

2025 대한바이러스학회 연구회연합 정기학술대회

The Korean Society of Virology

8.21(목) ~ 23(토)
한국여성수련원(강릉)



주 관 |
주 최 |



대한바이러스학회
The Korean Society of Virology

KVRI 기초과학연구원
한국바이러스기초연구소

KRICT 한국화학연구원
Korea Research Institute of Chemical Technology



LAB Total Solution

연구자의 안전과 과학의
미래를 설계하다

Introduce CHC

CHC LAB

실험실 가구·배기 장비·안전 장비 설계·제조 전문 기업.
실험대, 흡후드, 안전 캐비닛 등 기초 설비부터 맞춤형 설계, 제작,
설치, 유지관리까지 제공.

CHC Biotech

바이오 안전장비 전문 제조사. Biosafety Cabinet(BSC),
Laminar Flow Cabinet(LFC), Isolator 등
국제 기준을 충족하는 안전 장비를 국내 최초로 개발·제조.

HULAB

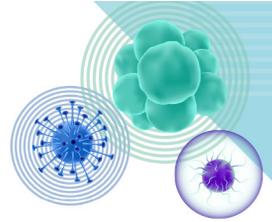
랩 컨설팅 전문기업. 설계, 구축, 유지보수까지
원스톱 맞춤형 솔루션을 제공하며 연구 환경과 운영 효율을 최적화.



Glovebox BSC Class III

외부와 완벽히 격리된 밀폐형 생물안전작업대 BL-3,
BL-4 등 고위험 병원체·감염성 검체 취급 시, 작업자의 안
전과 환경 보호를 보장하는 최고 등급 BSC.

국제 가이드라인	CDC, NIH, AG S 기준 준수	편리한 필터 무결성 테스트	Upstream/Downstream 포트 내장
고내구성 소재	STS 304/316, 라운드 용접 마감	다양한 시스템 연동	RTP, 덩크 탱크, 오토클레이브, BIBO 시스템 등
이중 HEPA 필터 시스템	유입·배출 시 각각 HEPA 필터 적용, > 99.997% @ 0.3µm	유지 음압 120 Pa	작업 중 발생 가능한 에어로졸 완벽 차단



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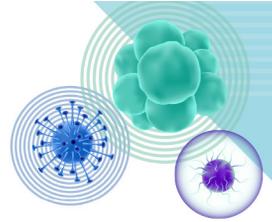
Program



8월 21일(목) 공동심포지엄 / 대강당

사회 : 김균환 교수(성균관대학교)

13:30-13:40	인사말 / 대한바이러스학회장 유승민 교수	
Session 1_ 호왕리 Memorial lecture 세션		
13:30-13:40	대한바이러스학회장 유승민 교수 (을지대학교 의과대학)	
13:50-14:20	Hantavirus and Prof. Ho Wang Lee 송진원 교수 (고려대학교 의과대학)	11
Session 2_ Boston-Korea 사업단 세션		
14:20-14:40	Emerging Bunyavirus Hemorrhagic Fever Research Center 조남혁 교수 (서울대학교 의과대학)	12
14:40-15:00	Discovery and validation of host-directed therapy targets against pan-respiratory viruses via multiomics approaches and CRISPR screening 송문정 교수 (고려대학교 생명과학대학)	13
Session 3_ ARPA-H 사업단 세션		
15:00-15:15	팬데믹 대비 감염병 난제 도전사업: 백신 및 치료제 개발 플랫폼 홍기종 교수 (가천대학교 의과대학)	
15:15-15:30	Development of a Decentralized System for mRNA vaccine production (DeCAFx) to Strengthen Pandemic Preparedness. 서상환 박사 (국제백신연구소)	14
15:30-15:45	백신 안정성 극대화를 위한 고품제형 mRNA-LNP 백신 마이크로니들 및 장기보관 기술 개발 김주영 박사 (퀵메디슨)	15
15:45-16:00	Coffee Break	
Session 4_ 한국화학연구원 세션		
16:00-16:30	Discovery of Antiviral Drug Candidates for Picornaviruses in KRICT 신진수 박사 (한국화학연구원)	16
16:30-17:00	Unraveling the Pathogenesis of SARS-CoV-2 Neuronal Invasion 권영찬 박사 (한국화학연구원)	17
Session 5_ 한국바이러스기초연구소(IBS) 세션		
17:00-17:30	Discovery and Characterization of Zoonotic Pathogens with Multi-Species and Multi-Organ Bat Organoids 최영기 소장 (한국바이러스기초연구소)	18
17:30-18:00	Peptides Targeting the SARS-CoV-2 RdRp NSP12 - NSP8 Interface: A Promising Antiviral Approach 안재우 박사 (한국바이러스기초연구소)	19
18:00-18:30	대한바이러스학회 정기총회 / 포스터 세션	
18:30-	간담회 / 경품	



Program



8월 22일(금) 연구회별 심포지엄 프로그램

간염 및 관련바이러스 연구회 강연장: 3층 301호

09:00-09:05	인사말/ 간염바이러스 연구회장 성균관대학교 김균환 교수	
Session 1		좌장: 김균환 교수 (성균관대학교 의과대학)
09:05-09:30	Novel immune-related anti-fibrosis target discovery using HBV-infected patient livers 성필수 교수 (가톨릭대학교 내과학교실)	23
09:30-09:55	Site-Specific m6A RNA Modifications Regulate Hepatitis C Virus Translation and Innate Immune Evasion 김진우 교수 (충남대학교 미생물·분자생명과학과)	24
09:55-10:20	Antiviral Strategies Targeting Hepatitis B Virus Replication 박성규 교수 (서울대학교 약학대학)	25
10:20-10:45	사진촬영 / Break time	
Session 2		좌장: 박성규 교수 (서울대학교 약학대학)
10:45-11:10	RIG-I-mediated antiviral signaling triggered by viral disruption of host RNA 이정현 교수 (서울시립대학교 생명과학과)	26
11:10-11:35	Single-cell landscape of immune responses in patients with acute hepatitis A virus infection 유호선 박사과정 (KAIST 의과대학원)	27
11:35-12:00	IFI35 suppresses the transcription of hepatitis B virus cccDNA via promoting HNF4α proteasomal degradation 김나연 박사과정 (성균관대학교 의과대학)	28
12:00-12:30	포스터 시상 / 대강당	

노로바이러스 연구회 강연장: 온라인

10:00-10:05	개회 / 노로바이러스 연구회장 전북대학교 명진종 교수	
10:05-10:15	사회자: 심포지움 개요 및 참석자 소개	
10:15-10:55	노로바이러스 분석법 국제표준(ISO) 추진 - PWI/NP 승인; WG32 - Norovirus 신설 및 컨비너 수입; WD 추진 전략 이규철 박사 (K-water 수석연구원)	
10:55-11:05	휴식	
11:05-11:55	ISO 노로바이러스 전문가 회의 - WD 승인 등 추진 전략 수립 ISO TC147/SC4 전문위원회 및 전문가협의체 구성원	
11:55-12:00	폐회 / 노로바이러스 연구회장 전북대학교 명진종 교수	

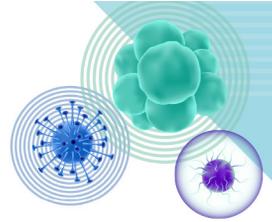
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신경계바이러스 연구회 강연장: 3층 303호

09:30-09:40	인사말 / 신경계바이러스 연구회장 한림대학교 최은경 교수	
09:40-10:00	Lentiviral and retroviral virus-like particles as a promising delivery platform for the SARS-CoV-2 nucleocapsid protein 정해윤 석사과정 (단국대학교)	31
10:00-10:20	Role of PAD2 in Prion-Induced Brain Pathology: An Ultrastructural Study 김태근 박사 (한림대학교 일송생명과학연구소)	32
10:20-10:40	A 3D Spheroid-Based Model of Prion Infection 박현정 박사 (한양대학교 약학기술연구소)	33
10:40-10:50	신경계바이러스연구회 간담회	
10:50-11:00	맺음말 / 신경계바이러스 연구회장 한림대학교 최은경 교수	
12:00-12:30	포스터 시상 / 대강당	

엔테로바이러스 연구회 강연장: 온라인

10:00-10:10	인사말 / 엔테로바이러스 연구회장 영남대학교 박호선 교수	
10:10-10:30	Cardiac-specific PDK4 deletion attenuates pyroptosis in CVB3-induced myocarditis model 김흥기 (중원대학교)	37
10:30-10:50	Sequence-specific mRNA interferases from Escherichia coli and Bacillus subtilis 박정호 (생명공학연구원)	38
10:50-11:20	Overcome virus-induced myocarditis; Development of anti-enterovirus drug 임병관 (중원대학교)	39
11:20-11:30	맺음말 / 엔테로바이러스 연구회장 영남대학교 박호선 교수	
12:00-12:30	포스터 시상 / 1층 대강의실	

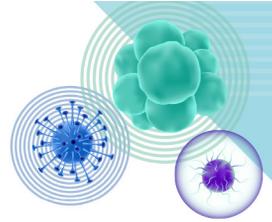


Program

수의바이러스 연구회		강연장: 3층 302호
09:00-09:05	인사말 / 수의바이러스 연구회장 전북대학교 조호성 교수	
Session 1		좌장: 오연수 교수 (강원대학교)
09:05-09:25	Application of virome for novel virus identification in animals 고영승 박사과정 (전북대학교)	43
09:25-09:45	Pharmaco-Net: An AI-Driven Structure-Based Drug Discovery Platform for supporting veterinary virus. 박영빈 이사 (CALICI Co.)	44
09:45-10:05	AI-Assisted Design and Immunogenicity Testing of a Nipah Virus Vaccine 우인옥 연구관 (국립보건연구원)	45
10:05-10:25	Coffee Break	
Session 2		좌장: 박최규 교수 (경북대학교)
10:25-10:45	Conditions for the Development of New Live Attenuated Vaccines: Focusing on Foot-and-Mouth Disease Vaccine 박종현 센터장 (농림축산검역본부)	46
10:45-10:05	Safety and immunogenicity assessment of novel inactivated canine distemper, adenovirus type 2, parvovirus and parainfluenza virus type 5 vaccine in dogs 양동균 연구관 (농림축산검역본부)	47
11:05-11:25	Evaluation and Development of a Statistically Optimized Risk-Based Surveillance Strategy for Foot-and-Mouth Disease in South Korea Saleem Ahmad 박사 (전남대학교)	48
11:25-11:30	맺음말 / 수의바이러스 연구회장 전북대학교 조호성 교수	
12:00-12:30	포스터 시상 / 대강당	

Program

아보바이러스 연구회		강연장: 1층 다목적실
09:00 - 09:10	인사말 / 아보바이러스 연구회장 고려대학교 의과대학 박만성 교수	
09:10-09:20	Key Elements and Technological Trends in mRNA Vaccine Development 남재환 교수 (가톨릭대학교)	53
09:20-09:30	Minimizing miRNA-Mediated Repression through 3' UTR Engineering Enhances mRNA Translation 윤수빈 박사과정 (가톨릭대학교)	54
09:30-09:40	mRNA-based IL-12 increases antigen-specific immune responses of personalized cancer vaccines. 조성제 박사과정 (가톨릭대학교)	55
09:40-10:00	Type I interferon-deficient mouse macrophages as a robust model for dengue antibody-dependent enhancement 이명신 교수 (울지대학교 의과대학)	56
10:00-10:20	Real-time Monitoring and Defining of Etiological Agents for Emerging Zoonotic Infectious Diseases Using Next-generation Sequencing 김원근 교수 (한림대학교 의과대학)	57
10:20-10:30	Evaluation of Vector Competence of <i>Culex tritaeniorhynchus</i> and <i>Culex pipiens pallens</i> for Japanese Encephalitis Virus Genotypes V (JEV-GV) 윤보람 보건연구사 (질병관리청 매개체분석과)	58
10:30-10:40	Fatal outcomes of SFTS and critical COVID-19 are associated with IL-10, IL-6, and TGF- β , And human infections of Hantaan virus were reported on Jeju Island, South Korea in 2024. 강수연 박사과정 (한양대학교)	59
10:40-10:50	Development and evaluation of mRNA vaccines encoding Glycoproteins for protection against <i>Bandavirus dabiense</i> 정다운 박사과정 (전북대학교)	60
10:50-11:00	Cross-Protective mRNA Vaccine Candidates for Old World Hantavirus 석종현 박사 (고려대학교)	61
11:00-11:10	Recombinant Bandavirus as an effective bivalent vaccine platform inducing protective immunity against intracellular pathogen and cancer 노효진 박사과정 (서울대학교)	62
11:10-11:20	The therapeutic potential of mRNA-encoded SFTSV human monoclonal antibody 이수연 박사과정 (가톨릭대학교)	63
11:20-11:30	맺음말 / 아보바이러스 연구회장 고려대학교 의과대학 박만성 교수	
12:00-12:30	포스터 시상 / 대강당	



Program

히피스바이러스 연구회		강연장: 2층 201호
09:00-09:05	인사말 / 히피스바이러스 연구회장 성균관대학교 의과대학 안진현 교수	
Session 1		좌장: 김의태 교수 (제주대학교)
09:05-09:30	DHT-AR Signaling Suppresses EBV-Positive Gastric Cancer via DNMT3A-MICA Pathway 강효정 교수 (경북대학교 약학대학)	67
09:30-09:55	Inherited chromosomally integrated Human Herpesvirus 6 김경란 교수 (창원경상대학교병원 소아청소년과)	68
09:55-10:20	RIG-I-mediated antiviral signaling triggered by viral disruption of host RNA 이정현 교수 (서울시립대학교)	69
10:20-10:40	Coffee Break	
Session 2		좌장: 최은영 교수 (건국대학교)
10:40-10:55	HCMV Tegument Protein pp28 Repositions Viperin to Promote Viral Egress 이재봉 석박통합 (연세대학교 의과대학, 서준영 교수 연구실)	70
10:55-11:10	Human cytomegalovirus long non-coding RNA counteracts nuclear cGAS to facilitate immune evasion 이성원 박사과정 (서울대학교 생명과학부, 안광석 교수 연구실)	71
11:10-11:25	Senescence of endothelial cells increases susceptibility to Kaposi's sarcoma-associated herpesvirus infection via CD109-mediated viral entry 연준희 박사 (을지대학교 의과대학, 이명신 교수 연구실)	72
11:25-11:40	Intracellular Acetyl-CoA Flux Induced by KSHV vIRF3-PKM2 Interaction Promotes the Disseminated Visceral Kaposi's Sarcoma 김영준 박사과정 (고려대학교 생명정보공학과, 이해라 교수 연구실)	73
11:40-11:50	맺음말 / 히피스바이러스 연구회장 성균관대학교 의과대학 안진현 교수	
12:00-12:30	포스터 시상 / 대강당	

Program

호흡기바이러스 연구회		강연장: 2-3층 대강당
09:00-09:05	인사말 / 호흡기바이러스 연구회장 국립보건연구원 신종바이러스연구센터 이주연 센터장	
09:05-09:25	Development of Broadly Neutralizing Antibodies Against SARS-CoV-2 variants 김현주 보건연구원(국립보건연구원)	77
09:25-09:45	A Cross-protective COVID-19 Vaccine Candidate using Newcastle Disease Virus as a Vaccine Vector 김정훈 박사과정 (고려대학교 의과대학)	78
09:45-10:05	Unveiling the Hidden Regulator of COVID-19 Immunopathology: NLRP12 이상준 교수 (울산과학기술원)	79
10:05-10:25	Zoonotic Risk Profiling of Bovine-derived H5N1 Influenza Virus via Genome-wide and Structural Evaluation 조승혜 박사과정 (고려대학교 의과대학)	80
10:25-10:45	Neutrophil Elastase: A Host Factor Driving SARS-CoV-2 Infectivity 안대균 책임연구원 (한국화학연구원)	81
10:45-11:05	Crossing the Species Divide: Insights into Animal-Origin Influenza Virus Spillover to Humans 이충용 교수 (경북대학교 의과대학)	82
11:05-11:10	맺음말 / 호흡기바이러스 연구부회장 경북대학교 의과대학 김성준 교수	
11:10-12:10	국립감염병연구소 공동주관 호흡기바이러스 연구 간담회	강연장 : 3층 303호
12:00-12:30	포스터 시상 / 대강당	



8월 22일(금) 연구회 교류

시간	사회: 김균환 교수(성균관대학교)
14:00-17:00	개별 연구회 교류 I



8월 23일(토) 연구회 교류

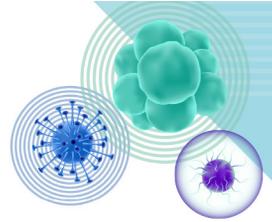
시간	사회: 김균환 교수(성균관대학교)
10:00-12:00	개별 연구회 교류 II

2025 대한바이러스학회
연구회연합 정기학술대회
The Korean Society of Virology

Abstracts of Lecture

공동세션

MEMO



Hantavirus and Prof. Ho Wang Lee

송진원^{1,2}

¹고려대학교 의과대학 미생물학교실, ²고려대학교 대학원 의과학과

한타바이러스는 분야바이러스 목(Order *Bunyvirales*)의 한타바이러스 과(family *Hantaviridae*)에 속하는 외피를 가진 음성 단일가닥 RNA바이러스이다. 한타바이러스는 3개의 분절로 이루어진 유전체를 보유하고 있으며 각 분절은 크기에 따라 large, medium, small로 불리며 각각 RNA 의존성 RNA 중합효소(RNA-dependent RNA polymerase), 두개의 표면 당단백질(Gn 및 Gc), 뉴클레오캡시드 단백질(nucleocapsid protein)을 암호화한다. 현재까지 알려진 주요 자연계 숙주동물로는 설치류, 박쥐, 두더지, 식충목을 포함하는 소형 포유동물이 있으며, 일부 바이러스 종은 인간에게 감염되어 질병을 일으키는 인수공통감염병의 원인 바이러스로 알려져 있다. 한타바이러스의 인간 감염은 감염된 설치류의 소변, 대변 및 타액을 비롯한 분비물을 에어로졸 형태로 흡입하였을 때 발생한다고 알려져 있으며, 드물게 물리는 경우에도 감염될 수 있다.

한타바이러스는 발병 형태에 따라 발열, 저혈압, 출혈 및 급성 신손상(acute kidney injury)을 동반하는 신증후군출혈열(hemorrhagic fever with renal syndrome, HFRS)과 두통, 무기력증, 근육통, 구토, 설사 및 호흡곤란과 기침과 같은 호흡기 증상을 동반하는 한타바이러스폐증후군(hantavirus pulmonary syndrome, HPS)로 나뉜다. HFRS는 한탄바이러스(*Orthohantavirus hantanense*), 서울바이러스(*Orthohantavirus seoulense*), 도브라바-벨그리드바이러스(*Orthohantavirus dobravaense*)에 의해 발생하며 유럽 및 아시아 등지에서 매년 약 150,000명의 환자가 1-12%의 사망률과 함께 보고되고 있다. HPS는 신놈브레바이러스(*Orthohantavirus sinnom-breense*), 뉴욕바이러스(New York virus), 안데스바이러스(*Orthohantavirus andesense*) 등에 의해 주로 발생한다. 환자는 주로 아메리카 대륙에서 발생하며, 매년 약 200여명의 환자와 최대 40%의 치명률을 보인다.

이러한 한타바이러스 유래 질병은 전 세계적으로 발병하고 있으며, 호흡기로 전파된다는 사실과 높은 사망률로 인해 공중보건에 큰 위협이 되고 있다. 국내에서는 매년 약 400건의 HFRS환자가 보고되고 있으며, 사망률은 1% 내외이다. 1976년, 고 이호왕 교수에 의해 한탄바이러스가 최초로 발견된 이후 1982년 서울바이러스, 2009년 임진바이러스, 2012년 제주바이러스 총 4종의 한탄바이러스가 국내에서 보고되었다.

특히 고 이호왕 교수는 6.25 전쟁에서부터 미국, 일본을 비롯한 여러 선진국에서 원인을 찾고자 하였으나 끝내 밝혀지 못한 신증후군출혈열의 원인바이러스를 최초로 발견 및 분리하였으며, 동시에 진단법 개발과 최초의 한타바이러스 백신인 '한타박스'를 개발 및 실용화하였다. 이러한 업적은 바이러스 발견자가 진단, 분리, 예방에 이르는 일련의 과정을 모두 완성한 세계 의학사에 길이 남을 업적으로 평가되고 있다. 이러한 공로를 인정받아 이호왕 교수는 미국 학술원 외국회원, 일본 학사원 명예회원, 대한민국 학술원 회원을 포함한 3개국 학술원 회원이라는 업적을 이뤘으며, 미국의 권위 있는 학술대회인 American Society of Virology (ASV)에서는 1996년부터 매년 뛰어난 연구 성과를 이룬 과학자를 선정해 'Ho-Wang Lee Lecture'라는 이름으로 특별 강연을 진행하며 이호왕 교수의 학문적 기여를 기리고 있다. 특히 2021년에는 노벨상 수상 유력 후보를 예측하는 클래리베이트 애널리틱스의 피인용 우수 연구자로 선정되기도 하였다.

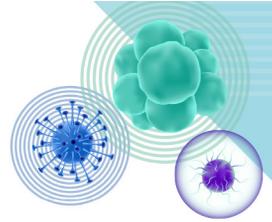
S 2-1

Emerging Bunyavirus Hemorrhagic Fever Research Center

Nam-Hyuk Cho

Department of Microbiology and Immunology, Seoul National University College of Medicine

Emerging Bunyaviruses such as SFTSV, HTNV, and RVFV pose serious public health risks due to their high fatality rates and epidemic potential, especially in vulnerable populations. This project aims to address these threats through a multidisciplinary collaboration between South Korean and U.S. scientists by establishing a clinical cohort and analyzing patient specimens using advanced multiomics and immunological tools. The project focuses on four major aims: elucidating Bunyavirus pathogenesis and virulence via specimen analysis and reassortment studies; developing and stabilizing vaccines using mRNA, protein nanoparticles, and viral vectors; identifying host-targeted antiviral and anti-inflammatory therapies; and validating immune responses and efficacy of vaccine and therapeutic candidates using organoid and animal models. Expected outcomes include identification of prognostic biomarkers for severe disease, discovery of therapeutic targets and neutralizing antibodies, development of multivalent vaccines, and creation of broad-spectrum antiviral drugs. By integrating clinical and experimental data, the project will significantly enhance our ability to predict outbreaks, develop effective countermeasures, and improve public health preparedness and patient outcomes against Bunyavirus infections.



S 2-2

Discovery and validation of host-directed therapy targets against pan-respiratory viruses via multiomics approaches and CRISPR screening

Moon Jung Song

Department of Biotechnology, College of Life Sciences and Biotechnology, Korea University, Seoul 02841, Republic of Korea

Respiratory viruses pose significant global health threats, as demonstrated by the COVID-19 pandemic. Traditional virus-specific approaches like vaccines and antivirals including monoclonal antibodies and small molecules, provide limited protection against rapidly emerging diverse viral threats, highlighting the need for broad-spectrum host-directed therapies (HDT) that target essential host proteins required by multiple viruses.

This collaboration between Dr. Moon Jung Song (Korea Bio-Defense Research Institute, Korea University) and Drs. Deborah T Hung and Seungmin Hwang (Broad Institute of MIT and Harvard) aims to develop novel HDT strategies against respiratory viruses. The partnership combines KBDRI's bio-defense expertise with advanced multiomics capabilities to: (1) validate targets from functional genomics screens for antiviral efficacy and drug discovery, and (2) identify novel HDT targets through unbiased multiomics analysis of host responses to viral infections in animal models.

Using state-of-the-art CRISPR/Cas9 screening and multidisciplinary approaches spanning virology, immunology, metabolism, structural biology, and medicinal chemistry, this research seeks to create broad-spectrum antiviral therapies effective against current and emerging respiratory viruses. By targeting shared host factors rather than virus-specific components, this work promises to advance treatment options that can be rapidly deployed against both known and unprecedented infectious threats.

Development of a Decentralized System for mRNA vaccine production (DeCAFx) to Strengthen Pandemic Preparedness

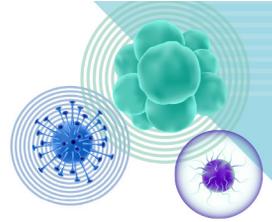
Sang Hwan Seo

Director, International Vaccine Institute

The COVID-19 pandemic demonstrated the promise of mRNA vaccines as a rapid-response platform, while also revealing critical gaps in global manufacturing capacity, equitable access, and timely deployment. To address these challenges and enhance preparedness for future pandemics, the International Vaccine Institute (IVI) is leading the development of DeCAFx—a *Decentralized and Accelerated mRNA Vaccine Production System*. DeCAFx is designed to enable scalable, regionally distributed, and time-sensitive mRNA vaccine manufacturing through modular infrastructure, standardized technologies, and pre-established technical partnerships.

Aligned with global initiatives such as CEPI's 100 Days Mission, DeCAFx aims to ensure vaccine production and distribution within weeks of pathogen identification. As part of this effort, IVI is advancing mRNA vaccine R&D through a global network of collaborators. These include prototype vaccines against Lassa fever (with SK bioscience) and Rift Valley fever (with Afrigen), platform validation using self-amplifying mRNA (with Karolinska Institute), and novel delivery systems such as microneedle patches (with QuadMedicine). IVI is also validating UTR-modified mRNA constructs (with Seoul National University) and evaluating an mRNA COVID-19 vaccine developed by Green Cross under KDCA support.

Through DeCAFx, IVI aims to integrate technological innovation, regional manufacturing, and regulatory readiness to build a sustainable and equitable vaccine ecosystem capable of responding rapidly to future pandemic threats.



S 3-2

백신 안정성 극대화를 위한 고품제형 mRNA-LNP 백신 마이크로니들 및 장기보관 기술 개발

김주영¹, 허혜진¹, 최인정¹, 김지석¹, 강아람¹, 이상욱², 백승기^{1*}, 송윤재^{3*}, 박정환^{3*}, 이재면^{4*}

¹(주)쿼드메디슨, ²엠큐렉스(주), ³가천대학교 바이오나노대학, ⁴연세대학교 의과대학

감염병 팬데믹 및 생물테러 등 공중보건 위기 상황에 대비하기 위한 백신 및 치료제의 사전 개발과 비축은 국가 보건안보의 핵심 전략이다. 특히 mRNA 백신은 플랫폼화된 유연한 생산성과 빠른 대응력으로 COVID-19 대유행에서 핵심적 역할을 수행했으나, 낮은 제제 안정성은 여전히 극복해야 할 주요 기술 과제로 남아 있다.

본 연구진은 mRNA-LNP 백신의 장기 보관 안정성을 극대화하기 위한 고품제형 마이크로니들 백신(P-MAP, Powder-attached Microneedle Array Patch) 기술을 개발하였다. 해당 기술은 동결건조된 mRNA-LNP 제제를 마이크로니들 팁의 점착성 표면에 직접 부착하는 방식으로, 기존 액상 기반의 마이크로니들 제조 공정이 요구하는 고농도 제형, 첨가제, 별도 건조 단계 등을 생략할 수 있는 무수·건식 코팅 기반의 제형 플랫폼이다.

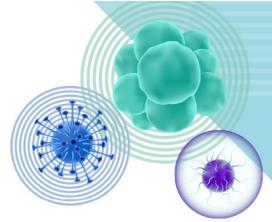
P-MAP은 수분 및 산소 노출을 최소화하여 mRNA의 분해를 방지하고, LNP 구조 및 생물학적 활성을 효과적으로 유지하는 장점을 갖는다. 또한, 해당 플랫폼은 다양한 백신 항원 적용이 가능하며, GMP 기준에 적합한 대량 제조공정으로 확장될 수 있어 향후 백신 비축 전략에 있어 실용적 솔루션을 제공할 수 있다.

Discovery of Antiviral Drug Candidates for Picornaviruses in KRICT

Shin, Jin Soo

Infectious Diseases Therapeutic Research Center, Korea Research Institute of Chemical Technology, Daejeon 34114, Republic of Korea

Picornaviruses are causative pathogens responsible for a wide range of diseases, including poliomyelitis, the common cold, hand-foot-and-mouth disease, meningitis, myocarditis, and hepatitis. Despite their clinical significance, no approved therapeutic agents are currently available for the treatment of picornavirus infections. Our research team aims to develop effective antiviral agents targeting picornaviruses. To this end, we have conducted high-throughput screening (HTS) to identify active compounds, followed by structure-activity relationship (SAR) studies to optimize derivatives and evaluate their antiviral efficacy, ultimately leading to the identification of lead compounds. Additionally, we are conducting mechanistic studies and drug-likeness optimization to derive potential drug candidates. Through these efforts, we aim to develop novel antiviral agents targeting DAA and HTAs, offering new therapeutic possibilities against picornavirus infections.



Unraveling the Pathogenesis of SARS-CoV-2 Neuronal Invasion

Gun Young Yoon¹, Gi Uk Jeong^{1,2}, Young Cheul Chung³, Won-Ho Shin³, and Young-Chan Kwon^{1,4}

¹Center for Infectious Disease Vaccine and Diagnosis Innovation, Korea Research Institute of Chemical Technology (KRICT), Daejeon, 34114, Republic of Korea, ²Division of Infectious Diseases, Department of Pediatrics, Boston Children's Hospital, Boston, MA, USA, ³Center for Bio-Signal Research, Korea Institute of Toxicology, Daejeon, 34114, Republic of Korea, ⁴Medical Chemistry and Pharmacology, University of Science and Technology (UST), Daejeon, 34114, Republic of Korea

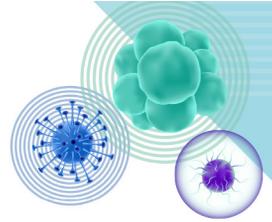
Recent studies suggest that SARS-CoV-2 infection can cause a variety of symptoms outside the lungs through neuronal invasion, but the links between neurological symptoms, neuroinflammation, and the immune response remain unclear. Here, we show that SARS-CoV-2 directly infects human microglia, triggering M1-like pro-inflammatory responses and cytopathic effects. In K18-hACE2 transgenic mice, microglial infection via intranasal exposure led to increased inflammatory cytokines and chronic microglial loss, indicating a central role for microglia in virus-induced neurological complications and identifying them as potential therapeutic targets. This study also addresses ocular manifestations of COVID-19. Intranasal infection in K18-hACE2 mice produced retinal inflammation and elevated ocular cytokines, while tracheal infection resulted in viral spread from the lungs to the brain and eyes along neural pathways. Fluorescence imaging confirmed ocular and neuronal infection, findings also replicated in Syrian hamsters, emphasizing the virus's neuroinvasive and ocular tropism. Long COVID is associated with persistent neurological symptoms, such as cognitive impairment, fatigue, and sleep disturbances, mechanisms of which are poorly understood. Infected mice demonstrated persistent brain viral RNA up to 90 days, reduced cortical NeuN (a neuronal marker), and downregulation of the HCRT (orexin) gene with lower hypothalamic expression. High-dose infection showed co-localization of SARS-CoV-2 nucleocapsid protein with orexin-producing neurons, and a negative correlation with HCRT mRNA, suggesting direct viral impairment of orexin function. Taken together, these results provide strong evidence that SARS-CoV-2 invades neuronal cells and microglia, triggers neuroinflammation, causes ocular and neurological complications, and disrupts orexin signaling, potentially contributing to long-term neurological symptoms and sleep disturbances characteristic of long COVID.

Discovery and Characterization of Zoonotic Pathogens with Multi-Species and Multi-Organ Bat Organoids

Hyunjoon Kim, Seo-Young Heo, Dongbin Park, Suhee Hwang, Yong-ki Lee, Jae-Woo Ahn, Se-Mi Kim, Issac Choi, Woohyun Kwon, Jaemoo Kim, Kanghee Kim, Boyeong Jeong, Jeong Ho Choi, Eun-ha Kim, Seung-Gyu Jang, Young Ki Choi*

Center for Study of Emerging and Re-emerging Viruses, Korea Research Institute, Institute for Basic Science (IBS), Daejeon, Republic of Korea

Zoonosis, an infectious disease that transmits from animals to humans, accounts for many historical outbreaks including COVID-19. Bats are well-recognized as key reservoirs for zoonotic pathogens, yet appropriate model systems to study these interactions have been limited. This gap hinders our ability to explore host-pathogen interactions and assess spillover risks comprehensively. To address this, we developed a collection of bat organoid models that encompass five species and three distinct organ types. With this model system, we could isolate and characterize bat-borne mammalian orthoreovirus and novel paramyxovirus, demonstrating their utility for simultaneous virome monitoring. These multi-species and multi-organ bat organoids present species- and tissue-specific replication patterns of multiple pathogenic virus families, including avian influenza viruses, revealing the zoonotic potential of avian-to-bat transmission. Overall, our innovative organoid platform offers a robust method for screening, isolating, and characterizing novel viruses, enhancing our ability to preempt and mitigate pandemic risks posed by bat-borne diseases.



Peptides Targeting the SARS-CoV-2 RdRp NSP12–NSP8 Interface: A Promising Antiviral Approach

Mark Anthony B. Casel^{1,2†}, Jae-Woo Ahn^{1†}, Hyunjoon Kim¹, Isaac Choi¹, Seung-Gyu Jang^{1,2}, Rare Rollon^{1,2}, Ho-Young Ji^{1,3}, Mina Yu^{1,2}, Seong Cheol Min², Min-Suk Song², and Young Ki Choi^{1,2*}

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Background: Although antiviral agents targeting viral proteases and polymerases are currently available, the emergence of resistant strains due to viral mutations continues to pose a significant challenge in the treatment of SARS-CoV-2 infections. Viral replication relies on the NSP12–NSP8–NSP7 complex, which enhances the activity of RNA-dependent RNA polymerase (RdRp). Among these components, NSP8 is critical for stabilizing the polymerase complex and supporting viral replication across diverse variants.

Objective: To disrupt the essential NSP12–NSP8 interaction, we designed four NSP8–derived peptides (N8-Pep α , N8-Pep α _cyc, N8-Pep β , and N8-Pep β D) targeting a conserved “hot spot” within the NSP12–NSP8 interface that governs complex stability and processivity.

Results: These peptides effectively inhibited RdRp activity by interfering with NSP12–NSP8 binding, leading to a marked reduction in SARS-CoV-2 replication in Vero E6 cells. Furthermore, intranasal administration of N8-Pep α or N8-Pep α _cyc (25 mg/kg) in BALB/c mice conferred strong antiviral protection, mitigating weight loss and reducing mortality upon infection with a mouse-adapted SARS-CoV-2 strain. Both prophylactic and therapeutic treatments significantly lowered viral titers and alleviated pathological damage in the nasal turbinates and lungs.

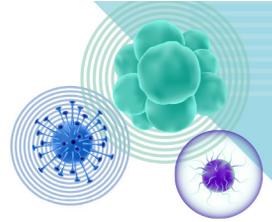
Conclusion: These findings establish the NSP12–NSP8 interface as a novel and highly conserved target for antiviral intervention. Interface-mimicking peptides derived from NSP8, particularly N8-Pep α and N8-Pep α _cyc, represent promising therapeutic candidates for disrupting RdRp complex assembly and effectively suppressing SARS-CoV-2 replication.

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간염 및 관련바이러스

MEMO



S 1-1

Novel immune-related anti-fibrosis target discovery using HBV-infected patient livers

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Understanding the involvement of these immune cells and other environmental factors provides a foundation for developing strategies to prevent the progression of CHB to liver cirrhosis and liver cancer and improve the management of HCC. To develop more effective therapies, further investigation is essential. Understanding the precise mechanisms through which innate immune cells interact with liver cells and drive inflammation and fibrosis could reveal new targets for innovative therapeutic interventions. Current treatments focus on managing metabolic syndrome and its components, but targeted anti-inflammatory strategies could help prevent or slow the progression of liver damage in CHB.

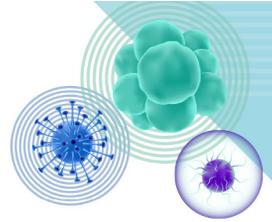
Recently, using HBV-infected human liver tissues, our group aimed to derive a unique protein signature predicting advanced liver fibrosis using multiplexed digital spatial protein profiling. Sixty-four portal regions of interest (ROIs) were selected for the spatial profiling. Using the results from the CD68⁺ area, a highly sensitive and specific immune-related protein signature (CD68, HLA-DR, OX40L, phospho-c-RAF, STING, and TIM3) was developed to predict advanced (F3 and F4) fibrosis. A combined analysis of single-cell RNA sequencing data from GEO datasets (GSE136103) and spatially-defined, protein-based multiplexed profiling revealed that most proteins upregulated in F0-F2 livers in portal CD68⁺ cells were specifically marked in tissue monocytes, whereas proteins upregulated in F3 and F4 livers were marked in scar-associated macrophages (SAMacs) and tissue monocytes. Internal validation using mRNA expression data with the same cohort tissues demonstrated that mRNA levels for TREM2, CD9, and CD68 are significantly higher in livers with advanced fibrosis. Overall, in patients with advanced liver fibrosis, portal MPs comprise of heterogeneous populations composed of SAMacs, Kupffer cells, and tissue monocytes. This is the first study that used spatially defined protein-based multiplexed profiling, and we have demonstrated the critical difference in the phenotypes of portal MPs between livers with early- or late-stage fibrosis.

Site-Specific m6A RNA Modifications Regulate Hepatitis C Virus Translation and Innate Immune Evasion

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N6-methyladenosine (m6A) is the most abundant internal modification of eukaryotic mRNAs and plays critical regulatory roles in viral infections. Hepatitis C virus (HCV), a major cause of chronic liver disease and hepatocellular carcinoma, utilizes m6A methylation to fine-tune its gene expression and subvert host immunity. In this study, we identify that the HCV genome harbors multiple m6A-modified sites, particularly in its untranslated regions and coding sequences, including the internal ribosome entry site (IRES) and NS5B coding region. These site-specific modifications exert distinct, functional roles in modulating viral translation and immune evasion. The essential m6A site at nucleotide 331 within the IRES stem-loop IV promotes efficient IRES-mediated translation of the viral polyprotein. This modification is specifically recognized by the m6A reader protein YTHDC2, whose RNA helicase activity, together with the host La antigen, facilitates IRES structural remodeling and enhances translation initiation. Disruption of this site or inhibition of YTHDC2 helicase function markedly impairs viral protein synthesis. Moreover, a distinct m6A site near nucleotide 8766 within the NS5B coding region suppresses innate antiviral signaling by reducing RIG-I-mediated recognition of viral RNA, indicating that HCV exploits m6A methylation to actively evade immune recognition. Together, our findings uncover site-specific role of m6A modifications promotes IRES-dependent translation and evades host innate immunity.



S 1-3

Antiviral Strategies Targeting Hepatitis B Virus Replication

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Hepatitis B virus (HBV) belongs to the Hepadnaviridae family and maintains its genome in the nucleus as episomal DNA. Although HBV is a DNA virus, it replicates through reverse transcription of a pregenomic RNA transcribed from the episomal, double-stranded circular DNA genome. A major problem associated with HBV infection is its contribution to the development of hepatocellular carcinoma (HCC). Treatment with nucleos(t)ide analogues (NAs) significantly reduces the risk of liver cirrhosis and HCC development. However, the risk of HBV-mediated liver disease still persists, as NAs do not completely cure chronic HBV infection. The main barrier to curing HBV is the persistence of covalently closed circular DNA (cccDNA) in the nucleus. While vaccination programs have reduced the incidence of new HBV infections, a large number of chronic carriers still exist worldwide. To eliminate cccDNA in chronic carriers, various treatment strategies have been explored, including combinations of antiviral agents targeting multiple steps of the HBV life cycle, immune modulators, and others. Nevertheless, aside from NAs, no other drugs have yet been approved for the treatment of HBV. In this presentation, we summarize recent advances in HBV drug development by various research groups, including our own. Furthermore, we provide insights into novel strategies for future HBV therapeutics.

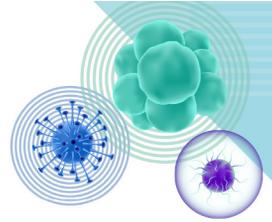
RIG-I-mediated antiviral signaling triggered by viral disruption of host RNA

Jung-Hyun Lee

Department of Life Science, University of Seoul

The cytosolic RNA sensor RIG-I plays a central role in innate antiviral immunity by detecting structured viral RNAs with 5'-triphosphates or short double-stranded features. While RIG-I was initially characterized in the context of RNA virus infection, our previous studies have shown that it also plays a critical role in host defense against DNA viruses including herpes simplex virus 1 (HSV-1) by sensing host-derived RNAs that mislocalized upon viral perturbation. We identified the 5S RNA pseudogene transcript RNA5SP141 as a physiological RIG-I ligand. During HSV-1 infection, the process of virus-induced host shutoff promotes the relocalization of RNA5SP141 from the nucleus to the cytoplasm and its unshielding, enabling RIG-I to recognize it and subsequently induce robust type I interferon responses. Furthermore, we have demonstrated that impaired RNA5SP141 biogenesis increases susceptibility to herpes simplex encephalitis, highlighting its importance in antiviral immunity.

Here, our new study reveals that HSV-1 infection promotes the selective packaging of RNA5SP141 into extracellular vesicles (EVs). These EVs are then released and delivered to uninfected cells. Interestingly, these EVs containing RNA5SP141 appear to be transferred preferentially to specific recipient cell types. This suggests a form of targeted intercellular communication that may prime select populations for antiviral responses. Although the molecular determinants of EV targeting and the downstream dynamics of RIG-I signaling in recipient cells are still being investigated, our findings provide a conceptual framework for EV-mediated immune amplification, extending antiviral surveillance beyond the initially infected cells.



Single-cell landscape of immune responses in patients with acute hepatitis A virus infection

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In hepatitis A virus (HAV) infection, the immune response plays a dual role, aiding in viral clearance in most healthy individuals but also contributing to severe liver damage in some elderly patients. Despite its importance, the specific roles of diverse immune cell populations in HAV infection remain incompletely understood. To address this, we performed CITE-seq and single-cell RNA sequencing (scRNA-seq) on peripheral blood mononuclear cells (PBMCs) from patients with acute hepatitis A, sampled during both the acute and convalescent phases, as well as from healthy controls. The composition of immune cell clusters varied significantly across disease stages. In CD8⁺ T cells, we observed increased frequencies of proliferating CD8⁺ T cells, effector memory (PD1⁺) CD8⁺ T cells, senescent (CD57⁺) CD8⁺ T cells, and NK-like (NKG2C⁺) CD8⁺ T cells during the acute phase. Proliferating and effector memory CD8⁺ T cells demonstrated elevated TCR-dependent activation scores, while senescent and NK-like subsets showed higher TCR-independent activation scores. Among CD4⁺ T cells, effector (PD1⁺ICOS⁺) CD4⁺ T cells were enriched in the acute phase and exhibited Th1-like and follicular helper-like features without CXCR5 expression. In the monocyte compartment, CXCL10⁺ monocytes were markedly increased during acute infection and expressed upregulated interferon-stimulated genes and higher CD8⁺ T cell-modulating score. Together, our immune landscape analysis highlights distinct subpopulations within CD8⁺ T cells, CD4⁺ T cells, and monocytes that are dynamically regulated during acute HAV infection. These findings provide a foundation for further studies to elucidate their contributions to disease pathogenesis.

IFI35 suppresses the transcription of hepatitis B virus cccDNA via promoting HNF4 α proteasomal degradation

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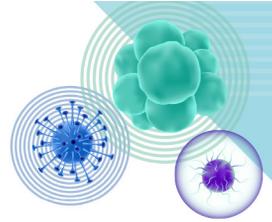
Hepatitis B virus (HBV) infection is a major health problem with hundreds of millions of people still chronically infected worldwide. Although it is known that cytokines can inhibit HBV replication in infected hepatocytes, much is still unknown about the underlying mechanisms or mediators. In this study, we systematically analyzed tumor necrosis factor- α (TNF- α) and interferon- γ (IFN- γ) induced proteins by proteomic analysis and identified interferon-inducible protein 35 (IFI35) as a novel host restriction factor for HBV replication. Overexpression of IFI35 suppressed HBV transcription, while its reduction showed the opposite effect. Mechanistically, IFI35 regulated the stability of hepatocyte nuclear factor 4 α (HNF4 α), which is essential for cccDNA transcription. IFI35 did not regulate the transcription of HNF4 α but rather promoted its degradation. We found that IFI35 recruits tripartite motif-containing protein 21 (TRIM21), an E3 ubiquitin-protein ligase, for K48-linked ubiquitination of HNF4 α . Results were further validated using patient-derived primary human hepatocytes (PHHs) and mouse model of HBV infection. Our results revealed that cytokines, especially IFN- γ , induced IFI35 in hepatocytes. IFI35 promoted the degradation of HNF4 α via the TRIM21-mediated ubiquitination, which, in turn, leads to the suppression of cccDNA transcription and viral replication. Our findings demonstrate that IFI35-TRIM21-HNF4 α axis may play a crucial role in TNF- α and IFN- γ induced suppression of HBV. Consequently, these results reveal a novel antiviral action of IFI35 against HBV. These findings may hold value in the development of alternative anti-HBV drugs.

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신경계바이러스

MEMO



Abstract

Lentiviral and retroviral virus-like particles as a promising delivery platform for the SARS-CoV-2 nucleocapsid protein

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The gag gene of human immunodeficiency virus type 1 (HIV-1) encodes a polyprotein precursor essential for viral particle assembly and budding. During virion maturation, the Gag polyprotein is proteolytically cleaved by the viral protease into multiple structural proteins crucial for viral infectivity. Because of its ability to promote particle formation, HIV-1 Gag has been extensively used for the generation of virus-like particles (VLPs). Similarly, expression of the gag gene from murine leukemia virus (MLV) alone is sufficient to induce VLP formation. Compared to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) VLPs, HIV-1 Gag VLPs yield substantially higher titers, likely due to their simpler and more efficient self-assembly and release mechanisms. The SARS-CoV-2 nucleocapsid (N) protein is widely used as a primary target in rapid antigen detection assays because of its high abundance, early expression, sequence conservation, and robust detectability. In this study, we investigated whether co-expression of Gag enables the incorporation of the SARS-CoV-2 N protein into VLPs. Transient co-transfection of HEK293T cells with plasmids encoding HIV-1 Gag-Pol (psPAX2), vesicular stomatitis virus G glycoprotein (VSV-G), and the SARS-CoV-2 N protein led to efficient packaging of N into HIV-1 Gag-derived VLPs. Similarly, co-expression of MLV Gag-Pol (pVPack-GP) with VSV-G and SARS-CoV-2 N resulted in MLV-based VLPs incorporating the N protein. Additionally, genetic fusion of the SARS-CoV-2 N protein to the C-terminus of HIV-1 or MLV Gag also promoted its incorporation into VLPs. HIV-1 Gag VLPs incorporating N protein served as reliable positive controls for SARS-CoV-2 rapid antigen diagnostic assays. These SARS-CoV-2 N protein-incorporating VLPs represent stable, noninfectious surrogates that mimic native virions and are suitable for lateral flow immunoassays, as well as for the validation and calibration of anti-N antibody detection assays in patient sera.

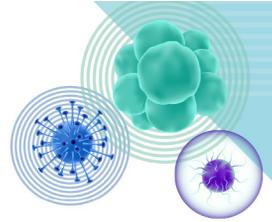
Abstract

Role of PAD2 in Prion-Induced Brain Pathology: An Ultrastructural Study

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Prion diseases, or transmissible spongiform encephalopathies (TSEs), are fatal neurodegenerative diseases affecting various mammals, including humans. These diseases are characterized by the accumulation of misfolded prion protein (PrP^{Sc}), derived from the normal cellular prion protein (PrP^C), leading to progressive brain degeneration and ultimately death. Peptidylarginine deiminases (PADs) are a family of posttranslational modification enzymes that catalyze the conversion of peptidylarginine to peptidylcitrulline in a calcium-dependent manner, a process known as citrullination (deamination). Of the five PAD isoforms identified in humans and rodents (PAD1-4, and PAD6), with PAD2 is predominantly expressed in the central nervous system (CNS). PAD2-mediated protein citrullination has been associated with neurodegenerative changes and implicated in proteinopathies such as prion and Alzheimer's diseases. Although the molecular and pathological roles of PAD2 have been studied, few investigations have focused on the ultrastructural changes related to PAD2 expression, particularly using transmission electron microscopy (TEM). In this study, wild-type and PAD2 knockout mice were infected with the 22L scrapie strain, a well-established prion disease model. Brain tissues were analyzed across five regions (cortex, cerebellum, striatum, hippocampus, and brainstem) to observe morphological and ultrastructural alterations in organelles such as mitochondria, endoplasmic reticulum, and Golgi complexes. Additionally, scrapie-associated structural changes were examined to further elucidate the role of PAD2 in prion pathogenesis [Grant: RS-2023-00247903].



Abstract

A 3D Spheroid-Based Model of Prion Infection

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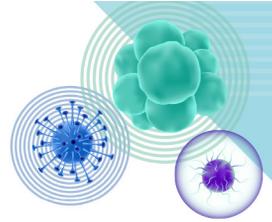
Prion diseases are transmissible and fatal neurodegenerative disorders characterized by the accumulation of misfolded prion protein (PrP^{Sc}) in the central nervous system. Although various *in vitro* models, such as 2D cultures, have been utilized to study prion replication, they often fail to replicate the structural and cellular complexity of the brain. 3D models such as brain organoids have shown promise in mimicking the architecture of brain tissue but are limited by variability and the infection protocols for long-term studies. Here, we present a novel 3D spheroid model of neurons and astrocytes derived from mouse neural stem cells (NSCs), to study the pathogenesis of prion diseases. This model was generated by inducing spheroid formation from NSCs followed by infection with Rocky Mountain Laboratory (RML) prion strains. RML infection-3D spherical models with neurons and astrocytes generated apoptosis and gliosis resembling a neural microenvironment for prion propagation and neurodegenerative processes. Additionally, the ability to support long-term prion transmission, secondary infection, and cryopreservation has been demonstrated. This innovative model enables long-term studies of prion dynamics and the evaluation of therapeutic interventions, bridging the gap between simple *in vitro* systems and *in vivo* models. Our findings demonstrate the utility of this 3D model as a valuable tool in prion research.

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엔테로바이러스

MEMO



Abstract

Cardiac-specific PDK4 deletion attenuates pyroptosis in CVB3-induced myocarditis model

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Pyroptosis is a highly inflammatory form of lytic programmed cell death that typically occurs during infection with intracellular pathogens. Coxsackievirus B3 (CVB3) is one of the most common pathogens for acute myocarditis in humans. It may induce myocarditis and progress to dilated cardiomyopathy. Pyruvate dehydrogenase kinase 4 (PDK4) is a metabolic enzyme that regulates cell metabolism through mitochondrial function. PDK4 levels increased in the hearts of mice during CVB3 infection. We hypothesized that PDK4 inhibition may be an effective strategy to prevent pyroptosis in CVB3 infection.

Cardiac-specific conditional knockout (*f/f*) mice for PDK4 were generated using cardiac-specific modified estrogen-Cre mice. PDK4 knockout (KO) mice were injected intraperitoneally with tamoxifen (1mg/ml) for 5 days and then sacrificed 4 weeks later. Cardiomyocytes isolated from the heart were treated with 10^8 PFU of CVB3 for 1 hour. Heart protein and RNA were extracted and used for western blot and qPCR analysis. PDK4 protein and RNA were eliminated, and PDH phosphorylation was decreased in KO compared to wild-type (WT) cardiomyocytes. However, there was no change in mitochondrial oxidative phosphorylation (OXPHOS) complex proteins. Furthermore, the mitochondrial dynamics regulators (OPA1, MFN1, MFN2, DRP1) showed no significant difference between KO and WT cardiomyocytes. To investigate the inflammatory response induced by CVB3 infection, mice were injected with tamoxifen, and three weeks later, they were directly infected with 2×10^4 PFU of CVB3. Seven days after infection, RNA was extracted from the hearts of mice and used for qPCR. Innate immune response inflammation-related genes *Nlrp1*, *MyD88*, *Irf7*, *Slfn4*, and *SAA2* were significantly increased in KO mice compared to WT mice. In contrast, there was a notable decrease in the expression of cytokines associated with pyroptosis, including *IL-18*, *Caspase-1*, *Irgm1*, and *Gbp5*.

In this study, we successfully generated PDK4 knockout mice and provided strong evidence for the protective effects in CVB3 infection-induced pyroptosis. It will be valuable to investigate the mechanistic role of PDK4 in protecting mitochondrial function during virus-induced cardiac inflammation and cell death.

Abstract

Sequence-specific mRNA interferases from *Escherichia coli* and *Bacillus subtilis*

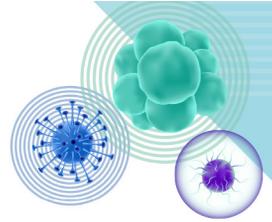
Jung-Ho Park

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MazF is a sequence-specific endoribonuclease, also known as an mRNA interferase, that plays a critical role in bacterial stress responses by cleaving intracellular mRNAs at defined recognition sequences. In *Escherichia coli*, MazF (MazF-ec) specifically recognizes and cleaves at ACA trinucleotide sequences, leading to global inhibition of protein synthesis and the selective expression of stress-responsive genes through the generation of leaderless mRNAs. In contrast, here we characterize MazF from *Bacillus subtilis* (MazF-bs), and demonstrate that it exhibits distinct substrate specificity by cleaving mRNAs at the pentanucleotide sequence UACAU. This longer and more complex recognition motif suggests a more selective post-transcriptional regulatory mechanism in *B. subtilis*.

Bioinformatic analysis reveals that MazF-bs homologues are widely conserved among Gram-positive bacteria, and display high sequence similarity, indicating a conserved functional role across diverse species. Intriguingly, the UACAU motif is significantly overrepresented in genes involved in the biosynthesis of secondary metabolites in *B. subtilis*, including nonribosomal peptide synthetases and polyketide synthases. This suggests that MazF-bs may contribute to the modulation of secondary metabolism under specific environmental or stress conditions, potentially linking toxin-antitoxin systems to metabolic adaptation and bacterial competitiveness.

Together, these findings illustrate that while MazF family members share a common mode of action as RNA interferases, their cleavage specificity and regulatory outcomes have diverged across species. This divergence reflects species-specific evolutionary pressures and highlights the potential for MazF systems to regulate distinct physiological pathways, ranging from programmed cell death in *E. coli* to secondary metabolite production in *B. subtilis*.



Abstract

Overcome virus-induced myocarditis; Development of anti-enterovirus drug

임병관

중원대학교, 생명과학과

심근염은 다양한 원인에 의해 심근에 염증이 유발되고 병증의 유발로 심근의 괴사와 심장의 섬유화 유도로 심장기능을 저하 심부전으로 진행되는 염증질환이다. 원인(cause), 조직학적, 면역조직 병리학적 소견, 임상 소견에 따라 다양하게 분류된다.

심장 생검은 심근염 진단에서 가장 큰 도움을 주지만 모든 병원에서 시행할 수 없고, 조직학적 검사 이후 임상적인 치료나 예후에 도움을 주지는 않아 그 유용성은 한계가 있다. 따라서, 임상적으로 2 주 이내 바이러스 질환의 병력이 있고 1) 특별한 원인 없이 troponin 이 상승하거나 2) 심근 손상의 심전도 변화가 있거나 3) 심초음파 또는 CMR에서 심장 기능 이상 소견이 보이면 급성 심근염 의심(possible subclinical myocarditis)으로 진단하고, 이들 환자에서 다음 4개의 임상 증상이 있으면(급성 심부전, 흉통, 실신 또는 거의-실신, 심근-심외막염) 심근염의 가능성이 있음(probable acute myocarditis)으로 진단한다. 그렇지만, 임상 증상과 관계없이 심근 생검에서 염증이 확인되면 심근염(definite myocarditis)으로 확진할 수 있다. 급성 심근염과 달리 만성 심근염은 특별한 원인 없이 악화될 수 있는데 이를 반영하는 생화학적/혈청학적 지표(serological biomarker)나 영상학적 검사는 없어 치료는 일반적인 만성 심부전치료에 따른다.

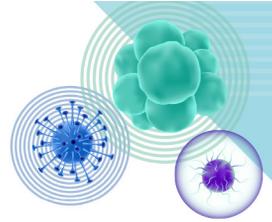
심근염 연구는 바이러스 검출과 면역반응의 유도와 작용 기작 검증이 주요한 부분으로 특정 바이러스 감염과 자가면역반응 유도를 통한 염증동물모델을 사용하여 이루어지고 있어 심근염 연구를 위한 마우스 strain에 따른 급, 만성 바이러스 심근염 모델에 대한 이해와 연구방법 그리고 면역반응에 대한 이해는 매우 중요하다고 할 수 있다.

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수의바이러스

MEMO



Application of virome for novel virus identification in animals

Young-Seung Ko¹, Sung-Hyun Moon¹, Taek Geun Lee¹, Da-Yun Bae¹, Yun-Chae Cho¹, Yeonsu Oh^{2*}, and Ho-Seong Cho^{1*}

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The virome encompasses the complete set of viral genetic material—both pathogenic and non-pathogenic—within a host or environment. With the advent of metagenomic next-generation sequencing (mNGS), virome analysis has enabled unbiased detection and characterization of both known and novel viruses, without requiring prior cultivation. While virome studies in human medicine have deepened our understanding of chronic infections, immunomodulation, and oncogenesis, similar approaches in veterinary and wildlife medicine have proven valuable for uncovering emerging viruses and enhancing zoonotic surveillance. In animals, virome analysis plays a critical role in identifying viral agents associated with unexplained clinical syndromes, respiratory and enteric diseases, and reproductive failures. Notably, virome-based studies in Korean bats have revealed diverse viral families, including coronaviruses, adenoviruses, rotaviruses, astroviruses, and pestiviruses—highlighting bats as reservoirs of zoonotic potential. Moreover, virome screening of lumpy skin disease (LSD) lesions in Vietnamese water buffaloes (*Bubalus bubalis*) unexpectedly identified *Ungulate tetraparvovirus 1*, alongside LSD virus (LSDV), demonstrating its utility in detecting previously unknown pathogens from clinical samples. Looking forward, virome analysis is expected to expand into areas such as abortion diagnostics, monitoring viral evolution in livestock populations, and evaluating viral communities in animal farming environments—such as airborne viruses in pig barns or waterborne viruses in aquaculture and livestock systems. These applications reinforce the virome's central role in advancing animal health, zoonotic risk assessment, and One Health strategies.

[Acknowledgements] This research was supported by 'The Government-wide R&D to Advance Infectious Disease Prevention and Control', Republic of Korea (grant number: RS-2023-KH140418).

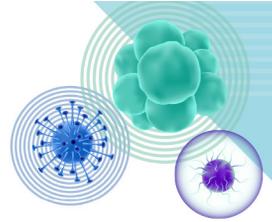
Pharmaco-Net: An AI-Driven Structure-Based Drug Discovery Platform for supporting veterinary virus

Park, Young Bin

Calici. Co.

Recent advances in structural biology of protein and artificial intelligence (AI) have opened new frontiers in rational drug discovery. Pharmaco-Net(<https://pharmaco-net.org>), developed by Calici Co., is an advanced AI-driven platform designed to harness the predictive power of protein 3D structures for efficient and biologically meaningful hit identification and optimization.

Traditional drug discovery approaches are often hampered by time-intensive and cost-prohibitive experimental workflows. Pharmaco-Net addresses these limitations by integrating high-fidelity protein structural data with proprietary AI algorithms to prioritize compounds with strong binding potential and mechanistic relevance—significantly reducing the resource burden associated with early-phase discovery. This platform enables rapid and accurate screening of both small molecules and peptides, followed by structure-based lead optimization, facilitating a more targeted and scalable approach to hit-to-lead progression. This presentation may provide an opportunity to discuss how these platforms can support and facilitate research in veterinary virology, particularly in areas such as drug development and related applications.



AI-Assisted Design and Immunogenicity Testing of a Nipah Virus Vaccine

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Nipah virus (NiV) was first identified in late 1998 in Kampung Sungai Nipah, Malaysia, from which its name is derived. Since 2001, NiV infections have been reported almost annually in various regions of Bangladesh. NiV is a prototype virus belonging to the genus Henipavirus within the Paramyxoviridae family and consists of a single-stranded negative-sense RNA genome. NiV is a bat-borne zoonotic pathogen that sporadically infects humans, causing severe respiratory illness, serious neurological disorders, encephalitis, and fatal outcomes, with mortality rates ranging from 40 to 75%. Currently, there are no approved vaccines or therapeutics for humans or animals, underscoring the urgent need for development. Two main strains of NiV have been identified: the Malaysian strain (NiVM) and the Bangladeshi strain (NiVB), each composed of multiple proteins. Among these, the surface glycoproteins fusion (F) protein and attachment (G) protein are exposed on the viral envelope's exterior. The primary role of the G protein is to mediate attachment of the virus particle to host cells, facilitating viral binding. In contrast, the F protein mediates the fusion of the viral envelope with the host cell membrane through structural changes, enabling viral entry. The G and F proteins of NiVM and NiVB share high sequence similarity, with 95.7% and 98.5% identity, respectively. In this study, recombinant proteins of both NiVM and NiVB G and F proteins, which are highly conserved and involved in virus-host cell binding, were utilized to develop and evaluate a recombinant protein vaccine. Consensus sequences for the G and F proteins from both strains were derived, and based on these, a chimeric sequence was designed. To enhance the stability of the trimeric form of the F protein, sequence optimization was performed using the proteinMPNN program. The resulting vaccine candidate was administered to mice to assess the immunogenicity of the vaccine antigen. The present study shows that the chimeric protein linking the NiV F protein to the G protein is a strong vaccine candidate. It presents the design of a NiV vaccine candidate developed to meet pandemic threats, highlighting an approach to strengthening preparedness and response capabilities against this deadly virus.

Conditions for the Development of New Live Attenuated Vaccines: Focusing on Foot-and-Mouth Disease Vaccine

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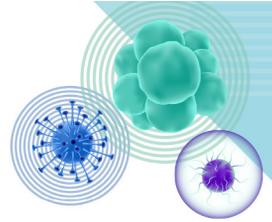
While inactivated vaccines are safe, they typically induce short-term immunity and require high-containment facilities for production. In contrast, live attenuated vaccines (LAVs) have the potential to elicit more robust, broader, and longer-lasting immune responses, mimicking natural infection. Foot-and-mouth disease (FMD) is a highly contagious viral disease that poses a significant threat to the global livestock industry. The control of FMD has primarily relied on vaccination with inactivated vaccines. However, developing effective FMD vaccines presents numerous challenges, including the existence of multiple serotypes and the rapid evolution of the virus, which often necessitates frequent vaccine updates.

This presentation aims to delineate the critical conditions and strategic considerations for the development of novel LAVs, addressing the inherent challenges and outlining a path toward safe and effective field application.

We first analyze the fundamental problems in developing LAVs. The primary concern is the genetic stability of the attenuated virus, as the high mutation rate of FMD virus (FMDV) increases the risk of reversion to virulence. This risk is a major safety barrier, potentially leading to iatrogenic outbreaks. To address this, a critical condition for modern LAV development is the use of reverse genetics to introduce multiple, synergistic, and stable attenuating mutations into the viral genome, thereby minimizing the probability of reversion.

Furthermore, we discuss essential precautions for both the development and field application phases. A successful LAV must be compatible with the "Differentiating Infected from Vaccinated Animals" (DIVA) strategy, which is crucial for surveillance and disease control. During development, rigorous evaluation of viral shedding, transmission potential, and safety in target and non-target species is mandatory. For field application, a comprehensive risk management plan is required. This includes robust post-vaccination surveillance systems to monitor for any adverse events or evidence of viral reversion. Anticipated field issues, such as vaccine-derived virus circulation, can be mitigated through phased deployment strategies, public awareness campaigns, and the availability of rapid companion diagnostics.

The development of a next-generation FMD LAV is a promising strategy for the effective control of FMD. However, its success hinges on fulfilling stringent conditions: ensuring genetic stability through advanced molecular engineering, incorporating a reliable DIVA principle, and implementing a meticulous risk management framework for field use. By addressing these challenges proactively, we can harness the full potential of LAVs to provide a powerful new tool for combating FMD.



S 2-2

Safety and immunogenicity assessment of novel inactivated canine distemper, adenovirus type 2, parvovirus and parainfluenza virus type 5 vaccine in dogs

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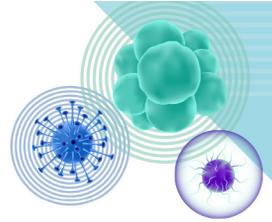
Canine distemper virus (CDV), adenovirus type 2 (CAV-2), parvovirus (CPV), and parainfluenza virus type 5 (CPIV-5) are highly contagious pathogens associated with significant mortality in puppies. Given the prevalence of these viruses in the Korean dog population, the development of a novel inactivated DAPP vaccine is essential for effective disease prevention. This study aimed to evaluate the safety and immunogenicity of an inactivated DAPP vaccine containing four virus strains: CD1901-200, APQA1701-100, CPV0901-201, and CPIV-5-120. CD1901 was passaged 200 times in Vero cells, while APQA1701-100 (CAV-2) was passaged 100 times in MDCK cells. CPV0901-201 and CPIV-5-120 were propagated in A72 cells. Two formulations of the inactivated DAPP vaccine were tested in guinea pigs to determine the optimal adjuvant. The selected formulation, containing Rehydra gel adjuvant, was then administered to dogs to assess safety and immune responses. Dogs receiving three doses of the vaccine exhibited no adverse reactions during the observation period. Virus neutralization antibody (VNA) titers measured at 7 weeks post-inoculation (WPI) demonstrated significantly enhanced humoral immune responses in vaccinated dogs compared to controls, with titers of 29.8, 119.4, 6,208, and 9.8 for CDV, CAV-2, CPV, and CPIV-5, respectively. These findings indicate that novel inactivated DAPP vaccine elicits a robust immune response and may serve as an effective preventive measure against major canine viral diseases.

Evaluation and Development of a Statistically Optimized Risk-Based Surveillance Strategy for Foot-and-Mouth Disease in South Korea

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Although South Korea implemented a nationwide FMD vaccination program with NSP/marker vaccines in 2011, sporadic outbreaks continued to occur—including major events in 2014~15 and subsequent years—highlighting the need to reassess and redesign the national serological surveillance system. This study presents a comprehensive evaluation and enhancement of the Foot-and-Mouth Disease (FMD) surveillance framework through integrated statistical modeling, risk factor analysis, and spatial epidemiology. Utilizing the latest NSP antibody surveillance data (2024), the Freedom From Disease (FFD) model was applied to determine optimal sample sizes and assess herd-level surveillance sensitivity. Under fixed parameters (1% design prevalence, 10% intra-herd prevalence, 95% diagnostic sensitivity, and 99.9% specificity), a limited sampling strategy of 16 animals per herd achieved a mean herd sensitivity of 0.89, requiring surveillance of 510 herds. A two-stage sampling design achieved the target of 95% herd-level sensitivity with 331 herds and approximately 4,803 animals. Individual sampling tables stratified by herd size were also developed for flexible field-level implementation. To identify immunization gaps, a nationwide Ridge regression analysis using SP antibody surveillance data from the past five years (2020–2024) revealed that low seropositivity was significantly associated with pig and goat farms, specific production systems (e.g., non-integrated breeding and feedlot types), sampling from slaughterhouses, and geographic regions such as Jeollanam-do, Jeju, and Daejeon. These findings suggest the need for targeted follow-up testing and supplemental vaccination in vulnerable subpopulations. Spatial-temporal associations between surveillance sensitivity and FMD outbreaks were assessed using Bayesian intrinsic conditional autoregressive (ICAR) models (2015–2019), which demonstrated that counties with a high proportion of farms below average herd sensitivity had a 4.68-fold increased FMD outbreak risk (95% CI: 2.92–7.87). Residual spatial effects indicated additional localized vulnerabilities beyond measured sensitivity. A case-control logistic regression further identified key FMD risk factors, including low SP antibody positivity (<0.70), specific pig production stages (e.g., sows, piglets), high farm and animal density, goat species. These findings underscore the importance of environmental, structural, and immunological drivers of FMD outbreaks. Together, this study provides scientific evidence supporting the need to redesign South Korea's FMD surveillance system. It proposes a statistically optimized, risk-based surveillance framework that enhances early detection, improves resource targeting, and strengthens compliance with international standards for FMD freedom recognition.



Together, these coordinated strategies provide a scientifically validated roadmap for optimizing FMD serological surveillance through statistically rigorous sampling, spatial risk targeting, and behavioral considerations, thereby enhancing early detection, immunity monitoring, and compliance with WOH standards for FMD freedom recognition in the future.

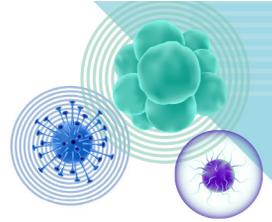
Acknowledgement: This research was supported by the Research and Development(R&D) project (Project No. Z-1543082-2025-25-01.) on the animal and plant quarantine inspection technology of the Animal and Plant Quarantine Agency in the Republic of Korea.

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연구회연합 정기학술대회
The Korean Society of Virology

Abstracts of Lecture

아보바이러스

MEMO



Abstract

Key Elements and Technological Trends in mRNA Vaccine Development

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In response to the COVID-19 pandemic in 2020, various vaccine platforms were developed, among which mRNA vaccines garnered significant attention. mRNA vaccines have demonstrated distinct advantages over conventional vaccine technologies, particularly in terms of rapid development, ease of manufacturing, high prophylactic efficacy, and an excellent safety profile. This presentation will examine the two essential components required for the development of mRNA vaccines and discuss future directions and prospects for the technology.

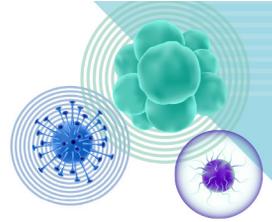
Abstract

Minimizing miRNA-Mediated Repression through 3' UTR Engineering Enhances mRNA Translation

Subin Yoon^{1,2}, Dahyeon Ha^{1,2}, Ayoung Oh¹, Sohee Jo^{1,2}, Seonghyun Lee^{1,2}, Soo-Yeon Lee^{1,2}, Jisun Lee¹, Jungmin Kim^{1,2}, Seongje Cho^{1,2}, Huijeong Choi^{1,2}, Yeeun Lee^{1,2}, Sanghyuk Jeon^{1,2}, Gitak Nam¹, Eun-Jin Choi^{1,2}, Sowon Lee^{1,2}, and Jae-Hwan Nam^{1,2*}

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The efficacy of mRNA-based vaccines, whether prophylactic or therapeutic, depends critically on the rational design of untranslated regions (UTRs) to maximize protein expression. While the 5' UTR primarily modulates translational efficiency, the 3' UTR is pivotal in regulating mRNA stability. In this study, we systematically constructed UTRs from highly expressed and immunogenic human and viral genes. Through computational prediction and experimental validation, we found that longer 3' UTRs tend to harbor more miRNA binding sites, which negatively correlate with protein expression levels. Notably, UTRs associated with high expression exhibited fewer predicted miRNA binding sites. To test the functional impact of miRNA binding, we designed and evaluated a series of modified 3' UTRs with reduced miRNA targetability. Using both luciferase reporter assays and therapeutic antibody expression systems, we demonstrated that these optimized UTRs significantly enhanced mRNA translation in vitro and in vivo. Antibody expression levels were markedly increased when paired with miRNA-depleted 3' UTRs, supporting the translational benefit of this strategy across different protein types. Our findings underscore the role of miRNA-mediated repression in limiting mRNA construct performance and demonstrate that strategic 3' UTR re-engineering can substantially improve the expression of both reporter and therapeutic proteins. This approach provides a powerful platform for enhancing the potency of mRNA vaccines and biologics.



Abstract

mRNA-based IL-12 increases antigen-specific immune responses of personalized cancer vaccines.

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mRNA-LNP platform is a versatile and promising technology for delivering gene of interest (GOI) by mimicking the mechanism of viral infection, and has several advantages, including the ability to deliver multi-antigens. Recently, mRNA-LNP-based personalized cancer vaccines (PCVs), which encode patient-specific neoantigens to induce cancer cell-specific immune responses, have shown positive results in several clinical trials for cancer immunotherapy. Here, we predicted colon cancer cell-specific MHC-I and MHC-II-restricted neoantigens and confirmed the induction of antigen-specific immune responses by mRNA-based cancer vaccine in a mouse model of colorectal cancer. Especially, co-administration of MHC-I and MHC-II antigens increased antigen-specific CD8+ T cell immune responses and induced a high anti-cancer efficacy. Furthermore, the therapeutic mRNA vaccines have also shown high anti-cancer efficacy in early cancer stage, indicating the importance of earlier cancer detection and earlier vaccination. In addition, combination therapy with immune checkpoint inhibitors (e.g. anti-PD-1 and -Tim-3 antibodies) or cytokines (e.g. IL-12) has also been shown to increase T cell immune responses and tumor growth inhibition. Overall, we propose the following points for high immunogenicity and effective anti-cancer treatment with PCVs. First, co-administration of MHC-I and MHC-II neoantigens will increase the antigen-specific immune responses of CD8+ T cells. Second, the combination therapy with immune stimulators that can increase the cell-mediated immune response, such as cytokines, enhances neoantigens-specific immune responses and has shown synergistic anti-cancer efficacy. These findings may contribute to an increase in cancer cell-specific immune responses and the clinical success of personalized cancer vaccines.

Abstract

Type I interferon-deficient mouse macrophages as a robust model for dengue antibody-dependent enhancement

Myung-Shin Lee

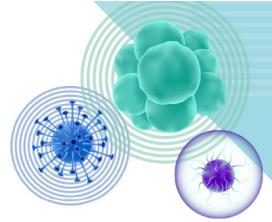
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Background and Objective: Monocytes and macrophages play pivotal roles in the pathogenesis of dengue virus (DENV) infection. Antibody-dependent enhancement (ADE) mediated by Fc receptors is recognized as a major mechanism underlying the increased severity and mortality associated with dengue hemorrhagic fever and dengue shock syndrome. However, the diversity of infection models used in previous studies and the lack of consistent results have posed significant challenges for effective ADE research. This study systematically compared dengue virus infection efficiency and ADE-mediated infection enhancement across various human and murine monocyte/macrophage cell lines.

Methods: Dengue virus infection rates were measured in various human and murine monocyte/macrophage cell lines, and ADE-mediated infection enhancement effects were quantitatively analyzed. The optimal infection model was selected for detailed analysis of infection dynamics and post-infection cytokine expression patterns.

Results: Among human cell lines, K562 cells exhibited the highest dengue virus infection rate and demonstrated significant ADE-mediated infection enhancement. In murine cell lines, Raw264.7 cells and immortalized macrophages derived from interferon-alpha receptor-deficient mice showed high infection efficiency with pronounced ADE-mediated infection enhancement. Notably, macrophages derived from interferon-alpha receptor-deficient mice demonstrated the highest infection efficiency, leading to their selection for comprehensive analysis of infection dynamics and post-infection cytokine expression.

Conclusions: This study demonstrates that macrophages derived from interferon-alpha receptor-deficient mice serve as an efficient and consistent in vitro model for dengue virus ADE research. This model, in conjunction with the AG129 mouse model, is expected to be valuable for investigating the pathogenic mechanisms of severe dengue virus infections such as dengue hemorrhagic fever and for therapeutic development.



Abstract

Real-time Monitoring and Defining of Etiological Agents for Emerging Zoonotic Infectious Diseases Using Next-generation Sequencing

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Emerging and re-emerging RNA viruses have recently caused outbreaks of infectious diseases, posing significant threats to public health, economy, and socio-cultural systems. Next-generation sequencing (NGS) plays a crucial role in establishing responsive strategies for zoonotic infectious diseases by enabling the acquisition of viral genome sequences, identification of etiology, and tracing of viral transmission routes. For real-time genome analysis of viruses from clinical cases, it is essential to rapidly secure samples, perform target-enriched sample preparation, apply next-generation sequencing, and utilize the bioinformatics-based analysis. We have established a clinical sample acquisition system for the study of hemorrhagic fever with renal syndrome (HFRS), severe fever with thrombocytopenia syndrome (SFTS), and fever of unknown origin. We developed sample preparation methods, including SISPA-based, amplicon-based, and target capture-based approaches. Additionally, we implemented Illumina sequencing and field-deployable MinION sequencing for NGS with the bioinformatic pipeline for viral genome analysis, named 'VirPipe'.

In these studies, we demonstrate the analysis of viral genome characteristics by obtaining whole-genome sequences directly from clinical samples of patients with SFTS occurring in South Korea, using Nanopore MinION sequencing. We present the results of evaluating the effectiveness of current molecular diagnostic methods for SFTS. Furthermore, in order to identify the etiological agent, metagenomic NGS is performed on clinical samples from suspected SFTS patients in which SFTSV was not detected. Previously, Gamak and Daeryong viruses, *Parahenipaviruses*, were discovered in shrew species in South Korea. We recently found Korean Langya virus, initially identified in febrile patients of unknown origin in China. In addition, novel paramyxoviruses were discovered in small mammals in Korea.

In conclusion, these studies highlight the real-time viral genome surveillance and exploration in preparedness and responsiveness for emerging infectious diseases. The discovery and genome characterization of novel zoonotic viruses are crucial for enabling rapid response and containment at the early stages of an outbreak, identifying effective therapeutic and vaccine targets, and guiding appropriate infectious disease control measures and policy decisions. Furthermore, these results provide insights into the development of NGS-based diagnostics for emerging infectious viruses.

Abstract

Evaluation of Vector *Competence of Culex tritaeniorhynchus* and *Culex pipiens pallens* for Japanese Encephalitis Virus Genotypes V (JEV-GV)

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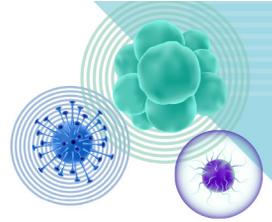
Japanese encephalitis virus (JEV) is a mosquito-borne zoonotic flavivirus that poses significant public health concerns across Asia. JEV is classified into five genotypes (G I–V), and its transmission is primarily mediated by *Culex* (*Cx.*) mosquitoes. Historically, genotype GIII was the most prevalent strain until the 1990s, after which genotype G I emerged as the dominant lineage in many endemic regions. In the Republic of Korea (ROK), genotype GV was first identified in 2010 and has since become the predominant genotype, suggesting a shift in viral ecology and successful local establishment. As vector competence varies by mosquito species and viral genotype, understanding the capacity of domestic mosquito vectors to transmit JEV GV is essential for guiding surveillance and control strategies.

Two common mosquito species in the ROK, *Culex tritaeniorhynchus* and *Culex pipiens pallens*, were evaluated for their vector competence for JEV genotype GV under controlled laboratory conditions. Adult female mosquitoes were orally infected with JEV GV and maintained under standardized temperature and humidity. At 14 days post-infection (dpi), mosquitoes were dissected and tested for viral RNA in their bodies (infection rate), legs/wings (dissemination rate), and saliva (transmission rate). Viral RNA detection was conducted using real-time reverse transcription PCR (RT-qPCR).

Culex tritaeniorhynchus exhibited high susceptibility to JEV GV infection, with an infection rate of 97.9% and a dissemination rate of 95.7% at 14 dpi. Viral RNA was detected in the saliva of 91.3% of infected individuals, indicating efficient transmission capability. These results demonstrate that *Cx. tritaeniorhynchus* supports robust viral replication and efficient dissemination to salivary glands.

In contrast, *Culex pipiens pallens* showed a lower infection rate of 36.9%, a dissemination rate of 42.2%, and a transmission rate of 31.1%. Despite the relatively lower competence, the detection of viral RNA in the saliva suggests a potential, albeit limited, role in JEV transmission.

This study confirms the high vector competence of *Culex tritaeniorhynchus* for JEV genotype GV, reinforcing its role as the primary vector in the ROK. However, the partial competence observed in *Cx. pipiens pallens* implies that this species could also contribute to JEV transmission, particularly in urban or peri-urban settings where it is more prevalent. These findings underscore the importance of species-specific surveillance and vector control strategies to effectively mitigate JEV risk.



Abstract

Fatal outcomes of SFTS and critical COVID-19 are associated with IL-10, IL-6, and TGF- β , And human infections of Hantaan virus were reported on Jeju Island, South Korea in 2024

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Severe fever with thrombocytopenia syndrome virus (SFTSV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause the hyperproduction of inflammatory cytokines, which have pathological effects in patient including severe or fatal cytokine storms. To characterize the effect of SFTSV and SARS-CoV-2 infection on the production of cytokines in severe fever with thrombocytopenia syndrome (SFTS) and COVID-19 patients, we performed an analysis of cytokines in SFTS and COVID-19 patients and also investigated the role of interleukin-10 (IL-10) in vitro studies: lipopolysaccharide-induced THP-1-derived macrophages, SFTSV infection of THP-1 cells, and SARS-CoV-2 infection of THP-1 cells. In this study, we found that levels of both IL-10 and IL-6 were significantly elevated, the level of transforming growth factor- β (TGF- β) was significantly decreased and IL-10 was elevated earlier than IL-6 in severe and critical COVID-19 and fatal SFTS patients, and inhibition of IL-10 signaling decreased the production of IL-6 and elevated that of TGF- β . Therefore, the hyperproduction of IL-10 and IL-6 and the low production of TGF- β have been linked to cytokine storm-induced mortality in fatal SFTS and severe and critically ill COVID-19 patients and that IL-10 can play an important role in the host immune response to severe and critical SARS-CoV-2 and fatal SFTSV infection.

Separately, we report the first confirmed cases of autochthonous human Hantaan virus (HTNV) infection on Jeju Island, South Korea, in 2024. Four laboratory-confirmed cases were identified, with clinical features consistent with hemorrhagic fever with renal syndrome (HFRS). Phylogenetic analysis revealed that the viral strains were closely related to HTNV sequences previously isolated from local rodent species (*Apodemus chejuensis*), suggesting localized zoonotic transmission and a distinct phylogeographic lineage.

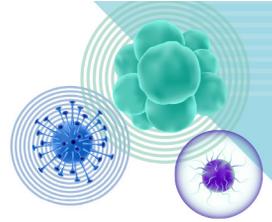
Abstract

Development and evaluation of mRNA vaccines encoding Glycoproteins for protection against *Bandavirus dabiense*

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Severe fever with thrombocytopenia syndrome (SFTS) is a tick-borne zoonotic disease caused by *Bandavirus dabiense* (SFTS virus, SFTSV), a negative-sense single-stranded RNA virus belonging to the genus *Bandavirus* in the family *Phenuiviridae*. SFTS was first reported in China in 2009, has since emerged across East Asia, including China, Japan and the Republic of Korea. In Korea, cases have been increasing steadily since 2013, with a high fatality rate of approximately 18.4%. However, there are currently no approved antiviral treatments and vaccines. In this study, we developed a safe and effective SFTS mRNA vaccine candidate encoding the full-length SFTSV glycoproteins, Gn and Gc. Our vaccine candidate harbors an equal amount of two mRNAs individually encoding full-length SFTSV Gn or Gc domains. The mRNAs were synthesized through by *in vitro* transcription with a 5' cap, SmartCap, and encapsulated in an ionizable lipid nanoparticle system, called STLNP. Robust expression of these Gn and Gc antigens was observed when human 293 T cells were transfected by the manufactured SFTSV mRNA formulation. We immunized mice twice three-week intervals with three doses of the mRNA vaccine candidate and collected blood samples from the immunized wild-type mice. The mRNA vaccine candidate elicited strong immunogenicity, as demonstrated by high levels of virus-neutralizing antibodies and total IgG. Also, the immunized mice showed a complete protection against a lethal dose of SFTSV without body weight loss and pathological trace. These findings indicate that our mRNA vaccine encoding glycoproteins represent a promising SFTS vaccine candidate for clinical development.



Abstract

Cross-Protective mRNA Vaccine Candidates for Old World Hantavirus

Jong Hyeon Seok, Jineui Kim, Yerin Hong, Jaek Choi, Jeonghun Kim, Minji Kim, Kisoong Kim, and Man-Seong Park

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Old World hantaviruses, including Hantaan virus (HTNV) and Seoul virus (SEOV), are major zoonotic pathogens that cause hemorrhagic fever with renal syndrome (HFRS) in Asia and Europe. However, current inactivated vaccines show limited efficacy and provide insufficient cross-protection against antigenic variants. To overcome these limitations, we generated mRNA hantavirus vaccine candidates encoding Phylogenetically Optimized Mosaic Antigens (POMA), designed from conserved sequence of old World hantavirus Gn, Gc proteins to induce cross-protection, incorporating stabilizing substitutions to enhance immunogenicity. Three H-POMA mRNA vaccines were generated through the Moderna mRNA Access program and evaluated in Balb/c mice. The H-POMA mRNA vaccine efficacy was assessed by quantifying viral loads in lung and kidney tissues, and immunogenicity analyzed by plaque reduction neutralization tests (PRNT), ELISA for Gn, Gc antigen-specific binding antibodies, and flow cytometric analysis of B cell responses. H-POMA mRNA vaccine candidates conferred superior protective efficacy compared to inactivated vaccine, inducing dose-dependent viral load reductions in both lung and kidney tissues along with elevated binding and neutralizing antibody levels. Sera from immunized mice exhibited cross-neutralizing activity against SEOV, supporting the effectiveness of the POMA antigen design strategy in overcoming serotype differences. Taken together, these findings indicate that the H-POMA mRNA antigen can be a promising vaccine candidate for broad protection against old World hantaviruses.

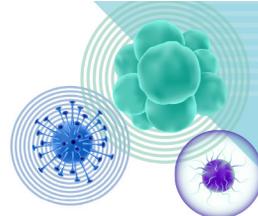
Abstract

Recombinant Bandavirus as an effective bivalent vaccine platform inducing protective immunity against intracellular pathogen and cancer

Hyo-Jin Ro^{1,2,†}, Yebeen Lee^{1,2,†}, Kyeongseok Jeon^{1,2}, Yujin Kim³, Seung Ho Baek³, Green Kim³, Joowan Kim^{1,2}, Jun-Gu Kang⁴, Na-Yoon Jang^{1,2,5}, Si-Hyeon Lee^{1,2}, Sun-Young Kim^{1,2}, Yu-Jin Kim^{1,2,5}, Na-Young Ha⁶, Yuri Kim⁷, Young-Ki Choi⁸, Jae U. Jung⁹, Jung Joo Hong^{3,10}, and Nam-Hyuk Cho^{1,2,4, 11*}

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Severe fever with thrombocytopenia syndrome virus (SFTSV) is an emerging tick-borne pathogen endemic to East Asia, associated with high mortality and lacking approved vaccines and therapies. We developed a live attenuated vaccine platform based on a recombinant SFTSV lacking the nonstructural (NS) gene, a major virulence factor suppressing type I interferon responses. The resulting Δ NS viruses, reassorted with the prevalent genotype B, exhibited attenuated replication in interferon-competent cells while maintaining the ability to infect and activate antigen-presenting cells. Immunization with Δ NS vectors elicited robust SFTSV-specific humoral and cellular immune responses in mice and non-human primates, complete protection against lethal challenge across multiple SFTSV genotypes, with durable immunity lasting up to 12 months. Moreover, Δ NS vectors encoding heterologous antigens, such as ovalbumin (OVA) or TSA56 from *Orientia tsutsugamushi*, induced strong antigen-specific T cell responses and conferred protective immunity against melanoma expressing OVA and scrub typhus. Mechanistically, Δ NS viruses directly promoted APC activation, enhanced antigen presentation, and reduced apoptosis in infected cells, supporting effective T cell priming. These results establish SFTSV Δ NS as a safe, immunogenic, and broadly protective vaccine candidate, as well as a versatile bivalent vector platform with potential applications against viral, intracellular bacterial, and tumor-associated antigens.



Abstract

The therapeutic potential of mRNA-encoded SFTSV human monoclonal antibody

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†These authors contributed equally to this work. *Corresponding authors

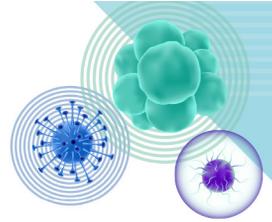
Severe fever with thrombocytopenia syndrome (SFTS), caused by the SFTS virus (SFTSV), has emerged as a significant public health concern in East Asia since 2009. The high mortality rate of SFTS underscores the urgent need for effective preventive and therapeutic interventions. Although a Gn-specific human monoclonal antibody, Ab10, herein referred to as the protein S/A-TEN, has been previously reported, its development has been hindered by the economic challenges and low yields of large-scale production. To address this limitation, we developed an mRNA encapsulated lipid nanoparticle to produce SFTSV-specific human mAbs (mRNA S/A-TEN). This novel approach facilitates small-scale production, potentially enabling direct human application. The mRNA S/A-TEN antibody obtained from the injected-mouse serum showed high neutralizing antibody titers. Furthermore, we found that injecting the mRNA S/A-TEN antibody into mice that were infected with lethal SFTSV resulted in 100% survival and assisted in a rapid recovery from organ failure. This study provides the first evidence that an mRNA-encoded SFTSV-specific human mAb can provide effective therapeutic protection against SFTSV infection, offering a promising therapeutic approach for the treatment of human SFTS.

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Abstracts of Lecture

허피스바이러스

MEMO



S 1-1

DHT-AR Signaling Suppresses EBV-Positive Gastric Cancer via DNMT3A-MICA Pathway

Hyojeung Kang

College of Pharmacy, Kyungpook National University, Daegu, Republic of Korea

Epstein-Barr virus-associated gastric carcinoma (EBVaGC) shows better survival outcomes in male patients, suggesting androgen involvement, yet the underlying mechanisms remain unclear. Our Kaplan-Meier analysis revealed that while high androgen receptor (AR) expression generally correlates with poor gastric cancer prognosis, EBV-positive patients with high AR expression showed improved survival, indicating paradoxical tumor-suppressive effects. We investigated dihydrotestosterone (DHT)-AR signaling using EBVaGC cell lines (SNU719, MKN1-EBV) with AR knockout/knockdown models generated via CRISPR/Cas9 and shRNA systems, employing comprehensive molecular analyses including ChIP-seq, whole genome bisulfite sequencing, and cytotoxicity assays with NK-92 cells and EBV-specific PBMCs, followed by xenograft validation in nude and NSG mice. DHT treatment activated dual tumor-suppressive mechanisms by first downregulating DNA methyltransferase 3A (DNMT3A) expression by 135.6%, leading to genome-wide DNA demethylation (methylated promoters: 81,952→54,294) that caused demethylation of MHC class I polypeptide-related sequence A (MICA) promoter regions, resulting in increased MICA expression and enhanced NK and T cell cytotoxicity against EBVaGC cells through NKG2D receptor interactions without inducing inflammatory cytokines, while simultaneously triggering EBV lytic/latent gene expression (BZLF1, EBNA1, LMP1), DNA damage response activation (ATM, H2AX, p53 phosphorylation), and pro-apoptotic miRNA upregulation (miR-204-5p), leading to early apoptosis and viral reactivation. Xenograft studies confirmed reduced tumor growth, increased lymphocyte infiltration, and enhanced viral gene expression in AR-positive tumors. This study reveals that DHT-AR signaling suppresses EBVaGC through DNMT3A downregulation-mediated epigenetic remodeling that enhances MICA-dependent immune responses and viral reactivation mechanisms, suggesting AR agonists as potential therapeutic agents for AR-positive EBV-associated gastric cancer, representing a paradigm shift from conventional androgen deprivation therapy and providing novel insights into the sequential hormonal-epigenetic-immune-viral interactions for personalized treatment strategies.

Inherited chromosomally integrated Human Herpesvirus 6

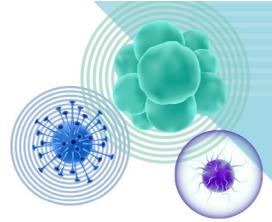
Kyung-Ran Kim^{1,2}, Doo Ri Kim³, Areum Shin³, Hwanhee Park⁴, Joon-sik Choi⁵, and Yae-Jean Kim^{3,6,7}

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Human herpesvirus 6 (HHV-6) is a lymphotropic virus that belongs to the Herpesviridae family, Betaherpesviridae subfamily, and the genus *Roseolovirus*. HHV-6 is an enveloped, double-stranded DNA virus that is approximately 160-200 nm in diameter and consists of two distinct species, HHV-6A and HHV-6B.

The seroprevalence for HHV-6 is 97% of the global population. Primary infection with HHV-6 typically occurs in children around two years of age. This infection manifests as roseola infantum, a self-limiting illness characterized by a three-day fever followed by a rash. HHV-6 is mainly transmitted through saliva and respiratory droplets. Following primary infection, HHV-6 sustains latency. While primary infection is generally benign, reactivation and primary infection can lead to severe complications such as encephalitis and graft-versus-host disease in hematopoietic cell transplant recipients.

HHV-6 can integrate into the telomere of human chromosomes. This integration into germline cells results in inherited chromosomally integrated (ici) HHV-6, which can be transmitted vertically. The prevalence of iciHHV-6 is between 0.5 and 2% in populations from Japan, the United States, and the United Kingdom. IciHHV-6 reported associations of various diseases, including Alzheimer's disease, depression, systemic lupus erythematosus, multiple sclerosis, angina pectoris, congestive heart failure, preeclampsia, and spontaneous abortion. Research is underway to develop vaccines and antiviral agents to prevent and treat HHV-6 infection.



S 1-3

RIG-I-mediated antiviral signaling triggered by viral disruption of host RNA

Jung-Hyun Lee

Department of Life Science, University of Seoul

The cytosolic RNA sensor RIG-I plays a central role in innate antiviral immunity by detecting structured viral RNAs with 5'-triphosphates or short double-stranded features. While RIG-I was initially characterized in the context of RNA virus infection, our previous studies have shown that it also plays a critical role in host defense against DNA viruses including herpes simplex virus 1 (HSV-1) by sensing host-derived RNAs that mislocalized upon viral perturbation. We identified the 5S RNA pseudogene transcript RNA5SP141 as a physiological RIG-I ligand. During HSV-1 infection, the process of virus-induced host shutoff promotes the relocalization of RNA5SP141 from the nucleus to the cytoplasm and its unshielding, enabling RIG-I to recognize it and subsequently induce robust type I interferon responses. Furthermore, we have demonstrated that impaired RNA5SP141 biogenesis increases susceptibility to herpes simplex encephalitis, highlighting its importance in antiviral immunity.

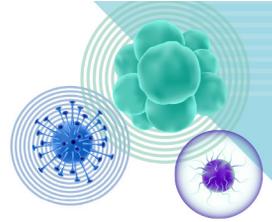
Here, our new study reveals that HSV-1 infection promotes the selective packaging of RNA5SP141 into extracellular vesicles (EVs). These EVs are then released and delivered to uninfected cells. Interestingly, these EVs containing RNA5SP141 appear to be transferred preferentially to specific recipient cell types. This suggests a form of targeted intercellular communication that may prime select populations for antiviral responses. Although the molecular determinants of EV targeting and the downstream dynamics of RIG-I signaling in recipient cells are still being investigated, our findings provide a conceptual framework for EV-mediated immune amplification, extending antiviral surveillance beyond the initially infected cells.

HCMV Tegument Protein pp28 Repositions Viperin to Promote Viral Egress

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Human cytomegalovirus (HCMV) relies on coordinated interactions between viral and host proteins to complete its life cycle. Viperin, an interferon-inducible antiviral protein, is normally localized to the endoplasmic reticulum (ER) but relocates to mitochondria during early HCMV infection and accumulates in the virus assembly compartment (vAC) at later stages. While early mitochondrial relocalization has been described, the mechanism underlying vAC targeting remained unclear. To investigate this, we performed a yeast two-hybrid screen using viperin as a bait and identified the tegument protein pp28 (UL99) as a direct interactor and key mediator of viperin relocalization. Co-immunoprecipitation and microscopy confirmed that pp28 binds viperin and is sufficient to recruit it to the vAC. Site-directed mutagenesis revealed that amino acids 12 to 14 (Glu12, Phe13, and Gly14) of pp28 are required for this interaction. Alanine substitution at these sites, pp28 mutant (12-14A), abolished viperin binding without affecting pp28 expression or localization. Infection with the recombinant HCMV expressing pp28 mutant (12-14A) resulted in significantly reduced extracellular viral titers, while intracellular titers remained unchanged. These findings demonstrate that the pp28-viperin interaction is dispensable for virion formation but essential for efficient virion release, revealing a novel mechanism by which HCMV exploits a host antiviral protein to enhance viral egress.



S 2-2

Human cytomegalovirus long non-coding RNA counteracts nuclear cGAS to facilitate immune evasion

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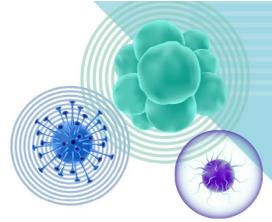
Viruses have evolved diverse immune evasion strategies including targeting host pattern recognition receptors (PRRs). The role of viral non-coding RNAs in modulating PRR activity is unclear. Here, we show that human cytomegalovirus (HCMV) produces long non-coding RNA4.9 that counteracts nuclear cyclic GMP-AMP synthase (cGAS)-mediated immune response to facilitate viral infection in human foreskin fibroblasts (HFFs). RNA4.9 interacts with host cGAS via its 75-nucleotide (nt) RNA region with predicted hairpin loops. Binding of RNA4.9 to cGAS inhibits cGAS enzymatic activity as well as downstream interferon response and facilitates productive viral replication. Sterically blocking the folding of 75-nt region with antisense oligonucleotides during HCMV infection restores cGAS activity and impairs viral replication. Additionally, we found that the specific localization of RNA4.9, which concentrates near HCMV DNA, is correlated with its efficient binding to cGAS and subsequent immune suppression. Our findings demonstrate viral non-coding RNAs as critical cGAS regulators and as potential therapeutic targets.

Senescence of endothelial cells increases susceptibility to Kaposi's sarcoma-associated herpesvirus infection via CD109-mediated viral entry

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The aging process is characterized by cellular functional decline and increased susceptibility to infections. Understanding the association between virus infection and aging is crucial for developing effective strategies against viral infections in older individuals. However, the relationship between Kaposi's sarcoma-associated herpesvirus (KSHV) infection, a cause of increased Kaposi's sarcoma prevalence among the elderly without HIV infection, and cellular senescence remains enigmatic. This study uncovered a link between cellular senescence and enhanced KSHV infectivity in human endothelial cells. Through a comprehensive proteomic analysis, we identified caveolin-1 and CD109 as host factors significantly upregulated in senescent cells that promote KSHV infection. Remarkably, CRISPR/Cas9-mediated KO of these factors reduced KSHV binding and entry, leading to decreased viral infectivity. Furthermore, surface plasmon resonance analysis and confocal microscopy revealed a direct interaction between KSHV virions and CD109 on the cell surface during entry, with recombinant CD109 protein exhibiting inhibitory activity of KSHV infection by blocking virion binding. These findings uncover a previously unrecognized role of cellular senescence in enhancing KSHV infection through upregulation of specific host factors and provide insights into the complex interplay between aging and viral pathogenesis.



Intracellular Acetyl-CoA Flux Induced by KSHV vIRF3-PKM2 Interaction Promotes the Disseminated Visceral Kaposi's Sarcoma

Yeong Jun Kim¹, Juhyeon Lim², Jae Jin Lee², Abhishek Kumar³, Shrute Kannappan⁴, Junjie Zhang⁵, Soochi Kim¹, Han-Jun Kim⁶, Kyeong Kyu Kim⁴, Zsolt Toth³, Hyungjin Eoh^{2,7}, and Hye-Ra Lee^{1,8*}

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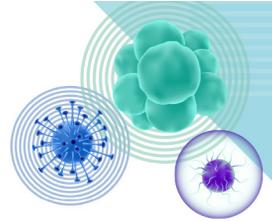
Kaposi's sarcoma (KS), induced by Kaposi's sarcoma-associated herpesvirus (KSHV), is a multicentric tumor of lymphatic endothelial origin. However, the fundamental molecular mechanisms underlying the malignancy leading to disseminated KS remain unclear. Here, we found that interaction between KSHV vIRF3 and PKM2 controls the metabolic switch of lymphatic endothelial cells (LECs), inducing disseminated visceral KS in xenograft models of KSHV-infected LECs. Mechanistically, vIRF3-PKM2 interaction elevates intracellular acetyl-CoA level by augmenting the PKM2 enzymatic activity, leading to SMAD5 acetylation, which contributes to the endothelial-mesenchymal transition (EndMT) of LECs. Notably, a vIRF3-derived short peptide acts as a potent and selective PKM2 antagonist, effectively regressing KS progression. Collectively, these results suggest that vIRF3 plays a pivotal role in KS malignancy, linking metabolic reprogramming of acetyl-CoA metabolism to cancer progression.

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호흡기바이러스

MEMO



Abstract

Development of Broadly Neutralizing Antibodies Against SARS CoV-2 variants

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Division of Emerging Virus and Vector Research, Center for Emerging Virus Research, National Institute of Health, Korea Disease Control and Prevention Agency, Osong 28159

The continuous emergence of SARS-CoV-2 variants has led to a reduction in the efficacy of existing antibody therapeutics, highlighting the need for new strategies to enhance neutralizing activity.

In this study, we aimed to improve the neutralizing potency of two previously developed anti-SARS-CoV-2 monoclonal antibodies using three approaches: (1) antibody combination, (2) isotype switching, and (3) generation of bispecific antibodies.

All three strategies resulted in improved neutralizing activity compared to individual monoclonal antibodies, with the bispecific antibody showing the most significant enhancement.

These findings provide valuable insight into the development of next-generation therapeutics against SARS-CoV-2 variants.

Abstract

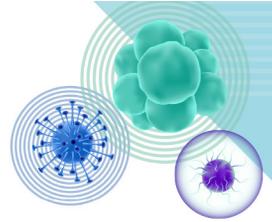
A Cross-protective COVID-19 Vaccine Candidate using Newcastle Disease Virus as a Vaccine Vector

Jeonghun Kim, Jong Hyeon Seok, Jineui Kim, Yerin Hong, Kissoon Kim, and Man-Seong Park*

Department of Microbiology, Institute for Viral Diseases, and Vaccine Innovation Center, College of Medicine, Korea University

Despite the rapid commercialization of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines, including mRNA vaccines, their effectiveness has declined due to the emergence of SARS-CoV-2 antigenic variants. The continuous emergence of SARS-CoV-2 variants emphasizes the need for effective vaccines that are capable of responding to emerging viruses. Moreover, mRNA vaccines face challenges in low-income countries due to their high production costs and cold storage requirement, leading to global inequity in vaccine distribution. Therefore, this study aimed to develop a cost-effective and highly efficacious vaccine that overcomes the current limitations of current SARS-CoV-2 vaccines

Based on phylogenetic analyses of the SARS-CoV-2 spike genes, two cross-reactive vaccine antigen candidates (POMA Omi 1 S and POMA Omi 2 S) were designed by using the Phylogenetically Optimized Mosaic Antigen (POMA) method. These antigens were applied to the Newcastle disease virus (NDV) vector to generate SARS-CoV-2 vaccine candidates, which demonstrated superior immunogenicity and protective efficacy compared with existing commercial NDV-based SARS-CoV-2 vaccines. These findings suggest that recombinant NDV-based vaccine may prove to be a promising strategy for developing a cost-effective and efficacious SARS-CoV-2 vaccine.



Abstract

Unveiling the Hidden Regulator of COVID-19 Immunopathology: NLRP12

SangJoon Lee

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SARS-CoV-2 has caused a global health crisis, with severe COVID-19 characterized by hyperinflammatory responses and immune dysregulation. Innate immune sensors are essential for antiviral defense, yet the complete network of immune sensing and inflammatory cell death pathways during SARS-CoV-2 infection remains unclear. In this study, we identify NLRP12 as a key innate immune sensor that mediates inflammatory cell death during SARS-CoV-2 infection. Using CRISPR-Cas9 screening and RNA-seq data analysis, we demonstrate that NLRP12 is upregulated in COVID-19 patients. Mechanistically, NLRP12 assembles a multi-protein complex with ASC, NLRP3, caspase-8, and RIPK3, coordinating multiple inflammatory cell death. Loss of NLRP12 significantly reduces activation of pyroptotic, apoptotic, and necroptotic markers both in vitro and in vivo. Moreover, NLRP12-deficient mice exhibit decreased inflammatory cytokine production, reduced cell death, and attenuated lung inflammation. These findings establish NLRP12 as a central regulator of inflammatory cell death and antiviral immunity, highlighting its potential as a therapeutic target for controlling immune responses in COVID-19.

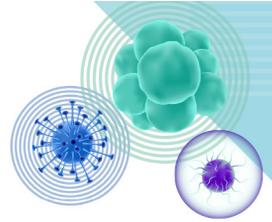
Abstract

Zoonotic Risk Profiling of Bovine-derived H5N1 Influenza Virus via Genome-wide and Structural Evaluation

Seunghye Cho¹, Sangyi Lee¹, Hyunbeen Kim¹, Sejik Park¹, Woojin Shin¹, Soyoung Lee¹, Kyuyoung Lee¹, Atanas V. Demirev¹, Man-Seong Park^{1,2,3}, and Jin Il Kim^{1,2,3}

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Extensive global surveillance has revealed an ongoing H5N1 influenza outbreak among dairy cattle in the United States, raising urgent concerns over its zoonotic potential. However, current genomic monitoring efforts often fail to incorporate critical molecular and structural determinants necessary for assessing cross-species transmission risk. In this study, we comprehensively evaluated the molecular evolution and host adaptation features of H5N1 clade 2.3.4.4 viruses, with a focus on viral mutations and their functional consequences. We performed structural analyses of hemagglutinin (HA) and neuraminidase (NA) interactions with both avian-type (α 2,3-linked) and human-type (α 2,6-linked) sialic acid receptors, key determinants of host specificity. Additionally, we assessed the binding affinity of the influenza polymerase complex (PB2, PB1, PA) to host ANP32A/B proteins, which are essential for efficient viral replication in mammalian cells. Notably, we observed variation in polymerase-host interactions among bovine-derived strains, indicating enhanced adaptation to mammalian hosts. By integrating structural receptor-binding analysis, polymerase-ANP32A/B compatibility profiling, and full-genome phylogenetic assessments, our study provides a robust framework for evaluating zoonotic risk. These findings underscore the necessity of genome-wide and functionally informed surveillance approaches to better anticipate and mitigate emerging threats posed by H5N1 viruses.



Abstract

Neutrophil Elastase: A Host Factor Driving SARS-CoV-2 Infectivity

Yu-Jin Kim^{1,8}, Su Jin Lee¹, Gun Young Yoon¹, Haesoo Kim¹, Wooseop Sim², Ji-Seung Yoo^{2,3}, Seil Kim^{4,5}, Sung Kyun Lee¹, Chonsaeng Kim¹, Nam-Hyuk Cho^{6,7}, Seong-Jun Kim^{9,10}, and Dae-Gyun Ahn^{1†}

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Infiltrating neutrophils, key immune biomarkers, are particularly prominent in severe COVID-19 cases, especially within lung tissue. This study explores the pathogenic role of neutrophil elastase, a major granular enzyme secreted by neutrophils during SARS-CoV-2 infection. Our findings suggest that neutrophil elastase plays a critical role in SARS-CoV-2 entry by significantly enhancing the membrane fusion of viral spike proteins. We demonstrated that human neutrophil elastase proteolytically processes SARS-CoV-2 spike proteins at newly identified sites adjacent to the S2' cleavage site, independent of TMPRSS2, as determined through mutational analysis. Transcriptome analysis revealed that, in the presence of neutrophil elastase, SARS-CoV-2-infected cells exhibit aberrant virus-induced inflammation, driven by increased viral propagation, abnormal NF- κ B activation, and DNA damage-associated inflammation. Importantly, the neutrophil elastase inhibitor, sivelestat, mitigates virus-induced lung pathology in infected mice, confirming its pathogenic role. These findings provide insights into viral exploitation of innate immunity and suggest potential therapeutic strategies.

Abstract

Crossing the Species Divide: Insights into Animal-Origin Influenza Virus Spillover to Humans

Chung-Young Lee

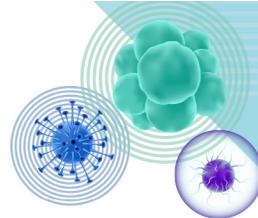
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Influenza A virus (IAV) has caused multiple pandemics throughout human history, highlighting the critical need to understand its transmission dynamics. While zoonotic spillover events from animals to humans are not uncommon, the mechanisms by which animal-origin IAVs overcome host-specific barriers remain incompletely understood. In this presentation, I will explore how animal influenza viruses breach the species barrier to infect humans, emphasizing key molecular determinants and host-pathogen interactions. Additionally, I will introduce a deep learning-based predictive framework we have developed to evaluate the pandemic potential of animal-origin IAVs, providing a novel tool to enhance influenza surveillance and risk assessment strategies.

2025 대한바이러스학회
연구회연합 정기학술대회
The Korean Society of Virology

Poster Presentation

MEMO



간염 1

N6-methyladenosine modification of hepatitis B virus RNAs differentially regulates viral life cycle depending on its position.

Geon-Woo Kim^{1,2} and Aleem Siddiqui¹

¹Division of Infectious Diseases and Public Global Health, University of California, San Diego, La Jolla, CA 92093, USA, ²Department of Microbiology and Molecular Biology, Chungnam National University, Yuseong-gu, Daejeon, Republic of Korea

간염 2

Dual function of Nucleus Accumbens-Associated Protein 2 as a Novel Host Factor in the Hepatitis B Virus Replication

Wonhee Kim¹ and Kyun Hwan Kim^{1,2,*}

¹Department of Metabiohealth, Institute for Cross-disciplinary Studies, Sungkyunkwan University, ²Viral Pathogenesis, Department of Precision Medicine, School of Medicine, Sungkyunkwan University

간염 3

Bardoxolone-Methyl (BARD) Suppresses Hepatitis B Virus Replication and Hepatocellular Carcinoma Development by Inhibiting Signal Transducer and Activator of Transcription 3 (STAT3) Signaling

Seo-Hyeon Park¹, Seung-Hoon Lee¹, Jae-Su Moon², and Geon-Woo Kim^{1*}

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간염 4

The Antiviral Effect of Heat Shock Transcription Factor, X-linked 1 on the Viral Replication of Hepatitis B Virus

Haena Yun¹ and Kyun-Hwan Kim^{1,2*}

¹Department of MetaBioHealth, Institute for Cross-disciplinary Studies, Sungkyunkwan University, ²Viral Pathogenesis, Department of Precision Medicine, School of Medicine, Sungkyunkwan University

간염 5

4'-Thiouridine Simultaneously Inhibits RdRp and NiRAN Activities of SARS-CoV-2 Nsp12

Myoung Kyu Lee^{1,#}, Minjae Kim^{3,#}, Yeon Seo Jeon^{1,2}, Hyun Su Ra^{1,2}, Jiwon Jeong^{1,2}, Meeheyin Kim^{1,2*}, and Lak Shin Jeong^{3*}

¹Infectious Diseases Therapeutic Research Center, Korea Research Institute of Chemical Technology (KRICT), Daejeon, 34114, Republic of Korea, ²Graduate School of New Drug Discovery and Development, Chungnam National University, Daejeon, 34134, Republic of Korea, ³Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul, 08826, Republic of Korea

간염 6

UNI418 Inhibits SARS-CoV-2 Entry via Disruption of Spike Protein Processing and Viral Endocytosis

Myoung Kyu Lee^{1,#}, Yejin Jang^{1,#}, Yuri Seo^{3,4,#}, Seon-gyeong Lee^{4,5,#}, Yeon Seo Jeon^{1,2}, Hyun Su Ra^{1,2}, Jiwon Jeong^{1,2}, Meeheyin Kim^{1,2*}, Joo-Yong Lee^{3*}, and Kyungjae Myung^{4,5*}

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간염 7

Hepatitis B virus (HBV)-Induced HOXD Antisense Growth-Associated Long Non-Coding RNA (HAGLR) Promotes the Viral Replication and Hepatocellular Carcinoma (HCC) Progression via Acting as Competitive Endogenous RNA (ceRNA)

Seung-Hoon Lee and Geon-Woo Kim*

Department of Microbiology & Molecular Biology, Chungnam National University, 99 Daehak-ro, Yuseong-gu, Daejeon, Korea

간염 8

Javanicin inhibits secretion of hepatitis B virus particles by targeting the core protein

Nayeon Park^{1†}, Gwang-Hoon Ko^{1†}, Yun Seo Park^{2†}, Jung-Ah Kang³, Sang Hee Shim^{2**}, and Sung-Gyoo Park^{1*}

¹College of Pharmacy and Research Institute of Pharmaceutical Science, Seoul National University, Seoul 08826, Republic of Korea, ²Natural Products Research Institute, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea, ³Bio-Nanotechnology Research Center, Korea Research Institute of Bioscience and Biotechnology, Daejeon, Republic of Korea

노로 1

Human Norovirus-Induced Inflammasome Activation: Unveiling the Role of NLRP6 in Intestinal Immunity

Sunghoon Park, Sung-Gyu Cho, Hyeon Woo Chung, Hwang Su Jin, Taehee Kim, and Jae Myun Lee*

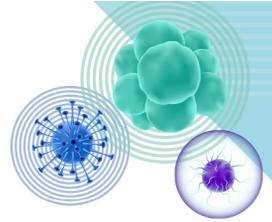
Department of Microbiology and Immunology, Yonsei University college of Medicine, Seoul, Republic of Korea

노로 1

Development of a Recombinant Baculovirus- Based Norovirus Vaccine and Evaluation of Systemic and Mucosal Immunogenicity in Mice

Doyoung Yoon, Youngjik Lee, Young Bong Kim, Hee-Jung Lee*

Department of Bio-medical Science and Engineering, Konkuk University, Seoul, Republic of Korea



수의 1

Development of a Portable Point-of-Care Assay for the Detection of Marine Mammal DNA Viruses, *Herpesviridae*, *Poxviridae*, and *Anelloviridae*

Shivani Rajoriya^{1,†}, Jieun Park^{1,†}, Seonghyeon Lee¹, Daehyun Kim¹, Augustine Natasha¹, Sara Puspareni Prayitno¹, Haryo Seno Pangestu¹, Minsung Lee¹, Nayeon Jang⁵, Min-Jeong Kim², Kyunglee LEE³, Seung Won Jung², Taek-Kyun Lee⁴, and Won-Keun Kim^{1,5*}

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수의 2

Field-deployable Molecular Assay of Marine Mammal RNA Viruses, *Orthomyxoviridae*, *Paramyxoviridae*, *Picornaviridae*, *Caliciviridae*, *Rhabdoviridae* and *Reoviridae*, Using a Franklin Thermocycler

Shivani Rajoriya^{1,†}, Jieun Park^{1,†}, Seonghyeon Lee¹, Daehyun Kim¹, Augustine Natasha¹, Sara Puspareni Prayitno¹, Haryo Seno Pangestu¹, Minsung Lee¹, Nayeon Jang⁵, Min-Jeong Kim², Kyunglee LEE³, Seung Won Jung², Taek-Kyun Lee⁴, and Won-Keun Kim^{1,5*}

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수의 3

Knowledge and Attitudes Toward Lumpy Skin Disease Virus in the Post-Outbreak Period: Evidence from Korean Cattle Farms, 2025

Seung-bum Kang, Jin-ho Jeong, Joo-young Park, Seo-yeon Shin, Ye-rim Jung, and Dae Sung Yoo*
Department of Veterinary Epidemiology, College of Veterinary Medicine, Chonnam National University, Gwangju, South Korea

수의 4

First Detection and Genome Characterization of Ungulate Tetraparvovirus 1 in an Asian Water Buffalo (*Bubalus bubalis*) in Vietnam

Young-Seung Ko¹, Da-Yun Bae¹, Taek Geun Lee¹, Yun-Chae Cho¹, Sung-Hyun Moon¹, Zoya Afzal², Jiyeon Park², Chaewon Yoon², Dae Sung Yoo³, Won-Keun Kim⁴, Yeonsu Oh^{2*}, and Ho-Seong Cho^{1*}

¹College of Veterinary Medicine and Bio-Safety Research Institute, Jeonbuk National University, Iksan 54596, Korea, ²College of Veterinary Medicine and Institute of Veterinary Science, Kangwon National University, Chuncheon 24341, Korea, ³Department of Preventive Veterinary Medicine, College of Veterinary Medicine, Chonnam National University, Gwangju 61186, Korea, ⁴Institute of Medical Science, College of Medicine, Hallym University, Chuncheon 24252, Korea

수의 5

Genomic Characterization of Rotavirus A from Korean Bats Reveals Evidence of Interspecies Transmission

Young-Seung Ko¹, Da-Yun Bae¹, Taek Geun Lee¹, Yun-Chae Cho¹, Sung-Hyun Moon¹, Zoya Afzal², Jiyeon Park², Chaewon Yoon², Sang Jin Lim³, Won-Keun Kim⁴, Ho-Seong Cho^{1*}, and Yeonsu Oh^{2*}

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수의 6

Comparison of Diagnostic Performance Between Commercial Kits for Simultaneous Detection of PRRSV-1, PRRSV-2, and PCV2 in Clinical Pig Samples

Da-Young Kim^{1,†}, Ho-Seok Do^{1,†}, Dong-Kyu Lee¹, Jonghyun Park^{1,2}, Ji-Hyeon Baek¹, Jung-Hoon Kwon¹, Won-Il Kim³, Seung-Chai Kim³, Hwan-Ju Kim³, Ki Beom Park⁴, Nam-Yeon Kim⁴, Choi-Kyu Park^{1*}, and Hye-Ryung Kim^{1,2*}

¹Animal Disease Intervention Center, College of Veterinary Medicine, Kyungpook National University, Daegu 41566, Republic of Korea, ²DIVA Bio Incorporation, Daegu 41519, Republic of Korea, ³College of Veterinary Medicine, Jeonbuk National University, Iksan 54596, Korea, ⁴Research & Development Center, Invirustech Co., Inc., Gwangju 61222, Korea

수의 7

Prevalence and Co-Infection Status of Psittacine Beak and Feather Disease Virus and Aves Polyomavirus 1 in Korean Psittacine Birds Determined by a Newly Developed Multiplex Real-Time PCR

Da-Young Kim¹, Jonghyun Park^{1,2}, Ji-Hyeon Baek¹, Yong-Gu Yeo^{1,3}, Jung-Hoon Kwon¹, Hye-Ryung Kim^{1,2*}, and Choi-Kyu Park^{1*}

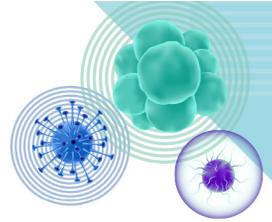
¹Animal Disease Intervention Center, College of Veterinary Medicine, Kyungpook National University, Daegu 41566, Republic of Korea, ²DIVA Bio Incorporation, Daegu 41519, Republic of Korea, ³Seoul Zoo, Gwacheon 13829, Republic of Korea

수의 8

In Silico Sequence Mining (ISSM): A Lightweight Tool for Rapid Viral NGS Data Analysis Without Large Databases

Min Chan Kim, Hye Ji Jung, Min Chang Kang, Ha Yeon Kim, Seong Sik Jang, Alain Chrysler Chamfort, Han Byul Lee, Hye Won Bae, and Hye Kwon Kim*

Department of Biological Sciences and Biotechnology, College of Natural Sciences, Chungbuk National University, Cheongju, Republic of Korea



수의 9

Development of a Luciferase-Tagged NiV Pseudovirus Animal Model Using rVSV for Vaccine Assessment

Seo Young Moon^{1,2}, Eun Bee Choi^{1,2}, Seungyeon Kim^{1,2}, Yookyoung Lee¹, Eun Young Jang¹, and Ouh In-Ohk^{1*}

¹Division of Vaccine Development Coordination, Center for Vaccine Research, National Institute of Infectious Diseases, National Institute of Health, Korea Disease Control and Prevention Agency, Cheongju, Republic of Korea, ²College of Veterinary Medicine & Institute for Veterinary Biomedical Science, Kyungpook National University, Daegu 41566, Republic of Korea

수의 10

First Emergence of Lumpy Skin Disease Virus in South Korea: Epidemiological Features and Implications

Dae-Sung Yoo¹, Jun Hee Han², Ho-Seong Cho³, Yeonsu Oh⁴, and Joo Young Park¹

¹College of Veterinary Medicine, Chonnam National University, Gwangju 61186, Republic of Korea, ²EpiCentre, School of Veterinary Science, Massey University, Palmerston North 4410, New Zealand, ³College of Veterinary Medicine & Biosafety Research Institute, College of Veterinary Medicine, Iksan 54596, Republic of Korea, ⁴College of Veterinary Medicine & Institute of Veterinary Science, Kangwon National University, Chuncheon 24341, Republic of Korea

수의 11

First Complete Genome Characterization of a Bat-Associated Pestivirus in Korea

Da-Yun Bae¹, Taek Geun Lee¹, Young-Seung Ko¹, Yun-Chae Cho¹, Sung-Hyun Moon¹, Zoya Afzal², Jiyeon Park², Chaewon Yoon², Sang Jin Lim³, Won-Keun Kim⁴, Yeonsu Oh^{2*}, and Ho-Seong Cho^{1*}

¹College of Veterinary Medicine and Bio-Safety Research Institute, Jeonbuk National University, Iksan 54596, Korea, ²College of Veterinary Medicine and Institute of Veterinary Science, Kangwon National University, Chuncheon 24341, Korea, ³Institute of Forest Science, Kangwon National University, Chuncheon 24341, Korea, ⁴Institute of Medical Science, College of Medicine, Hallym University, Chuncheon 24252, Korea

수의 12

Genetic Characterization of Korean Bat Coronaviruses via Virome Sequencing

Da-Yun Bae¹, Taek Geun Lee¹, Young-Seung Ko¹, Yun-Chae Cho¹, Sung-Hyun Moon¹, Zoya Afzal², Jiyeon Park², Chaewon Yoon², Sang Jin Lim³, Won-Keun Kim⁴, Ho-Seong Cho^{1*}, and Yeonsu Oh^{2*}

¹College of Veterinary Medicine and Bio-Safety Research Institute, Jeonbuk National University, Iksan 54596, Korea, ²College of Veterinary Medicine and Institute of Veterinary Science, Kangwon National University, Chuncheon 24341, Korea, ³Institute of Forest Science, Kangwon National University, Chuncheon 24341, Republic of Korea, ⁴Institute of Medical Science, College of Medicine, Hallym University, Chuncheon 24252, the Republic of Korea

수의 13

First Identification and Molecular Characterization of Psittacid Herpesvirus 1 from Pet Parrots in Korea

Ji-Hyeon Baek¹, Hye-Ryung Kim^{1,2}, Jonghyun Park^{1,2}, Yong-Gu Yeo^{1,3}, Oh-Deog Kwon¹, Seung-Chun Park^{1,4}, and Choi-Kyu Park^{1*}

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수의 14

Integrating Antibody Data, Surveillance Strategies, and Deep Learning Models into ABC-SMC Framework for Primary Case Detection in Livestock Disease Outbreaks

Dae sung Yoo^{1*}, Yeonsu Oh², and Ho-Seong Cho³

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수의 15

Development and Evaluation of Cap- and IRES-Based mRNA Vaccine Platforms Against Foot-and-Mouth Disease

Hye-Won Yu¹, Sowon Lee², Yun Ji Kim¹, Seonghyun Lee², and So-Hee Hong¹

¹Department of Microbiology, College of Medicine, Ewha Womans University, Seoul, Korea, ²Department of Biotechnology, Catholic University, Bucheon, Korea

수의 16

Genetic Diversity of Bat Astroviruses in Korean Bats Revealed by Virome Analysis

Yun-Chae Cho¹, Da-Yun Bae¹, Taek Geun Lee¹, Young-Seung Ko¹, Sung-Hyun Moon¹, Zoya Afzal², Jiyeon Park², Chaewon Yoon², Sang Jin Lim³, Won-Keun Kim⁴, Yeonsu Oh^{2*}, and Ho-Seong Cho^{1*}

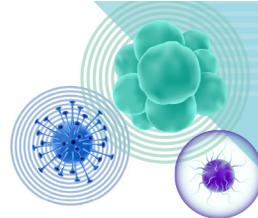
¹College of Veterinary Medicine and Bio-Safety Research Institute, Jeonbuk National University, Iksan 54596, Korea, ²College of Veterinary Medicine and Institute of Veterinary Science, Kangwon National University, Chuncheon 24341, Korea, ³Institute of Forest Science, Kangwon National University, Chuncheon 24341, Korea, ⁴Institute of Medical Science, College of Medicine, Hallym University, Chuncheon 24252, Korea

수의 17

Partial Genomic Sequences of Human Adenovirus C-like Strains Identified in Korean Bat

Yun-Chae Cho¹, Taek Geun Lee¹, Da-Yun Bae¹, Young-Seung Ko¹, Sung-Hyun Moon¹, Zoya Afzal², Jiyeon Park², Chaewon Yoon², Sang Jin Lim³, Won-Keun Kim⁴, Ho-Seong Cho^{1*}, and Yeonsu Oh^{2*}

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수의 18

Genomic and Amino Acid Mutation Analysis of Three H9N2 Low Pathogenic Avian Influenza Viruses Isolated from Poultry in Korea

Jiwon Kim, Jae-Eun Lee, Eun-Bin Lee, and Sungsu Youk*

Department of Microbiology, College of Medicine, Chungbuk National University, Cheongju, Republic of Korea

수의 19

Development of a Humanized MXRA8 Mouse Model for Chikungunya Virus Infection and Vaccine Efficacy Evaluation

EunBee Choi^{1,2}, Seungyeon Kim^{1,2}, SeoYoung Moon^{1,2}, In-Ohk Ouh¹, YooKyung Lee¹, and EunYoung Jang^{1*}

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수의 20

Evaluating the Impact of the Veterinary Prescription System on Antimicrobial Resistance Rates

Seo-Yeon Shin and Dae-sung Yoo*

Department of Veterinary Epidemiology, College of Veterinary Medicine, Chonnam National University, Gwangju, South Korea

신경계 1

PAFA and RT-QuIC as Platforms for Investigating Action Mechanism of Anti-Prion Agents

Yoochan Kang, Miryeong Yoo, Sanghoon Byun, Hyeri Kim, and Chongsuk Ryou*

Department of Pharmacy, College of Pharmacy and Institute of Pharmaceutical Science & Technology, Hanyang University, 55 Hanyangdaehak-ro, Sangnok-gu, Ansan 15588, Gyeonggi-do, Republic of Korea

신경계 2

A 3D Spheroid-Based Model of Prion Infection

Hyun Jung Park*, HyeRi Kim, Sanghoon Byun, and Chongsuk Ryou*

Department of Pharmacy, College of Pharmacy, and Institute of Pharmaceutical Science & Technology, Hanyang University ERICA, 55 Hanyangdaehak-ro, Ansan, Gyeonggi-do, 15588, Republic of Korea

신경계 3

Molecular and Pathological Impact of PAD2 Deficiency in Prion Disease with Integrated Ultrastructural Analysis

Mohd Najib Mostafa^{1,2}, Tae Keun Kim², Byung-Ki Jang², Hee Woo Choi², Myung Joo Choi², Yun Kyu Kim², Hyo Jeong Yu², Akihito Ishigami³, Yong-Sun Kim^{2,4}, and Eun-Kyoung Choi^{1,2*}

¹Department of Biomedical Gerontology, Graduate School of Hallym University, Seoul 07247, Republic of Korea, ²Ilson Institute of Life Science, Hallym University, Seoul 07247, Republic of Korea, ³Molecular Regulation of Aging, Tokyo Metropolitan Institute of Gerontology, Tokyo 173-0015, Japan, ⁴Department of Microbiology, College of Medicine, Hallym University, Chuncheon 24252, Korea

신경계 4

Lentiviral and retroviral virus-like particles as a promising delivery platform for the SARS-CoV-2 nucleocapsid protein

Hae Yun Jung, Hyeop Jin, Chaeun Oh, and Yong Tae Jung*

Department of Microbiology, College of Bio-Convergence, Dankook University, Korea

아보 1

Comparative Vector Competence of *Aedes albopictus* for Three Japanese Encephalitis Virus Genotypes (I, III, and V)

Ji-Young Kwon, Bo-Ram Yun, Ga Eun Kim, and Hee Il Lee*

Division of Vectors and Parasitic Diseases, Korea Disease Control and Prevention Agency, 187, Osongsaengmyeong 2-ro, Osong-eup, Heungdeok-gu, Chengju-si, Chungcheongbuk-do, Republic of Korea

아보 2

무주바이러스의 분자 진화와 인수공통감염 위험성 분석

김성균^{1,2}, 박경민^{1,3}, 김정아⁴, Sara P. Prayitno⁵, 김종우^{1,2}, 이승호⁶, 이재연^{1,2}, Augustine Natasha⁵, 이희일⁷, 김기순^{1,8}, 김원근^{5,9*}, 송진원^{1,2*}

¹고려대학교 의과대학 미생물학교실, ²고려대학교 의과대학 의과학과 BK21 프로그램, ³고려대학교 의과대학 바이러스병연구소, ⁴질병관리본부 감염병진단관리국 신종감염병과, ⁵한림대학교 의과대학 미생물학교실, ⁶국방과학연구소 제5부 제3연구개발원, ⁷질병관리본부 매개체분석과, ⁸고려대학교 의과대학 백신혁신센터, ⁹한림대학교 의과대학 의과학연구소

아보 3

Comparative Evaluation of mRNA-Encoded Antibody Structures Targeting SFTSV Gn

AYeon Kim^{1,2}, Jae-Yong Kim³, Soo-Yeon Lee^{1,2}, Yoo-Jin Bang³, Jung-Woo Lee³, Do-Hyung Kim³, Hye Won Kwak³, Hyeong-Jun Park³, Daeyeun Kim³, and Jae-Hwan Nam^{1,2,3*}

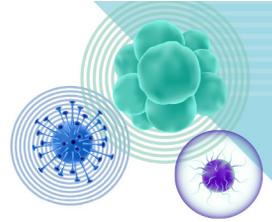
¹Department of Biotechnology, The Catholic University of Korea, Bucheon, 14662, Republic of Korea, ²BK21 plus Department of Biotechnology, The Catholic University of Korea, Bucheon, 14662, Republic of Korea, ³SMLbiopharm, Gwangmyeong, 14353, Republic of Korea

아보 4

Establishment of a Pseudovirus System for SFTSV Research

Jeong-In Kim^{1*}, Kee-Jong Hong^{1,2,3}, Munazza Fatima^{2,3}, Pil-Gu Park⁴, and Timothy An¹

¹Department of Bio-Medical Sciences, GAIST, Gachon University, Incheon, Korea, ²Department of Microbiology, Gachon University College of Medicine, Incheon, Korea, ³Lee Gil Ya Cancer and Diabetes Institute, Gachon University, Incheon, Korea, ⁴Department of Bio-Science, Gachon University College of BioNano Technology, Seongnam, Korea



아보 5

고정밀 나노포어 시퀀싱을 활용한 국내 한탄바이러스의 전장 유전체 감시 및 계통학적 다양성 연구

박경민^{1,2}, 김종우^{1,3}, 노주영¹, 김성규^{1,3}, 조희경^{1,3}, 김기진^{4,5}, 서예린⁶, 임태훈⁷, 이성현⁷, 이재연^{1,3}, 임승인⁸, 주영훈⁹, 이버들¹⁰, 윤석현¹¹, 박창보¹², 송동현¹³, 구세훈¹³, 이승호¹³, 이대상¹³, 김원근^{7,14}, 송진원^{1,2*}

¹고려대학교 의과대학 미생물학교실, ²고려대학교 의과대학 의과학과 BK21 프로그램, ³고려대학교 의과대학 바이러스성감염병 연구소, ⁴캐나다 브리티시컬럼비아주 버나비, 사이먼 프레이저 대학교 보건과학대학 감염병 유전체 및 원헬스 센터, ⁵캐나다 브리티시컬럼비아주 버나비, 사이먼 프레이저 대학교 분자생물학 및 생화학과, ⁶고려대학교 의과대학 예방의학교실, ⁷한림대학교 의과대학 미생물학교실, ⁸대한민국 육군 제5예방의무대, ⁹대한민국 육군 제1예방의무대, ¹⁰대한민국 육군 제3예방의무대, ¹¹대한민국 육군 제2예방의무대, ¹²대한민국 육군본부, ¹³국방과학연구소 제3기술연구본부 제5기술연구부, ¹⁴한림대학교 의과대학 의과학연구소

아보 6

넥스트스트레인을 활용한 한탄바이러스의 시공간 유전체 역학 및 시각화

박경민^{1,2}, 김기진^{3,4}, 김종우^{1,5}, 노주영^{1,5}, 김성규^{1,5}, 조희경^{1,5}, 서예린¹, 김진일^{1,2}, 박만성^{1,2}, 김원근^{6,7}, 송진원^{1,5*}

¹고려대학교 의과대학 미생물학교실, ²고려대학교 의과대학 바이러스병연구소, ³캐나다 브리티시컬럼비아주 버나비, 사이먼 프레이저 대학교 보건과학대학 감염병 유전체 및 원헬스 센터, ⁴캐나다 브리티시컬럼비아주 버나비, 사이먼 프레이저 대학교 분자생물학 및 생화학과, ⁵고려대학교 의과대학 의과학과 BK21 프로그램, ⁶한림대학교 의과대학 미생물학교실, ⁷한림대학교 의과대학 의과학연구소

아보 7

Activation of Toll-like receptor 2 is antiviral against Zika virus in microglia

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아보 8

울릉바이러스 발견 및 유전체 특성 분석

이재연^{1,2}, 박경민^{1,3}, 김종우^{1,2}, 김성규^{1,2}, 송동현⁴, 구세훈⁴, 이승호⁴, 이대상⁴, 김원근^{5,6}, 송진원^{1,2*}

¹고려대학교 의과대학 미생물학교실, ²고려대학교 의과대학 의과학과 BK21 프로그램, ³고려대학교 의과대학 바이러스병연구소, ⁴국방과학연구소 제5부 제3연구개발원, ⁵한림대학교 의과대학 미생물학교실, ⁶한림대학교 의과대학 의과학연구소

아보 9

Molecular identification of severe fever with thrombocytopenia syndrome virus in deer ked: Implications for disease transmission

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엔테로 1

Coxsackievirus B3 mRNA vaccine against CVB3-induced myocarditis in mouse model

Hong-Ki Kim¹, Ji-Hwa Shin¹, Jun-Gi Kim¹, Jae-Hwan Nam³, Ho-Sun Park², and Byung-Kwan Lim^{1*}

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42415, Republic of Korea, ³Department of Medical and Biological Sciences, The Catholic University of Korea, Gyeonggi-do, Bucheon, Republic of Korea

엔테로 2

Cardiac-specific PDK4 deletion attenuates pyroptosis in CVB3-induced myocarditis model

Hong-Gi Kim, Ji-Hwa Shin, Jun-Gi Kim, and Byung-Kwan Lim

Department of Biological Sciences, Jungwon University, Goesan-gun, Chungbuk, 28024, South Korea

허피스 1

Evidence for G-Quadruplex-Mediated Transactivation by the Immediate-Early 2 Transactivator of Human Cytomegalovirus

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²Biomedical Research Institute, Samsung Medical Center, Seoul 06351, Republic of Korea

허피스 2

ZNF451 Promotes HSV-1 Replication Under ICPO-Deficient Conditions

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Microbiology and Immunology, Jeju National University College of Medicine, ³Jeju Research Center for Natural Medicine, Jeju National University Core Research Institute

허피스 3

HSV-1 UL36 stabilizes ICPO Independent of its Deubiquitinase Activity

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Korea, ²Department of Microbiology and Immunology, Jeju National University College of Medicine, Jeju,

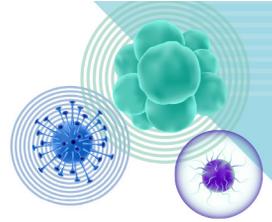
Republic of Korea, ³Jeju Research Center for Natural Medicine, Jeju National University Core Research Institute, Jeju, Republic of Korea

허피스 4

HP1BP3 is a histone-like G-quadruplex-binding protein that promotes Varicella-Zoster virus glycoprotein C expression and cell-free virion production

Woo-Chang Chung, Daegy Park, Eunmi Lee, and Jin-Hyun Ahn

Department of Microbiology, Sungkyunkwan University School of Medicine, Suwon 16419, Republic of Korea



허피스 5

CRISPR-Cas9-Mediated Integration of the Auxin-Inducible Degron System into VZV ORF61 for Controlled Protein Degradation

Seol Hwa Leem^{1,4}, Tae Hyoung Kim^{1,4}, Jeong Rae Yoo³, Kihye Shin^{2,4}, and Eui Tae Kim^{1,2,4}

¹Department of Biomedicine & Drug Development, Jeju National University Graduate School, Jeju, Republic of Korea, ²Department of Microbiology & Immunology, Jeju National University College of Medicine, Jeju, Republic of Korea, ³Department of Internal Medicine, Jeju National University College of Medicine, Jeju, Republic of Korea, ⁴Jeju Research Center for Natural Medicine, Jeju National University Core Research Institute, Jeju, Republic of Korea

허피스 6

A comprehensive analysis of human microglial models to evaluate the pathogenesis of Varicella Zoster Virus

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호흡기 1

First Report and Genomic Characterization of Parahenipavirus Langya virus in *Crocidura lasiura*, Republic of Korea

Augustine Natasha¹, Sarah E. Pye², Kyungmin Park^{3,4}, Shivani Rajoriya¹, Intae Yang¹, Jieun Park¹, Haryo Seno Pangestu¹, Minsung Lee¹, Daehyun Kim¹, Jongwoo Kim^{3,5}, Yeonsu Oh⁶, Carolina B. López², Jin-Won Song^{3,5*}, and Won-Keun Kim^{1,7*}

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호흡기 2

In Vitro and AI-based Antiviral Study of Tabamide A Derivative TA25 Using Lung Organoid Model for Human Rhinovirus

Bohyeon Kim^{1,¶}, Na Young Kwag^{2,¶}, Taehun Lim⁶, Jin Woo Kim³, Wonkyun Ronny Im³, Shivani Rajoriya¹, Jieun Park¹, Augustine Natasha¹, Daewoon Yoon², Divya Misra¹, Bat Ulzii Altanzula¹, Hennisa Hennisa¹, Minyoung Kim¹, Bo Min Kang¹, Young Bin Park⁵, Jeong Tae Lee⁴, Sung Ho Jeon³, Jinkyu Park^{2*}, and Won-Keun Kim^{1,5*}

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호흡기 3

Development of pan-coronavirus novel SARS-CoV-2 antiviral using phenotypic high-throughput screening

BoRa Lee¹, Aram Lee¹, Young Mi Kim¹, Jinyeong Heo², Dawoon Lee³, Hong-gun Lee², Joonseong Lee⁴, Sehan Lee⁴, Huijin Jung⁴, Woo Youn Kim⁴, Jiho Kim², David Shum², Seungtaek Kim³, and Inhee Choi^{1*}

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호흡기 4

Analysis of SARS-CoV-2 spike mutations in immunocompromised patients: canonical and non-canonical immune escape mechanisms

Jineui Kim, Jungmin Lee, Jong Hyeon Seok, Jeonghun Kim, Sohyun Lee, Yerin Hong, Dohee Kim, Minji Kim, Kisoan Kim, and Man-Seong Park*

Department of Microbiology, the Institute for Viral Diseases, and Vaccine Innovation Center, Korea University College of Medicine, Seoul 02841, Republic of Korea

호흡기 5

The DPP4-utilizing MERS-related bat coronavirus B20-180 may potentially exhibit enhanced cell entry through recombination and modification of the furin cleavage site

Van Thi Lo¹, Ngoc Thi Le^{2,3}, Min Chan Kim¹, Seong Sik Jang¹, Sun-Sook Kim⁴, Yong Gun Choi⁵, Chul Seung Lee⁶, Dae Gwin Jeong^{2,3}, and Hye Kwon Kim^{1*}

Van Thi Lo¹, Ngoc Thi Le^{2,3}, Min Chan Kim¹, Seong Sik Jang¹, Sun-Sook Kim⁴, Yong Gun Choi⁵, Chul Seung Lee⁶, Dae Gwin Jeong^{2,3}, and Hye Kwon Kim^{1*}

호흡기 6

국내 영아 폐렴 환자에서 확인된 신종 인간 코로나바이러스

박경민^{1,2+}, 신민수³⁺, Augustine Natasha⁴⁺, 김종우^{1,5}, 노주영¹, 김성규^{1,5}, 김보현⁴, 박지은⁴, 서예린¹, 조희경¹, 변관수⁶, 김지훈⁶, 이영선⁶, 심정옥⁷, 김원근^{4,8}, 송진원^{1,5*}

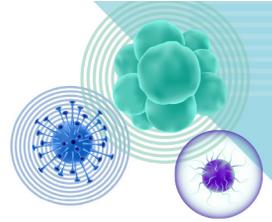
¹고려대학교 의과대학 미생물학교실, ²고려대학교 의과대학 바이러스병연구소, ³고려대학교 안산병원 소아청소년과, ⁴한림대학교 의과대학 미생물학교실, ⁵고려대학교 의과대학 의과학과 BK21 프로그램, ⁶고려대학교 구로병원 간질환센터, ⁷고려대학교 구로병원 소아청소년과, ⁸한림대학교 의과대학 의과학연구소

호흡기 7

Antisense Oligonucleotide Targeting Nipah Virus and Efficacy Evaluation Using a Fluorescent Reporter Cell System

Minwook Shin¹, Sukjoon Yoon², and Sungsu Youk³

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호흡기 8

Distinct Gene Expression Profiles Associated with Respiratory Syncytial Virus (RSV) Infection in Humans

Ha Young Oh^{1,2,3}, Se Sil Noh^{1,2,3}, and Hye Jin Shin^{1,2}

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호흡기 9

Development of a Broad-Spectrum DNA Vaccine Against Influenza A Viruses Using Baculoviral Gene Delivery System

Youngjik Lee, Sehyun Kim, Jungmin Chun, Aleksandra Nowakowska, Doyoung Yoon, Hee-Jung Lee, and Young bong Kim

Department of Biomedical Engineering, Konkuk university, Seoul, 05029, Republic of Korea

호흡기 10

Potential of Avian Paramyxovirus Type 14 as a Viral Vector

Jae-Eun Lee, Jiwon Kim, Eunbin Lee, Young Ki Choi, and Sungsu Youk

Microbiology Laboratory, College of Medicine, Chungbuk National University, Cheongju, South Korea

호흡기 11

Codon Optimization Strategies and Immunogenicity Comparative Study for Optimal mRNA Vaccine Candidate Discovery Against SARS-CoV-2 Omicron KP.2 Variant

Hye-Seon Jung^{1,2}, Hyeong-Jun Park², Hye Won Kwak², Jung Woo Lee², Soo-Yeon Lee¹, Yoo-Jin Bang², Jea-Yong Kim², Do-Hyung Kim², Song-Heun Shin², Hye-sik Chang³, Dae-Geun Kim², and Jae-Hwan Nam^{1,2*}

¹Department of Medical and Biological Science, The Catholic University of Korea, Bucheon, Gyeonggi-Do, Republic of Korea, ²R&D Research Center, SML Biopharm, Gwangmyeong, Gyeonggi-Do, Republic of Korea, ³Laboratory of Quantitative Molecular Biology, Seoul National University, Seoul, Republic of Korea

호흡기 12

Simulating Evolution of Coronavirus Spike Gene with Random Mutation and Similarity-Based Selection

Min Chan Kim, Hye Ji Jung, Seong Sik Jang, Van Thi Lo, and Hye Kwon Kim*

Department of Biological Sciences and Biotechnology, College of Natural Science, Chungbuk National University, Cheongju, Republic of Korea

호흡기 13

Isolation of a SARS-CoV-2 strain from pediatric patients in South Korea: Biologic and genetic characterization

Hee Chun Chung¹, Sung Jae Kim², Su Jin Hwang¹, Sung Hoon Park¹, Hyeon Woo Chung¹, Si Hwan Ko¹, Van Giap Nguyen³, and Jae Myun Lee^{1*}

¹Department of Microbiology and Immunology, Institute for Immunology and Immunological Diseases, Brain Korea 21 Project for Medical Science, Yonsei University College of Medicine, Seoul 03722, Korea, ²Department of Companion Animal Health, Kyungbuk University, Namyangju 12051, Korea, ³Department of Veterinary Microbiology-Infectious Diseases, Faculty of Veterinary Medicine, Vietnam National University of Agriculture, Hanoi, Vietnam

호흡기 14

Regulation of ISG15 secretion by the SARS-CoV-2 proteins through the LC3-derived secretory pathway

Kanghun Seo, Youngju Choi, Wonjin Bang, and Jin-Hyun Ahn

Department of Microbiology, Sungkyunkwan University School of Medicine, Suwon 16419, Republic of Korea

호흡기 15

Unmodified UTP mRNA Vaccine Provides Rapid and Superior Protection Against Canine H3N2 Influenza

Eun-Jin Choi^{1,2}, Jae seok Choi³, Jae-Yong Kim⁴, Hye Won Kwak⁴, Soo-Yeon Lee^{1,2}, Yoo-Jin Bang⁴, Do-Hyung Kim⁴, Hyeong-Jun Park⁴, Ayoung Oh¹, Dahyeon Ha^{1,2}, Subin Yoon^{1,2}, Sohee Jo^{1,2}, Jisun Lee¹, Daegeun Kim⁴, Woonsung Na⁵, and Jae-Hwan Nam^{1,2,4*}

¹Department of Medical and Biological Sciences, The Catholic University of Korea, ²BK21 Four Department of Biotechnology, The Catholic University of Korea, ³Interdisciplinary Graduate Program in Genetic Engineering, Seoul National University, ⁴SML biopharm, ⁵Department of Oral microbiology and Immunology, School of Dentistry, Seoul National University

호흡기 16

Diverse bat organoids provide pathophysiological models for zoonotic viruses

Seo-Young Heo^{1,2}, Yong-ki Lee¹, Kanghee Kim³, Boyeong Jeong¹, and Young Ki Choi^{1,2,3*}

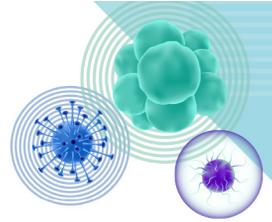
¹Center for Study of Emerging and Re-emerging Viruses, Korea Virus Research Institute, Institute for Basic Science (IBS), Daejeon 34126, Republic of Korea, ²Department of Metabiohealth, Sungkyun Convergence Institute, Sungkyunkwan University (SKKU), Suwon, Republic of Korea, ³College of Medicine and Medical Research Institute, Chungbuk National University, Cheongju, Republic of Korea

호흡기 17

Persistent Immune Imbalance in Post-Acute Sequelae of SARS-CoV-2: Neutrophil-Driven Pathology and Therapeutic Strategies from a *P. roborovskii* Hamster Model

Suhee Hwang^{1,2}, Dongbin Park¹, Yuri Jung¹, and Young Ki Choi^{1*}

¹Center for Study of Emerging and Re-emerging Viruses, Korea Research Institute, Institute for Basic Science (IBS), Daejeon, Republic of Korea, ²Department of Metabiohealth, Sungkyun Convergence Institute, Sungkyunkwan University (SKKU), Suwon, Republic of Korea



호흡기 18

Liquid-liquid phase separation mediated immune evasion of respiratory syncytial virus against oligoadenylate synthetase-RNase L pathway

Woo Yeon Hwang^{1,2}, Soohwan Oh^{2*}, and Young-Chan Kwon^{1,3*}

¹Center for Infectious Diseases Vaccine and Diagnosis Innovation (CEVI), Korea Research Institute of Chemical Technology (KRICT), Daejeon 34114, Republic of Korea, ²College of Pharmacy, Korea University, Sejong 300019, Republic of Korea, ³Medical Chemistry and Pharmacology, University of Science and Technology (UST), Daejeon, 34114, Republic of Korea

호흡기 19

Dose-Dependent Modulation of mRNA Vaccine Expression and Immune Response by dsRNA Contamination

Sohee Jo^{1,2}, Jisun Lee¹, Subin Youn^{1,2}, Seonghyun Lee^{1,2}, Seongje Cho¹, Youngran Cho^{1,2}, Ayoung Oh^{1,2}, Dahyeon Ha^{1,2}, Huijeong Choi^{1,2}, Jungmin Kim^{1,2}, Gahyun Roh¹, Sowon Lee¹, Hyo-Jung Park^{1,2}, and Jae-Hwan Nam^{1,2}

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호흡기 20

Cholesterol Sulfate Restricts SARS-CoV-2 Infection by Modulating Intracellular Cholesterol Trafficking and Autolysosome Formation

Su Jin Hwang¹, Sung-Jin Kim³, Seok Jun Moon^{2*}, and Jae Myun Lee^{1*}

¹Department of Microbiology and Immunology, Yonsei University College of Medicine, ²Department of Oral biology, Yonsei University College of Dentistry, ³Oral Histology and Developmental Biology, Seoul National University School of Dentistry

호흡기 21

Development of a Broad-Lineage, REASSURED- Compliant Rapid Diagnostic Test for Lassa Virus Using Optimized Monoclonal Antibody Pairs

Hwachul Shin¹, Myung-Min Choi², Minji Lee¹, Jinwon Kim¹, Hwajung Yi¹, and Yoon-Seok Chung^{1*}

¹Division of High-Risk Pathogens, Department of Laboratory Diagnosis and analysis, Korea Disease Control and Prevention Agency, Cheongju, Korea, ²Division of Laboratory Diagnosis and Analysis, Gyeongnam Regional Center for Disease Control and Prevention, Busan, Republic of Korea

호흡기 22

Genomic Surveillance of Monkeypox Virus Reveals the Evolutionary Framework and Transmission Dynamics in South Korea

Chi-Hwan Choi, Minji Lee, Sang Eun Lee, Gyuri Sim, Hwachul Shin, Jin-Won Kim, Hwajung Yi, and Yoon-Seok Chung*

Division of High-risk Pathogens, Bureau of Infectious Disease Diagnosis Control, Korea Disease Control and Prevention Agency, Cheongju, Republic of Korea

호흡기 23

Prolonged MPXV shedding and emergence of Tecovirimat resistance in an immunocompromised person living with HIV: Evidence from genomic surveillance in South Korea.

Minji Lee, Chi-Hwan Choi, Sang Eun Lee, Jin-Won Kim, Gyuri Sim, Hwachul Shin, Jeong hyun Lee, Hwajung Yi, and Yoon-Seok Chung*

Division of High-risk Pathogens, Department of Laboratory Diagnosis and analysis, Korea Disease Control and Prevention Agency, Cheongju, South Korea

기타 1

Kinetically activating nanovaccine mimicking multidimensional immunomodulation of natural infection for broad protection against heterologous viruses in animal models

Sang Nam Lee^{2,5}, Jaemoo Kim^{1,5}, Young-Il Kim^{1,5}, D.K. Haluwana^{4,5}, Ryouhno Eun^{2,5}, Wooyoung Kim¹, Suhyeon Oh^{1,3}, Jong-Soo Lee^{4*}, Young Ki Choi^{1*}, and Yong Taik Lim^{2*}

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기타 2

Organ-Specific Delivery of Ionizable Lipid Nanoparticles to the Spleen Enhances mRNA Expression and Immunity

Jungmin Kim^{1,2}, Seo-Hyeon Bae^{1,2}, Huijeong Choi^{1,2}, Yeeun Lee^{1,2}, Sohee Jo^{1,2}, Seonghyun Lee^{1,2}, Subin Yoon^{1,2}, Dahyeon Ha^{1,2}, Ayoung Oh^{1,2}, Youngran Cho^{1,2}, Seongje Cho¹, Sowon Lee¹, Sanghyuk Jeon^{1,2}, Hyo-Jung Park^{1,2}, Jisun Lee¹, Hyewon Youn^{3,4}, and Jae-Hwan Nam^{1,2*}

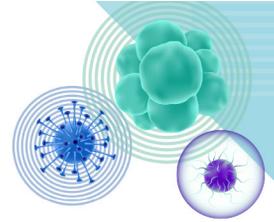
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기타 3

Unmodified UTP is not always best friend for mRNA Cancer Vaccines: Prove from IL-12 mRNA in mEER tumor mice model

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기타 4

Development of Neutralization-Based Serological Standards Using Gardasil 9 Clinical Samples in Korea

Heewon Bang, Aleksandra Nowakowska, Jungmin Chun, Youngjik Lee, Hee-Jung Lee, and Young Bong Kim*

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기타 5

Eighteen-Month Persistence of Neutralizing Antibodies Following Mpxv Infection in South Korea: A Longitudinal Analysis

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기타 6

TLR7/8 Agonist-Integrated Lipid Nanoparticles Enhance Immune Responses of N1-Methyl-Ψ-Modified mRNA Vaccines for Preventive and Therapeutic Applications

Huijeong Choi^{1,2}, Seonghyun Lee^{1,2}, Hyejin Kim^{3,4,5}, Seo-Hyeon Bae^{1,2}, Sohee Jo^{1,2}, Jungmin Kim^{1,2}, Yeeun Lee^{1,2}, Dahyeon Ha^{1,2}, Ayoung Oh^{1,2}, Subin Yoon^{1,2}, Sanghyuk Jeon^{1,2}, Yu-Sun Lee^{1,2}, Youngran Cho^{1,2}, Seongje Cho¹, Gahyun Roh¹, Sowon Lee^{1,2}, Jayaraj Gowda^{3,4}, Hyo-Jung Park^{1,2}, Jisun Lee¹, Daesub Song⁶, Soo Bong Han^{3,4*}, and Jae-Hwan Nam^{1,2,7*}

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기타 7

Development of HPV mRNA Vaccine and Evaluation Indicators

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기타 8

Baculovirus-Delivered DNA Vaccine Platform for Broad Protection Against Novel JEV Genotypes

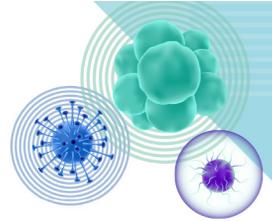
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연구회연합 정기학술대회
The Korean Society of Virology

Abstracts of Poster

MEMO



간염 1

N6-methyladenosine modification of hepatitis B virus RNAs differentially regulates viral life cycle depending on its position.

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N6-methyladenosine (m6A) RNA methylation most prevalently occurs in cellular and viral RNAs. Here, we investigated the m6A functions in the hepatitis B virus (HBV) life cycle. We identified a single m6A consensus motif at nucleotide position 1907. All HBV transcripts bear this motif at the 3' end epsilon structure, but pregenome RNA (pgRNA) carries this motif twice, at 5' and 3' epsilon structures, owing to the terminal redundancy of sequences at its 5' and 3' end. Interestingly, m6A methylations differentially regulated the HBV life cycle dependent on its position. 3' m6A modification reduced viral RNA stability, affecting corresponding viral protein expression, but 5' m6A modification is essential for pgRNA encapsidation to synthesize viral DNA. Besides, we found that HBV X (HBx) protein recruits host methyltransferases to nuclear HBV DNA to induce co-transcriptional m6A methylation. This study highlights the pivotal role of m6A methylation in the HBV life cycle.

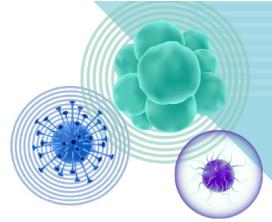
간염 2

Dual function of Nucleus Accumbens-Associated Protein 2 as a Novel Host Factor in the Hepatitis B Virus Replication

Wonhee Kim¹ and Kyun Hwan Kim^{1,2,*}

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Hepatitis B virus (HBV) establishes chronic infections by finely tuning viral transcription and maintain the stability of its RNA in hepatocytes. These processes are critically influenced by host factor, yet the molecular mechanism remain incompletely understood. Here we identify nucleus accumbens-associated protein 2 (NACC2), a protein with BTB and BEN domains, as a host factor that modulated HBV replication and is downregulated by cytokine stimulation, as demonstrated in our study. NACC2 recruits the nucleosome remodeling and deacetylase (NURD) complex to transcriptionally repress MDM2, leading to enhanced stability of the antiviral protein P53. Functional studies reveal that NACC2 knockdown inhibits HBV replication through post-transcriptional regulation of viral RNA, whereas overexpression reduces HBV replication through P53 stabilization. Our findings reveal that NACC2 exerts opposing effect on HBV: promoting replication by post-transcriptionally regulating viral RNA while suppressing replication through p53 stabilization. Given that NACC2 expression is diminished by cytokine signaling, it may act as a crucial link between immune responses and viral persistence. These results highlight NACC2 as a promising target for therapeutic intervention and underscore the importance of host factors that bridge viral replication with host immune regulation. Future studies will further delineate the mechanism underlying NACC2-mediated post-transcriptional control of HBV RNA and its potential role in chronic infection management.



간염 3

Bardoxolone-Methyl (BARD) Suppresses Hepatitis B Virus Replication and Hepatocellular Carcinoma Development by Inhibiting Signal Transducer and Activator of Transcription 3 (STAT3) Signaling

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Hepatitis B virus (HBV) is an enveloped DNA virus that belongs to the Hepadnaviridae family. The genome of the HBV consists of a 3.2 kb partially double-stranded DNA molecule. HBV infection contributes to the development of hepatocellular carcinoma (HCC). Current frontline therapeutics for chronic HBV, such as nucleos(t)ide analogues (Entecavir and Tenofovir), aim to inhibit viral replication and mitigate pathogenesis progression. Additionally, immunomodulatory agents, including pegylated interferon (PEG-IFN) α -2a and PEG-IFN α -2b, bolster the host's immune response against HBV infection. However, these therapeutic agents exhibit limitations in treating HBV-mediated HCC patients due to prevalent impaired liver function or liver disorders. In this study, we conducted a comprehensive analysis of 594 FDA-approved drugs for their capacity to inhibit HCC progression using human liver-derived HCC organoids and identified 39 compounds as promising drug candidates. Among these, Bardoxolone-methyl (BARD) dramatically decreased HBV replication by regulating STAT3 signaling pathways. Therefore, our results suggest that BARD is a potential drug for targeting both HBV and HCC and provides the roles of STAT3 signaling pathways in the mechanisms of HBV-mediated HCC development.

The Antiviral Effect of Heat Shock Transcription Factor, X-linked 1 on the Viral Replication of Hepatitis B Virus

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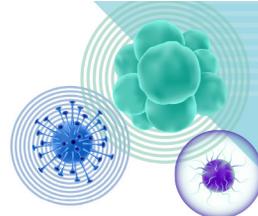
About 250 million people are chronically infected with hepatitis B virus (HBV), and approximately 1.2 million new infections occur annually. Despite the availability of preventive vaccines and antiviral nucleos(t)ide analogs, the persistence of covalently closed circular DNA (cccDNA) as a viral minichromosome in infected hepatocytes makes complete eradication of HBV challenging.

Heat shock transcription factors (HSFs) are activated by various stressors such as heat, chemicals, tumors, and pathogens. They bind to heat shock elements (HSEs) to regulate transcription. While HSF1 has been well studied and linked to HBV replication and HBV-related hepatocellular carcinoma, the functions of other HSF family members remain unclear.

In this study, we identified heat shock transcription factor, X-linked 1 (HSFX1), encoded on the X chromosome, as a novel regulator of HBV replication. Upregulating HSFX1 expression significantly decreased HBV DNA levels and the secretion of viral proteins (HBeAg and HBsAg) in a dose-dependent manner, as determined by Southern blotting and ELISA. As confirmed by Northern blotting, HSFX1 suppressed HBV RNA levels without affecting cccDNA levels (Hirt DNA extraction).

Mechanistically, HSFX1 repressed HBV transcription by inhibiting enhancer and promoter activity, as demonstrated by luciferase assays. However, HSFX1 did not affect the HBV RNA stability. Moreover, HSFX1 downregulated transcription of HBV through modulation of hepatocyte nuclear factors (HNFs). However, the mechanism by which HSFX1 knockdown influences HBV transcription remains unclear.

In conclusion, our findings suggest that HSFX1 negatively regulates HBV transcription in hepatocytes. These results provide new insight into the potential of HSFX1 as a therapeutic target for hepatitis B. Further research is needed to fully elucidate the molecular mechanisms of HSFX1 in viral infection under cellular stress conditions.



4'-Thiouridine Simultaneously Inhibits RdRp and NiRAN Activities of SARS-CoV-2 Nsp12

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To date, three direct-acting antivirals (DAAs) have been globally approved for the treatment of SARS-CoV-2 infection: nirmatrelvir (Paxlovid™; Pfizer), an Mpro protease inhibitor, and two nucleoside analog inhibitors of Nsp12 RdRp, molnupiravir (Lagevrio™; MSD) and remdesivir (Veklury®; Gilead Sciences). The RdRp inhibitors interfere with viral RNA synthesis by acting as ribonucleoside analogs. Molnupiravir induces G-to-A mutations that ultimately lead to lethal mutagenesis. Remdesivir, an adenosine analog, is incorporated into viral RNA but induces delayed chain termination. Both nucleoside analogs inhibit the RdRp function of Nsp12. AT-527 (bemnifosbuvir), developed by Atea Pharmaceuticals, induces not only termination of RNA elongation but also inhibition of Nsp9-NMPylation and -RNAylation by binding to the NiRAN domain of Nsp12. In this study, we identify nucleoside analogs that inhibit the functions of RdRp and NiRAN. Through screening of a nucleos(t)ide-focused chemical library, we identified 4'-thiouridine (1) as a potent antiviral agent against SARS-CoV-2 in Vero cells, with an EC₅₀ value of 1.71 μM and a CC₅₀ value exceeding 100 μM. Its triphosphate metabolite, compound 8, inhibited the RNA-dependent RNA polymerase activity of the SARS-CoV-2 Nsp12-Nsp7-Nsp8(2) complex, terminating nascent RNA synthesis through misincorporation. Additionally, compound 8 suppressed the function of the NiRAN domain of Nsp12, effectively blocking both RNAylation and NMPylation of Nsp9. Pharmacokinetic analysis in mice showed excellent oral bioavailability of compound 1. Oral administration at 100 mg/kg/day, twice daily for 5 days, protected mice from lethal SARS-CoV-2 infection, resulting in 40% survival and near-complete recovery of body weight by day 14 postinfection. Compound 1 also exhibited broad-spectrum activity against various coronaviruses and other RNA viruses. These findings highlight that compound 1 is a promising orally available antiviral candidate.

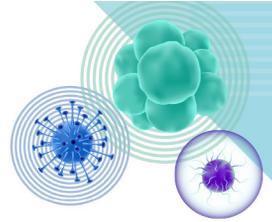
간염 6

UNI418 Inhibits SARS-CoV-2 Entry via Disruption of Spike Protein Processing and Viral Endocytosis

Myoung Kyu Lee^{1,#}, Yejin Jang^{1,#}, Yuri Seo^{3,4,#}, Seon-gyeong Lee^{4,5,#}, Yeon Seo Jeon^{1,2}, Hyun Su Ra^{1,2}, Jiwon Jeong^{1,2}, Meeheyin Kim^{1,2*}, Joo-Yong Lee^{3*}, and Kyungjae Myung^{4,5*}

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Since coronavirus entry into host cells is important for viral infectivity and pathogenesis, this step is critically considered as a target for therapeutic intervention. SARS-CoV-2 has multiple entry pathways. Direct membrane fusion pathway occurs at the cell surface and involves direct fusion with the plasma membrane. The virus first binds to the ACE2 receptor on the host cell surface through its spike protein. Subsequently, the TMPRSS2 cleaves the spike protein, exposing the fusion peptide. Endocytosis-mediated pathway involves internalization of the virus through clathrin-mediated endocytosis. After ACE2 binding, the virus-receptor complex is internalized into endosomal vesicles. The spike protein can be processed by cathepsin L enzyme in the acidic endosomal environment to produce the fusion-capable S2 subunit, without requiring TMPRSS2. PIKfyve has been identified as a promising drug target to treat SARS-CoV-2 infections (apilimod, YM201636 and SGC-PIKFYVE1). In addition, PIP5Ks produce ptdlns(4,5)P2 on clathrin-coated vesicles, which are required for SARS-CoV-2 entry. However, the effects of inhibiting PIP5K on SARS-CoV-2 endocytic processes and cellular entry have been elusive. In this study, we identified UNI418, a dual PIKfyve and PIP5K1C inhibitor, as a new chemical agent that inhibits SARS-CoV-2 entry into host cells. UNI418 inhibited the proteolytic activation of cathepsins, which is regulated by PIKfyve, resulting in the inhibition of cathepsin L-dependent proteolytic cleavage of the SARS-CoV-2 spike protein into its mature form, a critical step for viral endosomal escape. We also demonstrated that UNI418 prevented ACE2-mediated endocytosis of the virus via PIP5K1C inhibition. Our results identified PIKfyve and PIP5K1C as potential antiviral targets and UNI418 as a putative therapeutic compound against SARS-CoV-2.



간염 7

Hepatitis B virus (HBV)-Induced HOXD Antisense Growth-Associated Long Non-Coding RNA (HAGLR) Promotes the Viral Replication and Hepatocellular Carcinoma (HCC) Progression via Acting as Competitive Endogenous RNA (ceRNA)

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Hepatitis B virus (HBV) is an enveloped DNA virus that belongs to the Hepadnaviridae family. Approximately 254 million people are chronically infected with HBV worldwide, and around 1.2 million people become newly infected each year. It infects hepatocytes and induces chronic inflammation, thereby serving as a major risk factor for cirrhosis and hepatocellular carcinoma (HCC). HBV-mediated HCC contributes significantly to global liver cancer mortality, with an estimated 1.2 million deaths annually, highlighting the necessity of further investigation into HBV-HCC pathogenesis and treatment. Long noncoding RNAs (LncRNAs) have gained widespread attention in recent years due to their functions in cancer, inflammation, and other diseases. Notably, a growing number of lncRNAs have been found to play roles in HBV development and HCC progression. In this study, we identified the HOXD antisense growth-associated long non-coding RNA (HAGLR) as a key regulator of HBV replication and HCC development. HAGLR, previously reported to be highly expressed in HCC, functions as a competing endogenous RNA (ceRNA) by sponging various microRNAs. Our findings reveal that HBV infection upregulated HAGLR expression, which subsequently sponges miR-30a-5p, miR-130a-3p, miR-29a-3p, miR-148a-3p, and miR-191-5p, resulting in enhanced HBV replication and accelerated HCC progression. These results suggest that HAGLR, as a dual regulator of HBV replication and HCC progression, may serve as a therapeutic target for patients with HBV-mediated HCC.

간염 8

Javanicin inhibits secretion of hepatitis B virus particles by targeting the core protein

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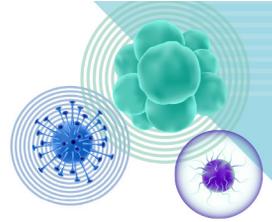
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Hepatitis B virus (HBV) is the primary cause of liver disease. Nucleot(s)ide analogues such as Entecavir are commonly used to treat HBV infection; however, although these drugs attenuate the virus, they are not a cure. Therefore, it is important to find a novel anti-HBV compounds that enable complete remission of chronic hepatitis B (CHB) infection.

We screened 190 natural product libraries using the HepG2.2.15 cell line. Additionally, anti-HBV activities were assessed across genotypes C and D. The mechanism underlying the inhibition of HBV replication by the identified compound was elucidated through cell-based assays.

We identified a hit compound called Javanicin, which is derived from the endophytic fungus JS169. The IC₅₀ of Javanicin is < 500 nM, and the selectivity index (SI = CC₅₀/ IC₅₀) is > 10. Javanicin induced proteasome-mediated degradation of the HBV core protein, and reduced the amount of HBV capsid protein. Javanicin and Entecavir acted synergistically, and were more effective than either drug alone. Additionally, structural analysis showed that Javanicin carries several modifiable moieties, which may lead to development of derivatives.

Javanicin is a novel class of HBV capsid assembly inhibitors, functioning by inducing proteasome-mediated degradation. Furthermore, when paired with Entecavir, Javanicin holds potential as a curative treatment for CHB.



Human Norovirus-Induced Inflammasome Activation: Unveiling the Role of NLRP6 in Intestinal Immunity

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Human norovirus (HNoV) is a major cause of viral gastroenteritis globally, yet the mechanisms by which it interacts with host innate immunity remain poorly understood. The development of human intestinal enteroid (HIE) models has enabled direct investigation of HNoV replication and immune responses in physiologically relevant epithelial tissues. We examined the role of the HNoV NS7 protein, an RNA-dependent RNA polymerase (RdRp), in modulating inflammasome responses. Using *in vitro* reconstitution assays and *ex vivo* HIE models, we assessed the activation of canonical inflammasomes, focusing on NLRP3 and NLRP6. NLRP6-deficient HIEs were generated to determine its role in viral restriction. The NS7 protein directly interacted with both NLRP3 and NLRP6, promoting inflammasome assembly, caspase-1 cleavage, and secretion of IL-1 β and IL-18. In HIEs, HNoV infection triggered canonical inflammasome activation, marked by ASC speck formation, gasdermin D processing, and increased IL-18 production. Strikingly, NLRP6 knockout abrogated inflammasome responses and resulted in enhanced HNoV replication, suggesting that NLRP6 plays a key role in antiviral defense in the intestinal epithelium. Our findings identify the HNoV NS7 protein as a novel activator of canonical inflammasome pathways and establish NLRP6 as a critical regulator of innate immune responses in intestinal epithelial cells. This study provides new insight into how HNoV exploits or is restricted by inflammasome signaling and suggests that modulation of inflammasome activity may offer therapeutic potential in controlling norovirus infection.

Development of a Recombinant Baculovirus-Based Norovirus Vaccine and Evaluation of Systemic and Mucosal Immunogenicity in Mice

Doyoung Yoon, Youngjik Lee, Young Bong Kim, Hee-Jung Lee*

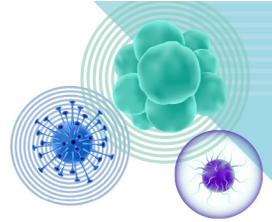
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Human norovirus (HuNoV) is a leading cause of acute viral gastroenteritis worldwide, posing significant health risks, especially for infants and the elderly. Although vaccine development has progressed, no HuNoV vaccine has been approved to date. In this study, we developed a recombinant baculovirus-based vaccine, AcHERV-HuNoVs, utilizing the AcHERV platform to deliver the VP1 capsid protein of HuNoV. The GII.4 and GII.17 genotypes, currently predominant in the Korean population, were selected as vaccine targets.

To assess immunogenicity, BALB/c mice were immunized with AcHERV-HuNoVs or virus-like particle (VLP)-based control vaccines. VLPs were produced and purified from insect cells for use as either controls or antigens in immunological assays.

AcHERV-HuNoVs vaccination induced robust systemic humoral responses, as shown by high serum IgG titers. It also elicited mucosal humoral immunity, reflected in increased IgA levels in serum and fecal samples. Furthermore, vaccinated mice demonstrated strong systemic cellular immunity, including antigen-specific IFN- γ production and elevated cytokine secretion in splenocytes. Notably, enhanced mucosal cellular immune responses were observed, with increased cytokine production and upregulation of mucosa-associated gene expression in mesenteric lymph nodes.

Collectively, these findings indicate that AcHERV-HuNoVs can induce broad systemic and mucosal immune responses without the need for external adjuvants, supporting its potential as a safe and effective HuNoV vaccine platform.



수의 1

Development of a Portable Point-of-Care Assay for the Detection of Marine Mammal DNA Viruses, *Herpesviridae*, *Poxviridae*, and *Anelloviridae*

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DNA viruses pose significant threats to marine mammals and are responsible for infectious disease-related mass mortality events (ID-MMEs). Continuous monitoring and timely detection is critical to mitigate outbreak response in marine mammals. However, the absence of field-deployable testing can delay outbreak management. In this study, a sensitive SYBR green-based real-time PCR (qPCR) for the point-of-care (POC) detection of DNA viruses was developed on a portable Biomeme Franklin thermocycler. A ten-fold dilution series of plasmid DNA representing virus genes were used as template to produce standard curves to quantify the sensitivity of the assay. Furthermore, the primers were designed in the present study to amplify the targeted fragment of viruses from the *Herpesviridae*, *Anelloviridae* and *Poxviridae* families. To assess the assay on clinically relevant samples, we spiked pooled whale liver DNA with dilutions of virus standard templates. The performance of Franklin thermocycler was compared to a laboratory based qPCR platform, QuantStudio 3. The Franklin method demonstrated its sensitivity and specificity for detection of DNA viruses. The LOD of the Franklin assay was 10^4 copies/ μ L of the template, allowing detection of target virus genes in 90 minutes. The simple operation and smartphone connectivity of the Franklin thermocycler makes it a suitable POC diagnostic tool. Overall, this study highlights the potential of this low- cost, rapid, and field-adaptable molecular diagnostic tool for on-site surveillance and management of DNA virus outbreaks in marine mammals.

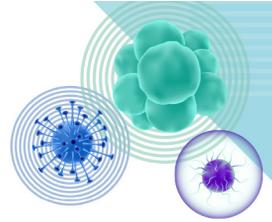
수의 2

Field-deployable Molecular Assay of Marine Mammal RNA Viruses, *Orthomyxoviridae*, *Paramyxoviridae*, *Picornaviridae*, *Caliciviridae*, *Rhabdoviridae* and *Reoviridae*, Using a Franklin Thermocycler

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RNA viruses have been identified as the primary cause for Infectious disease-related mass mortality events (ID-MMEs) in marine mammals. In this study, we have validated the development and utility of point-of-care diagnostics for marine mammal viruses using handheld device, Franklin thermocycler for field diagnostics of marine mammal viruses. Franklin thermocycler enable offline analysis on a smartphone, displaying the results, and can be used in small spaces when fully charged, fulfilling all of its potential and advantages as a point-of-care testing (POCT) device. To address challenges in assessing the target marine mammalian virus positive clinical samples, we used synthetic biology approach for assessment of virus templates inserted in plasmids. This allowed us to establish a system for synthesizing and storing virus templates, which can serve as positive controls. The target marine mammal infecting RNA viruses included influenza A virus (IAV) H13N2 and H4N6, Phocine distemper virus (PDV), Otarine picobirnavirus (OTBV), Phopivirus (Phopi), Harbour porpoise rhabdovirus (HPRV), Steller sea lion reovirus (SSRV), and Walrus calicivirus (WCV). Compared to lab-scale equipment, Franklin was able to sensitively and specifically detect the intended virus. This developed POCT enables rapid and accurate diagnosis of marine mammal viruses in resource-limited environments, facilitating timely intervention to mitigate the spread of infection to marine ecosystems and other species, including humans. Despite these advances, several challenges remain, including the optimization of RNA extraction for point-of-care diagnostics and obtaining clinical samples. In conclusion, this study highlights the potential value of point-of-care diagnostic tests in response to viral diseases in marine mammals.



수의 3

Knowledge and Attitudes Toward Lumpy Skin Disease Virus in the Post-Outbreak Period: Evidence from Korean Cattle Farms, 2025

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Lumpy skin disease (LSD), resulting from infection with Lumpy skin disease virus, is a very infectious disease and primarily infects buffalo and cattle. Weight loss, skin nodules, fever, and reduced milk yields are consequences of LSD. Sporadic incidents continued to be reported during 2024, even though lumpy skin disease, after first appearing in South Korea in October 2023 and then progressing throughout the nation, raised a question regarding potential endemicity and shed light upon an imminent necessity to sustain measures to contain and regulate the disease.

Identifying which strands of knowledge and which attitudes drive farmers to change their on farm biosecurity behavior regarding LSD is the primary focus of this study. Despite early governmental recognition of LSD as a transboundary threat and the implementation of preventive measures, the virus's incursion and local spread highlight a critical disconnect between policy design and field-level uptake, underscoring the urgent need to investigate farmers' knowledge and attitudes that may compromise the effectiveness of national disease control strategies. To generate empirical data, the first national cross-sectional survey from South Korea will survey cattle farm operators regarding their knowledge of LSD epidemiology and their perceptions concerning key biosecurity interventions, including vaccination, disinfection, and measures to control vectors, as well as their perceived risk and potential impact of disease outbreaks, and their level of trust in government livestock disease control policies and attitudes toward their implementation. To ensure representativeness and reliability of the survey data for informing effective policy-making and educational program development, this study employed region-based stratified sampling based on cattle farming indicators—such as the number of farms, herd size, and density—at the municipal (si/gun/gu) level across the country.

This work was supported by Korea Institute of Planning and Evaluation for Technology in Food, Agriculture and Forestry (IPET) through High-Risk Animal Infectious Disease Control Technology Development Project, funded by Ministry of Agriculture, Food and Rural Affairs (MAFRA) (RS-2024-00399814).

First Detection and Genome Characterization of Ungulate Tetraparvovirus 1 in an Asian Water Buffalo (*Bubalus bubalis*) in Vietnam

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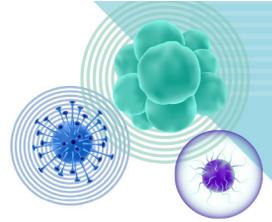
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Parvoviruses (family *Parvoviridae*) are small, non-enveloped, single-stranded DNA viruses that infect a wide range of vertebrate hosts. Within the subfamily *Parvovirinae*, the genus *Tetraparvovirus* comprises viruses primarily associated with ungulates. *Ungulate tetraparvovirus 1* (formerly known as bovine hokovirus) has been sporadically detected in cattle across several countries, but its presence in Southeast Asia has remained largely uninvestigated.

In this study, a nearly complete genome (4,981 nucleotides) of *Ungulate tetraparvovirus 1* was recovered from a skin swab of a domestic water buffalo (*Bubalus bubalis*) in Vietnam and designated NIVR-B12-2024. Sequence analysis revealed 93.33% nucleotide identity with the *Bovine hokovirus* HK1 strain reported in Hong Kong. Phylogenetic analysis based on the NS1 and VP1 regions confirmed its placement within genotype I of *Ungulate tetraparvovirus 1*. Comparative genetic analysis further supports the division of this virus into at least two genotypes (I and II), consistent with previous findings.

This report provides the first molecular evidence of *Ungulate tetraparvovirus 1* in Vietnamese livestock. The successful detection using a non-invasive skin swab sample underscores the utility of field-adaptable sampling methods for parvoviral surveillance. While the pathogenic potential of this virus remains unclear, its identification in water buffalo expands the known host and geographic range of the virus. These findings emphasize the need for broader molecular surveillance across Southeast Asia to better understand the ecology, evolution, and potential health impact of *Ungulate tetraparvovirus 1* in domestic animal population.

This work was supported by Korea Institute of Planning and Evaluation for Technology in Food, Agriculture and Forestry (IPET) through High-Risk Animal Infectious Disease Control Technology Development Project, funded by Ministry of Agriculture, Food and Rural Affairs (MAFRA) (RS-2024-00400152).



수의 5

Genomic Characterization of Rotavirus A from Korean Bats Reveals Evidence of Interspecies Transmission

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Bats are natural reservoirs for a broad range of viruses, including those with zoonotic potential. Rotavirus A (RVA), a leading cause of diarrhea in humans and animals, accounted for 35.2% of diarrhea-related deaths in children under five years of age globally in 2021 – the highest among all single pathogens. While various RVA genotypes and interspecies transmission events have been reported in bats worldwide, the genomic features of bat-associated RVA strains in Korea remain poorly characterized.

In this study, metagenomic next-generation sequencing was performed on intestinal tissue samples collected in 2024 from three insectivorous bat species (*Rhinolophus ferrumequinum*, *Hypsugo alaschanicus*, and *Miniopterus fuliginosus*) in Gangwon Province, South Korea. Viral contigs were identified using Kaiju and confirmed by BLASTx against the NCBI RefSeq database. Phylogenetic analyses of the VP7 and VP4 gene segments were conducted using MAFFT and IQ-TREE under the GTR+G+I model.

A near-complete RVA genome, comprising nine of eleven segments (assembled into twelve contigs), was recovered from a single *R. ferrumequinum* specimen. The VP7 gene (856 bp) exhibited 98.0% nucleotide identity with a rabbit-derived RVA strain (GeneBank: MK751437.1) and was assigned to genotype G3. The VP4 gene (1,592 bp) showed 80.3% identity with a Chinese bat strain (LZHP2/2015 P[3]) and clustered most closely with the P[10] genotype, despite notable sequence divergence.

Phylogenetic analysis revealed that both segments were more closely related to RVA strains from non-bat hosts, suggesting possible interspecies transmission or reassortment. These findings provide the first genomic insight into RVA in Korean bats and highlight their potential role in the evolution and dissemination of RVA. Continued surveillance, combined with studies on viral isolation, pathogenicity, and host range, is needed to assess the public health relevance of bat-derived RVA.

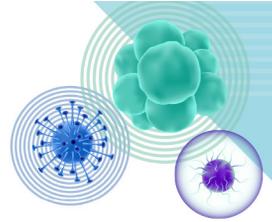
This research was supported by 'The Government-wide R&D to Advance Infectious Disease Prevention and Control', Republic of Korea (grant number: RS-2023-KH140418).

Comparison of Diagnostic Performance Between Commercial Kits for Simultaneous Detection of PRRSV-1, PRRSV-2, and PCV2 in Clinical Pig Samples

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Porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2) are the primary viral pathogens associated with porcine respiratory disease complex (PRDC), a multifactorial syndrome that severely affects pig health and productivity. PRRSV is classified into two genotypes: European type 1 (PRRSV-1) and North American type 2 (PRRSV-2), which co-circulate with PCV2 in Korean pig herds. Several multiplex real-time quantitative reverse transcription-polymerase chain reaction (mqRT-PCR) kits are commercially available for the differential detection of PRRSV-1, PRRSV-2, and PCV2; however, it remains unclear which are most suitable for identifying field strains currently circulating in Korean pig herds. In this study, the diagnostic performance of a newly developed mqRT-PCR kit (N kit), capable of differentially detecting PRRSV-1, PRRSV-2, and PCV2, was compared with that of four commercially available kits (A, B, C, and D) in Korea. Analytical assessments revealed that the newly developed N kit demonstrated high specificity, a detection limit of <10 copies/reaction, and high precision, with intra- and inter-assay coefficients of variation (CVs) below 3.2%. In clinical testing using 160 field samples, the N kit showed the highest detection rates for PRRSV-1 (46.9%), PRRSV-2 (70.0%), and PCV2 (61.3%), outperforming the other kits: A (29.4%, 61.3%, 34.4%), B (29.4%, 41.3%, 36.9%), C (40.0%, 61.9%, 50.6%), and D (36.9%, 31.3%, 50.6%), respectively. Additionally, the N kit identified the highest rate of triple co-infections (21.9%) compared to A (6.9%), B (5.6%), C (6.9%), and D (7.5%). These results demonstrate that the diagnostic performance of the N kit is superior in detecting genetically diverse PRRSV and PCV2 strains currently circulating in Korea. This study provides essential comparative data for swine practitioners and diagnostic laboratories, supporting the selection of appropriate mqRT-PCR kits for reliable diagnosis and improved control of PRRSV and PCV2 in Korean pig herds.



Prevalence and Co-Infection Status of Psittacine Beak and Feather Disease Virus and Aves Polyomavirus 1 in Korean Psittacine Birds Determined by a Newly Developed Multiplex Real-Time PCR

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Psittacine beak and feather disease virus (PBFDV) and Aves polyomavirus 1 (APyV) are among the most prevalent viral agents affecting parrot species worldwide, often cause chronic infections and high mortality rates in both wild and captive birds. Early diagnosis and isolation of infected birds are key to preventing the transmission of these viruses to healthy birds. Therefore, there is an urgent need to develop a rapid and sensitive diagnostic method for detecting the virus in suspected birds in the field. In this study, we developed a duplex quantitative PCR (dqPCR) assay with TaqMan probes for the simultaneous detection of PBFDV and APyV in psittacine birds in Korea. The assay was designed to amplify the PBFDV V1 gene and the APyV T gene within a single reaction tube, enabling rapid and differential identification of both viruses. The developed dqPCR assay demonstrated high specificity, with no amplification observed for unrelated avian pathogens. The detection limit was below 50 genome copies per reaction for both PBFDV and APyV, representing a tenfold improvement in sensitivity compared to conventional PCR. And precision testing confirmed the assay's reproducibility, with intra- and inter-assay coefficients of variation remaining below 5%. In the clinical evaluation, a total of 87 clinical samples, including feathers, blood, and swabs from psittacine birds, were analyzed using the dqPCR assay. The detection rates were 55.2% (48/87) for PBFDV and 13.8% (12/87) for APyV. And a co-infection rate of 12.6% (11/87) was higher than the rates reported in Chile, Bangladesh, and Brazil, but similar to the rates reported in Taiwan and Eastern Turkey. Conclusively, the newly developed dqPCR method offers a fast, sensitive, and field-applicable diagnostic tool and in suspected psittacine birds, that will be useful for etiological diagnosis, epidemiological studies, and the control of these virus infections.

In Silico Sequence Mining (ISSM): A Lightweight Tool for Rapid Viral NGS Data Analysis Without Large Databases

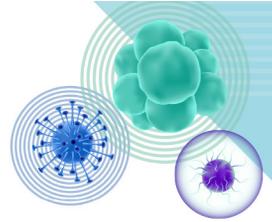
Min Chan Kim, Hye Ji Jung, Min Chang Kang, Ha Yeon Kim, Seong Sik Jang, Alain Chrysler Chamfort, Han Byul Lee, Hye Won Bae, and Hye Kwon Kim*

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Advances in next-generation sequencing (NGS) have brought significant innovation to life sciences and diagnostics. However, data accessibility and a lack of user-friendly analysis tools remain significant challenges in virology. Viral genome databases are not only limited in terms of representation and standardization, but are often unsuitable for accurate and sensitive virus detection, especially in NGS-based workflow environments. Consequently, viral sequence analysis often relies on large public databases, such as NCBI's nt (nucleotide) or nr (nonredundant protein) databases. These databases are extremely large and require significant time and computing resources for analysis.

To overcome these limitations, we developed In Silico Sequence Mining (ISSM), a standalone Windows-based GUI software. ISSM enables rapid and user-friendly detection of similar sequences in raw NGS files (FASTA or FASTQ format) based on probe sequences, such as PCR/qPCR primers or biomarkers. Leveraging a RapidFuzz-based fuzzy matching algorithm, ISSM can identify highly similar, if not perfectly identical, sequences. Notably, ISSM does not require downloading or building large reference databases, such as nt or nr, and operates as a single executable file (.exe) without installation or environment configuration, significantly reducing time and resource usage.

We validated ISSM using viral NGS datasets, including SARS-CoV-2 and feline coronavirus (FCoV), as well as clinical samples from HIV and cancer patients. This demonstrated that ISSM accurately detects true positive sequences with high sensitivity. These results suggest that ISSM offers a practical and intuitive alternative for viral sequence detection, probe validation, pathogen screening, and precision medicine applications, even in data or resource constrained environments.



Development of a Luciferase-Tagged NiV Pseudovirus Animal Model Using rVSV for Vaccine Assessment

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Nipah virus (NiV), a highly pathogenic member of the *henipavirus* genus in the *Paramyxoviridae* family, is a bat-borne zoonotic pathogen first identified during a severe outbreak in Malaysia in the mid-to-late 1990s. NiV continues to cause recurrent outbreaks in South Asia, particularly in Bangladesh and India, and poses a significant transboundary threat to global health. Due to its high mortality and epidemic potential, NiV has been classified as a high priority pathogen by the Centers for Disease Control and Prevention (CDC), World Health Organization (WHO), and Coalition for Epidemic Preparedness Innovations (CEPI), underscoring the urgent need for effective medical countermeasures, particularly vaccines. However, research on NiV is limited due to the requirement for biosafety level 4 (BSL-4). In this study, we demonstrated a pseudovirus-based animal model using a recombinant vesicular stomatitis virus (rVSV) vector system, which allows for safe experimentation under biosafety level 2 (BSL-2) conditions. Luciferase-tagged Nipah pseudoviruses were inoculated into Balb/c mice, Syrian golden hamsters, and C57BL/6-based human ephrin B2-B3 transgenic (TG) mice. Pseudovirus infection was monitored by measuring luciferase luminescence at 4-, 6-, and 24-hours post-inoculation. The highest luminescence signals were observed at 6 hours in Balb/c mice, 4 hours in Syrian golden hamsters, and 6 hours in human ephrin B2-B3 TG mice. Although further optimization of the time points and infection conditions is required, this pseudovirus-based animal model provides a valuable tool for the evaluation of vaccine efficacy and antiviral strategies against NiV under lower biosafety conditions, which may accelerate NiV vaccine development.

First Emergence of Lumpy Skin Disease Virus in South Korea: Epidemiological Features and Implications

Dae-Sung Yoo¹, Jun Hee Han², Ho-Seong Cho³, Yeonsu Oh⁴, and Joo Young Park¹

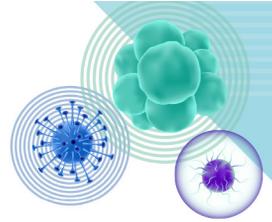
¹College of Veterinary Medicine, Chonnam National University, Gwangju 61186, Republic of Korea, ²EpiCentre, School of Veterinary Science, Massey University, Palmerston North 4410, New Zealand, ³College of Veterinary Medicine & Biosafety Research Institute, College of Veterinary Medicine, Iksan 54596, Republic of Korea, ⁴College of Veterinary Medicine & Institute of Veterinary Science, Kangwon National University, Chuncheon 24341, Republic of Korea

Lumpy Skin Disease (LSD) is a vector-borne transboundary viral disease in cattle, caused by a Capripoxvirus and characterized by causing skin nodules, fever, abortion, and reduced milk yield. The first outbreak of LSD in South Korea occurred on October 19, 2023, marking it as a nationally significant emerging disease. Notably, the initial case was identified by a farmer, not through official surveillance systems, raising concerns that the virus had already spread undetected among multiple farms. This delayed recognition highlights the need to reconstruct early transmission dynamics prior to government intervention in order to understand the intrinsic spread of the disease.

Focusing on the pre-intervention phase of the outbreak, we selected 77 LSD-infected farms reported between October 19 and November 10, 2023, as case farms, based on their estimated infection dates occurring before October 19—prior to the implementation of national control measures. A total of 90,602 registered cattle farms across South Korea served as controls. Spatial cluster analysis using a Bernoulli model identified one significant high-risk area, which was used for transmission modeling. A Bayesian spatio-temporal framework was then constructed to incorporate both within- and between-farm dynamics.

Within-farm transmission was modeled using a compartmental SIR structure, while between-farm transmission was represented as a distance-dependent process scaled by the number of cattle at the source farm using an alternative fat-tailed kernel. Force of infection was calculated under varying parameter combinations and fitted to observed epidemic data using a Poisson likelihood framework. This comparison enabled the inference of the key transmission parameters via MCMC sampling. Based on the best-fitting parameters, we will estimate the between-farm basic reproduction number (R_0) to quantify LSD transmissibility prior to intervention.

This study is expected to provide one of the first quantitative assessments of the intrinsic, unmitigated transmissibility of LSD, based on infection dynamics observed before any control measures were implemented. By establishing a rare estimate of baseline transmission potential, the findings may



serve as a valuable reference point for evaluating the effectiveness of interventions such as vaccination or selective culling. These insights are also expected to contribute to the development of early-warning systems and inform preparedness strategies for future incursions of transboundary animal diseases in South Korea.

This work was supported by Korea Institute of Planning and Evaluation for Technology in Food, Agriculture and Forestry (IPET) through High-Risk Animal Infectious Disease Control Technology Development Project, funded by Ministry of Agriculture, Food and Rural Affairs (MAFRA) (RS-2024-00399814).

First Complete Genome Characterization of a Bat-Associated Pestivirus in Korea

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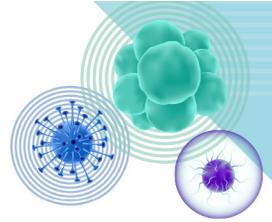
¹College of Veterinary Medicine and Bio-Safety Research Institute, Jeonbuk National University, Iksan 54596, Korea, ²College of Veterinary Medicine and Institute of Veterinary Science, Kangwon National University, Chuncheon 24341, Korea, ³Institute of Forest Science, Kangwon National University, Chuncheon 24341, Korea, ⁴Institute of Medical Science, College of Medicine, Hallym University, Chuncheon 24252, Korea

Bats are established reservoirs for a wide array of zoonotic viruses; however, the diversity and distribution of bat-associated viruses in South Korea remain insufficiently explored. The genus Pestivirus (family *Flaviviridae*) includes several economically important pathogens affecting livestock, such as *Bovine viral diarrhoea virus 1* (BVDV-1) and *Classical swine fever virus* (CSFV). Emerging evidence indicates that pestiviruses may also circulate in wildlife hosts, including bats and rodents. Notably, the atypical porcine pestivirus, a pathogen implicated in neonatal piglet disease, shares genetic similarity with *Rhinolophus affinis* bat pestivirus (*RaPestV-1*), a pestivirus previously identified in bats.

In this study, virome analysis was conducted using next-generation sequencing (NGS) on oral swab samples collected from bats in Gangwon Province, South Korea. A complete pestivirus genome (11,316 nucleotides) was recovered from a *Rhinolophus* species and designated RF-O-3_251. The genome encodes a polyprotein of 3,644 amino acids and shares 91.98% nucleotide identity and 97.94% amino acid similarity with a Chinese bat pestivirus strain (LN2020). BLASTP and phylogenetic analyses confirmed that this strain clusters within the bat pestivirus clade, showing the highest similarity to the reference strain WXG28496.1.

This study presents the first report of a complete bat pestivirus genome from South Korea, offering molecular evidence of pestivirus circulation among indigenous bat populations. The high level of similarity to known pestiviruses emphasizes the potential for interspecies transmission, including spillover into domestic livestock. Although constrained by sample size and geographic coverage, these findings underscore the urgent need for expanded surveillance and further investigation into the pathogenicity, host range, and zoonotic potential of bat-derived pestiviruses.

This research was supported by 'The Government-wide R&D to Advance Infectious Disease Prevention and Control', Republic of Korea (grant number: RS-2023-KH140418).



Genetic Characterization of Korean Bat Coronaviruses via Virome Sequencing

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Bats are well-established natural reservoirs for a variety of zoonotic viruses, including severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), and Ebola virus. Coronaviruses (CoVs), members of the *Coronavirinae* subfamily, are classified into four genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*. Among these, *Alphacoronavirus* and *Betacoronavirus* primarily infect mammals, with bats playing a central ecological role in their maintenance and transmission.

In this study, we conducted virome analysis using next-generation sequencing (NGS) on samples collected from four bat species in South Korea. Sample types included oral swabs, feces, and intestinal tissues. A total of 30 partial CoV genomic sequences (ranging from 523 to 1,992 bp) were identified, exhibiting 93.93% to 99.06% nucleotide identity with known reference strains. Phylogenetic analysis demonstrated that all CoVs sequences derived from oral swabs and two from fecal samples belonged to the *Alphacoronavirus* genus. Notably, two CoV strains isolated from the intestinal tissues of greater horseshoe bats (*Rhinolophus ferrumequinum*) clustered within the *Betacoronavirus* genus. One strain (RF-T-2024-I1_3) showed 99.84% sequence identity to *Sarbecovirus* sp. isolate LN2020E (GenBank: OK017797.1) from China, while the other (RF-T-2024-I1_53) was closely related (99.84%) to the Korean *Sarbecovirus* strain 16BO133 (GenBank: KY938558.1).

Although based on partial genomic sequences, these findings offer valuable insights into the genetic diversity and circulation of bat coronaviruses in South Korea. Continued surveillance and full-genome sequencing efforts are essential to assess their zoonotic potential and implications for public health preparedness.

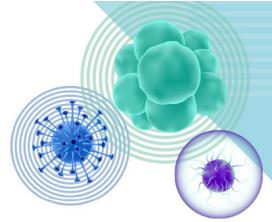
This research was supported by 'The Government-wide R&D to Advance Infectious Disease Prevention and Control', Republic of Korea (grant number: RS-2023-KH140418).

First Identification and Molecular Characterization of Psittacid Herpesvirus 1 from Pet Parrots in Korea

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Twelve parrots raised in an aviary in Gyeongsangbuk-do, Korea, died acutely over a two-week period. Six of those were submitted to the Veterinary Diagnostic Laboratory in the College of Veterinary Medicine at Kyungpook National University for etiological diagnosis. To identify the causes of sudden death in pet parrots, molecular screening was performed targeting major psittacine viral pathogens, including Psittacine beak and feather disease virus (PBFDV), Avian bornavirus (ABV), Psittacid herpesvirus 1 (PsHV-1), Avian polyomavirus (APV), and Avian paramyxovirus serotype 1 (APMV-1). Five major viral pathogens were tested by previously described assays: PCR for PBFDV, APV, and PsHV-1; reverse transcription PCR (RT-PCR) for ABV and APMV-1. As a result, all six parrots tested positive for PBFDV, with three samples positive for ABV and one (rosella parakeet) positive for PsHV-1. Notably, one parrot (rosella parakeet) was confirmed to be coinfecting with three viruses: ABV, PBFDV, and PsHV-1. To date, in Korea, there have been reports on the genetic characterization of PBFDV and APV, but no reports on PsHV-1. Accordingly, the PsHV-1-positive sample was subjected to genetic characterization and genotyping through PCR amplification. The UL16 gene (nucleotides/nt 1-419) of the PsHV-1-positive rosella parakeet was amplified using the primer set previously described by Tomaszewski et al. (2003), and the PCR product was sequenced using the Sanger's method by a commercial company (BIONICS, Daejeon, South Korea). The resulting sequences were analyzed and assembled using Geneious Prime software. The partial UL16 gene sequence of the PsHV-1 was successfully obtained in this study and it was deposited in the National Center for Biotechnology Information GenBank database (strain KPsHV-1, GenBank accession number PQ645140). The partial UL16 gene was sequenced and compared with those of global PsHV-1 strains with different genotypes were retrieved from the GenBank database. The KPsHV-1 strain was closely related to the genotype 1 PsHV-1 strain previously reported in the USA, showing 100% nucleotide identity with strain 97-0001 (GenBank accession number AY372243). The results showed that KPsHV-1 is clustered with other genotype 1 strains reported from the USA and Brazil while being distinct from genotype 2, 3, and 4 PsHV-1 strains. This is the first report for genotype identification of PsHV-1 circulating in Korean psittacine birds. These findings contribute to our understanding of the epidemiology and genetic characteristics of PsHV-1 among pet parrots in Korea.



Integrating Antibody Data, Surveillance Strategies, and Deep Learning Models into ABC-SMC Framework for Primary Case Detection in Livestock Disease Outbreaks

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Identifying the primary case is critical for effective outbreak response and disease control in livestock populations. Traditional approaches often rely solely on temporal and spatial patterns of reported cases, without integrating serological or surveillance-type data. Furthermore, advances in machine learning offer new opportunities for dynamic outbreak modeling and source attribution.

This study aims to develop and evaluate a comprehensive analytical framework that integrates antibody test data, surveillance modality (active vs. passive), and herd-level characteristics within a spatially explicit ABC-SMC (Approximate Bayesian Computation Sequential Monte Carlo) model. We further explore the utility of graph neural networks (GNNs) and long short-term memory networks (LSTMs) for enhancing primary case detection and modeling outbreak dynamic. A field dataset comprising PCR and antibody results, surveillance types, herd size, geographical coordinates, and report dates was assembled from livestock holdings. The integrated approach improved accuracy in primary case detection compared to traditional models excluding antibody and surveillance data. Incorporation of GNN/LSTM modules further enhanced model performance, particularly in settings with complex spatial or temporal dependencies. The method demonstrated robust estimation of transmission and detection parameters, and yielded probabilistic rankings of candidate primary herds. Our study highlights the value of combining serological and surveillance-type data with state-of-the-art simulation and machine learning approaches for outbreak source detection. The presented framework is adaptable to diverse livestock diseases and surveillance contexts, and provides a foundation for more targeted, data-driven interventions in animal health management.

This work was supported by Korea Institute of Planning and Evaluation for Technology in Food, Agriculture and Forestry (IPET) through High-Risk Animal infectious Disease Control Technology Development Program, funded by Ministry of Agriculture, Food and Rural Affairs (MAFRA)(grant number: RS-2024-00400522)

Development and Evaluation of Cap- and IRES-Based mRNA Vaccine Platforms Against Foot-and-Mouth Disease

Hye-Won Yu¹, Sowon Lee², Yun Ji Kim¹, Seonghyun Lee², and So-Hee Hong¹

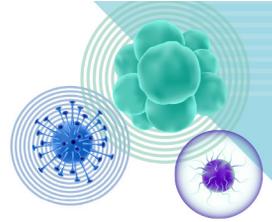
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mRNA vaccine technology has emerged as a promising platform for infectious disease response due to its rapid production, high immunogenicity, and scalability. In this study, we developed two mRNA vaccine platforms for application against foot-and-mouth disease virus (FMDV), a highly contagious livestock pathogen. One was a cap-based platform (CUK 3-1), and the other was an IRES-based platform using elements from EMCV and FMDV serotype O. As the gene of interest, we used an FMDV virus-like particle (VLP) construct composed of VP4-VP2-VP3-VP1-2A-Pro-3C.

The mRNAs were synthesized and purified for each platform, formulated into lipid nanoparticles (LNPs), and intramuscularly injected into 8-week-old female C57BL/6 mice twice at 2-week intervals. Sera were collected two weeks after the second immunization and analyzed by ELISA for FMDV-specific antibodies.

Among the IRES-based platforms, the EMCV IRES construct induced the highest antibody titers, while the cap-based platform consistently elicited significantly stronger immune responses overall. These findings suggest that while IRES-based approaches are functional, the cap structure provides a more robust platform for antigen expression.

This study demonstrates that both cap- and IRES-based mRNA vaccine platforms can elicit antibody responses against FMDV, with the cap-based platform showing superior immunogenicity. These results highlight the potential for mRNA technology to be applied not only to human diseases but also to veterinary vaccines, offering meaningful scientific and societal contributions to livestock disease control and agricultural biosecurity.



Genetic Diversity of Bat Astroviruses in Korean Bats Revealed by Virome Analysis

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Bats (order *Chiroptera*) represent approximately 20% of all mammalian species and serve as reservoirs for a wide array of viruses, many of which have zoonotic potential. Among these, astroviruses—non-enveloped, positive-sense single-stranded RNA viruses of the family *Astroviridae*—have been detected in diverse bat populations globally. The family comprises two genera: *Mamastrovirus*, infecting mammals, and *Avastrovirus*, associated with birds. While astroviruses are traditionally linked to gastroenteritis, certain strains have recently been implicated in neurological disease in both humans and animals.

Despite global interest, bat astroviruses (BtAstVs) remain undercharacterized in South Korea, with limited surveillance efforts since their first detection in 2016. In this study, virome analysis using next-generation sequencing was conducted on samples from four bat species (*Rhinolophus ferrumequinum*, *Hypsugo alaschanicus*, *Miniopterus fuliginosus*, and *Myotis aurascens*) collected in Gangwon Province. Sixteen partial BtAstV sequences were identified from *M. fuliginosus* and *M. aurascens*. Amino acid sequence identities compared to reference strains in the NCBI RefSeq database ranged from 67.10% to 89.85%, with most sequences mapping to the *Mamastrovirus* ORF1ab polyprotein region.

Notably, one sequence (MF-F-1_4) showed only 49.96% identity to a Vietnamese bat astrovirus (YP009333174.1) and did not cluster within any established astrovirus lineage, suggesting the existence of a potentially novel lineage. These results highlight the substantial genetic diversity of BtAstVs circulating in Korean bat populations and underscore their potential role in astrovirus evolution. Expanded surveillance, full-genome sequencing, and cross-species pathogenicity studies are warranted to better understand their ecological and zoonotic significance.

This research was supported by 'The Government-wide R&D to Advance Infectious Disease Prevention and Control', Republic of Korea (grant number: RS-2023-KH140418).

Partial Genomic Sequences of Human Adenovirus C-like Strains Identified in Korean Bat

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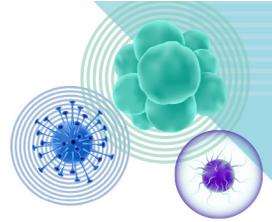
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Next-generation sequencing (NGS) has revolutionized the detection of diverse viruses in both humans and animals, significantly advancing our understanding of viral diversity and host range. Bats, in particular, are recognized as important reservoirs of zoonotic viruses, leading to increased global efforts in bat virome surveillance. Adenoviruses (AdVs) are double-stranded DNA viruses that infect a broad spectrum of vertebrate hosts and are commonly associated with respiratory and gastrointestinal illnesses, though many infections remain subclinical. To date, ten species of bat-associated adenoviruses have been identified.

In this study, we conducted virome analysis of samples collected from multiple bat species inhabiting South Korea to investigate the presence of adenoviruses with potential zoonotic relevance. A total of 11 partial adenoviral genome sequences (509–889 bp) were recovered. Sequence alignment revealed 99.21–100% nucleotide identity with known reference strains. Phylogenetic analysis placed these sequences within the Human adenovirus C (HAdV-C) group, yet they formed distinct lineages from previously reported bat-derived HAdV-C strains. The identified sequences originated from *Rhinolophus ferrumequinum*, *Hypsugo alaschanicus*, and *Miniopterus fuliginosus*.

These findings suggest that insectivorous bats in Korea may harbor adenoviruses genetically related to human strains, possibly reflecting independent evolutionary trajectories or historical cross-species transmission events. Further studies involving full-genome sequencing, virus isolation, and pathogenicity testing are essential to better assess the zoonotic potential and public health implications of these viruses.

This research was supported by 'The Government-wide R&D to Advance Infectious Disease Prevention and Control', Republic of Korea (grant number: RS-2023-KH140418).



Genomic and Amino Acid Mutation Analysis of Three H9N2 Low Pathogenic Avian Influenza Viruses Isolated from Poultry in Korea

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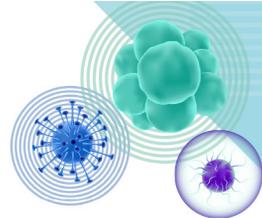
Three strains of H9N2 low pathogenic avian influenza viruses are isolated from domestic poultry in Chungcheongbuk-do province in Korea in 2024-2025, and full genome sequences were analyzed for their phylogenetic relationships and key amino acid mutations. Phylogenetic analysis revealed that all strains belonged to the Y280 lineage, with several mutations associated with mammalian adaptation and increased pathogenicity. Notably, all three viruses harbored A588V mutation in PB2, while one additionally carried K526R, a combination known to enhance replication efficiency in mammalian hosts. The K526R substitution was previously identified in some Korean H9N2 isolates in 2020, and this is the first time it has been detected again since then. The HA segments of all strains exhibited I155T, Q226L and G228S mutations (H3 numbering), suggesting enhanced affinity for human-like α 2,6-linked sialic acid receptors. Collectively, these findings highlight the zoonotic potential of currently circulating H9N2 strains in Korea and underscore the need for continued molecular surveillance and risk assessment of avian influenza viruses with pandemic potential.

Development of a Humanized MXRA8 Mouse Model for Chikungunya Virus Infection and Vaccine Efficacy Evaluation

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Chikungunya virus is a mosquito-borne infectious disease, an enveloped, benign single-stranded RNA virus belonging to the Togaviridae family and the Alphavirus genus, and is one of the lethal pathogens with Biosafety Level 3 that causes chikungunya fever. In January 2017, Chikungunya virus was added to the list of WHO research and development blueprints at the Annual Review Meeting in Geneva, Switzerland, and Chikungunya virus was mentioned in Serious diseases necessitating further action as soon as possible, as of May 2016, and it is a virus of increasing importance as it is included in CEPI's 100-day plan and the domestic development priority pathogen designated by the Korea Disease Control and Prevention Agency. Currently, vaccines targeting Chikungunya virus include the inactivated vaccine (ixchiq) from Valneva and the VLP vaccine (Vimkunya) from Bavarian Nordic, and various companies and researchers are developing vaccines using various vaccine platforms such as mRNA. The receptor for the virus is known as matrix-remodelling associated 8 (MXRA8), which is a cell surface protein that regulates bone and cartilage formation, vascular elongation, and maintenance of the blood-brain barrier. MXRA8 is also called DICAM and limitrin, and has two Ig-like domains on its surface. In order to establish conditions for an animal model of chikungunya virus infection, a humanized mouse that overexpresses the human MXRA8 receptor will be generated to confirm the infection protection ability against chikungunya virus and use it to evaluate the efficacy of a chikungunya vaccine, which will be helpful in constructing a vaccine library.



Evaluating the Impact of the Veterinary Prescription System on Antimicrobial Resistance Rates

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Antimicrobial resistance (AMR) refers to the ability of microorganisms such as bacteria to survive by developing resistance to specific antibiotics. This phenomenon makes treating infectious diseases increasingly difficult and has emerged as a serious global public health concern. Recognizing the severity of this issue, the Korean government has been working to manage antimicrobial resistance rates based on a One Health approach, with veterinary prescription requirements being part of these efforts. This study investigated the impact of the expanded implementation of prescription-required veterinary medicines, which took effect on November 13, 2022, on antimicrobial resistance rates and evaluated the policy's effectiveness.

The evaluation methodology was as follows. Using AMR survey data, we calculated monthly antimicrobial resistance rates for six bacterial species (*Campylobacter sp.*, *E. coli*, *E. faecalis*, *E. faecium*, *Salmonella sp.*, *Staphylococcus aureus*) detected in domestically distributed livestock products (cattle, pigs, chickens, ducks) against various antibiotics from February 2017 to December 2023. Monthly antimicrobial resistance rates were categorized into pre- and post-policy implementation periods for comparative analysis and visualized using heat maps. Interrupted time series (ITS) analysis was conducted to assess whether the policy intervention resulted in significant changes in both the level and slope of antimicrobial resistance rates, with findings subsequently visualized. A Bayesian structural time series (BSTS) model was employed to predict counterfactual antimicrobial resistance rates that would have occurred in the absence of policy intervention, enabling causal inference and data visualization.

The analysis results varied depending on bacterial species, livestock type, and antibiotic. Detailed results and their interpretations will be provided in subsequent work.

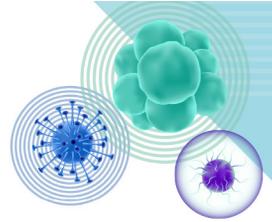
This work was supported by Korea Institute of Planning and Evaluation for Technology in Food, Agriculture and Forestry (IPET) through High-Risk Animal Infectious Disease Control Technology Development Project, funded by Ministry of Agriculture, Food and Rural Affairs (MAFRA) (RS-2024-00400522).

PAFA and RT-QuIC as Platforms for Investigating Action Mechanism of Anti-Prion Agents

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Prion diseases are neurodegenerative disorders caused by the accumulation of the infectious, misfolded prion proteins (PrP^{Sc}) that resulted from the conversion of normal prion proteins (PrP^C). PrP^{Sc} plays a central role in diseases neurotoxicity and transmission. Evaluating the inhibition of PrP^{Sc} formation and aggregation is considered an effective approach for identifying anti-prion agents. PrP aggregation formation assay (PAFA) and Real-time quaking induced conversion (RT-QuIC) were established as complementary platforms for screening potential anti-prion compounds. PAFA enables the assessment of a potential ability of an agent to suppress the self-aggregation of partially denatured, molten-form recombinant PrP under controlled in vitro conditions, reflecting its capacity to reflect early misfolding and aggregation events. In contrast, RT-QuIC measures the seeded conversion of recombinant PrP in the presence of brain-derived PrP^{Sc} seeds, thereby enabling the assessment of a potential agent's effect on prion propagation and seed amplification. These complementary analyses allow distinguish whether the observed decrease in PrP^{Sc} levels in culture cells and animals is a result of spontaneous aggregation inhibition, seed conversion, or both. Several agents were examined using PAFA and RT-QuIC to investigate the action mechanism through which the agents modulate prion pathology. Initially, western blot analysis demonstrated that poly-L-arginine (PLR), compound 7x and 7y, extracts of *Curcuma phaeocaulis* Valeton (Zingiberaceae, CpV) reduced PrP^{Sc} levels. PAFA and RT-QuIC were subsequently employed to assess their effects on PrP propagation and aggregation. PLR did not inhibit PrP aggregation, whereas compounds 7x, 7y, and CpV showed significant suppression of PrP^{Sc} formation and aggregation. These findings indicate that PLR likely acts through a different mechanism compared to compounds 7x, 7y, and CpV extract. This finding provides mechanistic insights into the anti-prions activity of the tested compounds and highlight their potential for application to discover therapeutics for prion disease.



A 3D Spheroid-Based Model of Prion Infection

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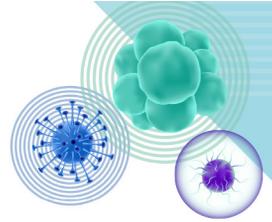
Prion diseases are transmissible and fatal neurodegenerative disorders characterized by the accumulation of misfolded prion protein (PrP^{Sc}) in the central nervous system. Although various *in vitro* models, such as 2D cultures, have been utilized to study prion replication, they often fail to replicate the structural and cellular complexity of the brain. 3D models such as brain organoids have shown promise in mimicking the architecture of brain tissue but are limited by variability and the infection protocols for long-term studies. Here, we present a novel 3D spheroid model of neurons and astrocytes derived from mouse neural stem cells (NSCs), to study the pathogenesis of prion diseases. This model was generated by inducing spheroid formation from NSCs followed by infection with Rocky Mountain Laboratory (RML) prion strains. RML infection-3D spherical models with neurons and astrocytes generated apoptosis and gliosis resembling a neural microenvironment for prion propagation and neurodegenerative processes. Additionally, the ability to support long-term prion transmission, secondary infection, and cryopreservation has been demonstrated. This innovative model enables long-term studies of prion dynamics and the evaluation of therapeutic interventions, bridging the gap between simple *in vitro* systems and *in vivo* models. Our findings demonstrate the utility of this 3D model as a valuable tool in prion research.

Molecular and Pathological Impact of PAD2 Deficiency in Prion Disease with Integrated Ultrastructural Analysis

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Prion diseases, or transmissible spongiform encephalopathies (TSEs), are fatal neurodegenerative diseases caused by the accumulation of misfolded prion protein (PrP^{Sc}) and accompanied by pronounced astrocytosis, reflected by increased glial fibrillary acidic protein (GFAP) expression. Peptidylarginine deiminase 2 (PAD2), predominantly expressed in the central nervous system, catalyzes protein citrullination and has been implicated in neurodegeneration. While the role of PAD2 in protein modification has been explored, its influence on the molecular and pathological mechanisms of prion disease—and the associated ultrastructural alterations—remains poorly defined. In this study, wild-type (WT) and PAD2 knockout (KO) mice were intraperitoneally inoculated with the 22L scrapie strain. Disease progression was assessed through survival analysis, clinical scoring, and comprehensive molecular and histopathological evaluation across five brain regions (cortex, cerebellum, striatum, hippocampus, brainstem). PAD2 KO mice exhibited markedly accelerated disease progression and reduced survival compared to WT controls. Unexpectedly, molecular assays revealed decreased accumulation of PrP^{Sc} and reduced GFAP expression in KO brains, which was further confirmed by histopathological examination. To complement these findings, transmission electron microscopy demonstrated more frequent mitochondrial abnormalities, increased autophagic vesicles, and widespread organelle disruption in KO neurons. These results suggest that PAD2 deficiency shifts prion pathogenesis away from the classical “PrP^{Sc} – astrocytosis” axis toward alternative neurotoxic pathways, including mitochondrial dysfunction and autophagy dysregulation. This divergence likely underlies the paradoxical combination of reduced prion/astrocytic markers and accelerated clinical decline, highlighting PAD2 as a potential regulator of cellular resilience in neurodegenerative disease [Grant: RS-2023-00247903].



신경계 4

Lentiviral and retroviral virus-like particles as a promising delivery platform for the SARS-CoV-2 nucleocapsid protein

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The *gag* gene of human immunodeficiency virus type 1 (HIV-1) encodes a polyprotein precursor essential for viral particle assembly and budding. During virion maturation, the Gag polyprotein is proteolytically cleaved by the viral protease into multiple structural proteins crucial for viral infectivity. Because of its ability to promote particle formation, HIV-1 Gag has been extensively used for the generation of virus-like particles (VLPs). Similarly, expression of the *gag* gene from murine leukemia virus (MLV) alone is sufficient to induce VLP formation. Compared to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) VLPs, HIV-1 Gag VLPs yield substantially higher titers, likely due to their simpler and more efficient self-assembly and release mechanisms. The SARS-CoV-2 nucleocapsid (N) protein is widely used as a primary target in rapid antigen detection assays because of its high abundance, early expression, sequence conservation, and robust detectability. In this study, we investigated whether co-expression of Gag enables the incorporation of the SARS-CoV-2 N protein into VLPs. Transient co-transfection of HEK293T cells with plasmids encoding HIV-1 Gag-Pol (psPAX2), vesicular stomatitis virus G glycoprotein (VSV-G), and the SARS-CoV-2 N protein led to efficient packaging of N into HIV-1 Gag-derived VLPs. Similarly, co-expression of MLV Gag-Pol (pVPack-GP) with VSV-G and SARS-CoV-2 N resulted in MLV-based VLPs incorporating the N protein. Additionally, genetic fusion of the SARS-CoV-2 N protein to the C-terminus of HIV-1 or MLV Gag also promoted its incorporation into VLPs. HIV-1 Gag VLPs incorporating N protein served as reliable positive controls for SARS-CoV-2 rapid antigen diagnostic assays. These SARS-CoV-2 N protein-incorporating VLPs represent stable, noninfectious surrogates that mimic native virions and are suitable for lateral flow immunoassays, as well as for the validation and calibration of anti-N antibody detection assays in patient sera.

Comparative Vector Competence of *Aedes albopictus* for Three Japanese Encephalitis Virus Genotypes (I, III, and V)

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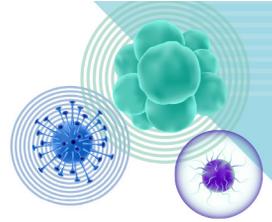
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Japanese encephalitis virus (JEV), a mosquito-borne flavivirus, is a major cause of viral encephalitis in Asia. While *Culex tritaeniorhynchus* is recognized as the primary vector, *Aedes albopictus* has recently been implicated in potential JEV transmission based on the detection of viral RNA in field-collected specimens in the Republic of Korea (ROK). However, its vector competence for JEV remains poorly understood. This study aimed to evaluate the susceptibility and transmission potential of *Ae. albopictus* following oral exposure to JEV.

Ae. albopictus mosquitoes (F43 generation), originally collected from Incheon, ROK, were reared under controlled laboratory conditions. Females (5–7 days old) were orally infected with JEV genotypes GI, GIII, or GV (1.0×10^6 – 1.0×10^7 PFU/mL) using a Hemotek membrane feeding system. At 7 and 14 days post-infection (dpi), mosquitoes were dissected to assess infection (midgut), dissemination (legs–wings), and transmission potential (head–thorax, saliva). JEV RNA was detected using qRT-PCR targeting the NS5 gene, and infectious virus titers were determined by TCID₅₀ assay in BHK-21 cells. All experiments were performed in a BSL-3 facility (Permit No. KCDC-18-3-04).

Vector competence of *Ae. albopictus* was evaluated for three JEV genotypes (GI, GIII, GV) at 7 and 14 dpi by assessing infection rate (IR), dissemination rate (DR), and transmission rate (TR), including salivary positivity. Overall, JEV genotype-dependent differences were observed in the infected mosquitoes. At 7 dpi, GV- and GIII-infected mosquitoes showed higher DRs (75.9% and 68.4%, respectively) compared to GI (42.9%). By 14 dpi, GV-infected mosquitoes exhibited the highest vector competence, with a DR of 100.0%, TR of 71.7%, and saliva positivity of 36.7%, indicating robust transmission potential. GIII-infected mosquitoes showed moderate competence (DR 76.9%, TR 39.3%, saliva 6.6%), while GI infection remained largely confined to the midgut with minimal TR (4.0%) and salivary detection. Temporal analysis confirmed that GV continued to disseminate and accumulate in salivary tissues over time, whereas GI showed little progression. These findings suggest that *Ae. albopictus* is more competent for transmitting JEV genotypes GIII and GV than GI under laboratory conditions.

Our findings demonstrate that *Ae. albopictus* exhibits genotype-dependent vector competence for JEV. Under controlled laboratory conditions, *Ae. albopictus* was capable of supporting infection, dissemination, and transmission of JEV genotypes GIII and GV, with GV showing the highest transmission potential at both individual and population levels. In contrast, GI infection remained largely restricted to the midgut, with minimal evidence of dissemination or salivary transmission. These results suggest that *Ae. albopictus*, a mosquito species widely distributed in the ROK, may contribute to JEV transmission dynamics, particularly for GV.



무주바이러스의 분자 진화와 인수공통감염 위험성 분석

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신증후군출혈열은 설치류가 매개하는 오르토타바이러스(*Orthohantavirus*) 속 바이러스에 의해 발생하는 인수공통감염병으로, 유라시아 전역에서 중요한 공중보건 문제로 인식되고 있다. 유럽에서는 매년 푸말라바이러스(*Puumala virus*, PUUV)에 의한 수천 명의 유행성 신장병(nephropathia epidemica) 환자가 발생하며, 유행성 신장병 환자에서는 혈소판 감소증과 급성 신손상 등을 동반한 한탄바이러스 감염에 비해 비교적 경미한 증상이 나타난다. 오르토타바이러스 푸말라엔스(*Orthohantavirus puumalaense*) 종에 속하는 무주바이러스(*Muju virus*, MUJV)는 대한민국 내 비단털들쥐(*Craseomys regulus*)를 자연 숙주로 하지만, 이에 대한 유전적 다양성과 인체 감염 가능성에 관한 연구는 아직 제한적이다.

본 연구에서는 2012년부터 2023년까지 대한민국 23개 지역에서 포획된 185마리의 비단털들쥐를 대상으로 MUJV의 혈청학적 및 분자학적 유병률을 평가하였다. 혈청학적 검사 결과, 163마리 중 5마리(3.1%)에서 PUUV 특이 면역글로블린G(IgG) 항체가 검출되었으며, 역전사중합효소연쇄반응법(RT-PCR)을 이용한 분자학적 검사에서도 동일한 5마리(2.7%)에서 MUJV RNA가 확인되었다. 특히, 강원도 철원군에서 처음으로 MUJV가 분자학적으로 확인되어 MUJV의 기존 알려진 분포 지역을 확장하였다. 앰플리콘 기반의 나노포어 염기서열분석법(Amplicon-based nanopore sequencing)을 통해 MUJV의 전장 유전체 염기서열을 확보할 수 있는 방법을 개발하였으며, 계통발생학적 분석 결과 강원도와 전라북도에서 채집된 MUJV 균주 사이의 명확한 계통지리학적 분화가 관찰되었다. Bayesian 방법을 이용한 MUJV의 진화속도 분석 결과, S, M, L 분절에서 각각 8.4×10^{-3} , $2.6-7.0 \times 10^{-3}$, 1.8×10^{-2} substitutions/site/year의 속도로 추정되었다. 인수공통감염 위험성 분석 결과에서는 MUJV 균주의 대부분이 중간에서 높은 수준의 인간 감염 가능성을 지닌 것으로 평가되었다.

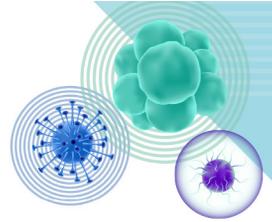
본 연구는 국내 MUJV의 유전적 분자 진화와 인수공통감염 위험성을 종합적으로 평가한 연구이며, 향후 공중보건학적 관점에서 MUJV에 대한 지속적이고 포괄적인 감시와 추가적인 연구의 필요성을 강조한다.

Comparative Evaluation of mRNA-Encoded Antibody Structures Targeting SFTSV Gn

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Severe fever with thrombocytopenia syndrome (SFTS) is a tick-borne infectious disease first reported in China in 2009, caused by the SFTSV (Severe fever with thrombocytopenia syndrome virus (SFTSV)). It presents with high fever, thrombocytopenia, and leukopenia, often leading to high mortality. Currently, no approved vaccines or antiviral treatments exist. In this study, we developed mRNA-LNPs encoding monoclonal antibodies targeting the Gn glycoprotein of SFTSV in three structures: (1) separate mRNAs for heavy and light chains (H/L), (2) a single-chain construct linking heavy and light chains via a flexible peptide (H+L), and (3) an scFv fused to an Fc domain (scFv). These formats were assessed for in vitro expression and neutralization. The linker-connected heavy-light chain format showed superior neutralizing activity. In IFNAR knockout mice challenged with SFTSV, this construct significantly improved survival. These results show the therapeutic potential of mRNA-based monoclonal antibodies and the impact of antibody format on functional efficacy in mRNA-based therapeutics.



Establishment of a Pseudovirus System for SFTSV Research

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Severe Fever with Thrombocytopenia Syndrome (SFTS) is caused by the Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV), which poses a serious public health threat due to its high fatality rate and lack of effective treatments. The SFTSV G glycoprotein (Gn/Gc) is crucial for host cell infection and is a key target for vaccine development. Since SFTSV requires biosafety BSL-3 facilities, research and therapeutic development are limited. To overcome this, we generated VSV- and lentivirus-based pseudotyped viruses expressing the SFTSV G glycoprotein and assessed their infectivity to explore their potential as research models. The VSV-based pseudotyped virus was produced using the Δ G VSV system, while the lentivirus-based pseudotyped virus was generated using a third-generation lentiviral system. Infectivity was evaluated by GFP and luciferase expression. The VSV-based pseudotyped virus was successfully produced. Although the infection efficiency did not significantly differ from the control VSV without the G protein, we succeeded in improving the virus purity through wash and antibody treatment, contributing to improved purity. However, further research is needed to improve yield. In contrast, the lentivirus-based pseudotyped virus showed low infection efficiency, making its successful production uncertain.

This study aimed to establish a pseudotyped virus system for SFTSV research under BSL-2 conditions. The VSV-based system successfully improved purity, whereas the lentivirus-based system showed low infectivity, limiting its use as a research model. The VSV system may be a better option, and optimization of virus production methods is needed to improve yield.

고정밀 나노포어 시퀀싱을 활용한 국내 한탄바이러스의 전장 유전체 감시 및 계통학적 다양성 연구

박경민^{1,2}, 김종우^{1,3}, 노주영¹, 김성규^{1,3}, 조희경^{1,3}, 김기진^{4,5}, 서예린⁶, 임태훈⁷, 이성현⁷, 이재연^{1,3}, 임승인⁸, 주영훈⁹, 이버들¹⁰, 윤석현¹¹, 박창보¹², 송동현¹³, 구세훈¹³, 이승호¹³, 이대상¹³, 김원근^{7,14}, 송진원^{1,2*}

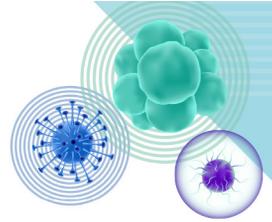
¹고려대학교 의과대학 미생물학교실, ²고려대학교 의과대학 의과학과 BK21 프로그램, ³고려대학교 의과대학 바이러스성감염병연구소, ⁴캐나다 브리티시컬럼비아주 버나비, 사이먼 프레이저 대학교 보건과학대학 감염병 유전체 및 원헬스 센터, ⁵캐나다 브리티시컬럼비아주 버나비, 사이먼 프레이저 대학교 분자생물학 및 생화학과, ⁶고려대학교 의과대학 예방의학교실, ⁷한림대학교 의과대학 미생물학교실, ⁸대한민국 육군 제5예방의무대, ⁹대한민국 육군 제1예방의무대, ¹⁰대한민국 육군 제3예방의무대, ¹¹대한민국 육군 제2예방의무대, ¹²대한민국 육군본부, ¹³국방과학연구소 제3기술연구본부 제5기술연구부, ¹⁴한림대학교 의과대학 의과학연구소

한탄바이러스(*Orthohantavirus hantanense*, HTNV)는 신증후군출혈열(Hemorrhagic Fever with Renal Syndrome, HFRS)의 주요 원인 병원체로, 국내에서는 경기도 및 강원도 지역에서 지속적인 발생이 보고되고 있다. 본 연구는 고정밀 나노포어 시퀀싱 기술과 생물정보학 분석을 활용하여 HTNV 전장 유전체를 획득하고, 감염원 추적 및 유전적 다양성을 평가하고자 수행되었다.

2022년부터 2023년까지 경기도, 강원도, 광주광역시 11개 지역에서 총 579마리의 설치류를 채집하였으며, 이 중 등줄쥐(*Apodemus agrarius*) 498마리를 대상으로 IFA를 통한 혈청학적 분석과 RT-PCR을 통한 분자생물학적 분석을 실시하였다. 혈청 양성률은 13.1% (65/498), 폐 시료를 이용한 RNA 양성률은 혈청 양성 개체 중 26.2% (17/65)로 확인되었다.

RNA 양성 시료를 이용한 앰플리콘 기반 고정밀 나노포어 시퀀싱을 이용한 분석 결과, 경기도 및 강원도에서 확보한 시료로부터 총 15주의 완전한 HTNV 전장 유전체를 획득하였다. 또한 Graph-incompatibility-based Reassortment Finder (GiRaF)를 이용한 유전체 재편성 분석을 통해 파주시 및 연천군에서 획득한 3주의 HTNV에서 L분절 재편성체(reassortant)를 확인하였다.

본 연구 결과는 국내 HTNV의 시공간적 감시 해상도를 향상시키고, 신변종 바이러스 계통 및 발생 지역의 유전적 특성을 규명하는 데 기여하였다. 또한 HFRS 유행 지역에서의 유전자 기반 진단 및 방역 전략 수립에 있어 나노포어 시퀀싱과 생물정보학의 응용 가능성을 제시하며, 효과적인 공중 보건 대응을 위한 과학적 기반을 마련하였다.



아보 6

넥스트스트레인을 활용한 한탄바이러스의 시공간 유전체 역학 및 시각화

박경민^{1,2}, 김기진^{3,4}, 김종우^{1,5}, 노주영^{1,5}, 김성규^{1,5}, 조희경^{1,5}, 서예린¹, 김진일^{1,2}, 박만성^{1,2}, 김원근^{6,7}, 송진원^{1,5*}

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한탄바이러스(*Orthohantavirus hantanense*, HTNV)는 등줄쥐(*Apodemus agrarius*)를 자연 숙주로 하는 인수 공통감염병 병원체로, 동아시아 지역에서 유행하며 신증후군출혈열의 주요 원인으로 알려져 있다. 본 연구에서는 HTNV의 시공간적 유전체 역학과 돌연변이 양상을 실시간으로 시각화하기 위해, Nextstrain 플랫폼을 기반으로 한 지역 맞춤형 분석 환경을 구축하였다. GenBank로부터 확보한 S, M, L 세 유전체의 완전 코딩 서열과 수집 시기, 숙주, 지리정보(GPS 등)를 포함한 메타데이터를 통합하여 데이터베이스를 구성하고, Snakemake 기반 분석 파이프라인을 통해 일관된 계통분석과 시공간적 시각화를 구현하였다. 계통수와 지리정보를 통합한 분석 결과, 대한민국을 포함한 동아시아 지역에서의 계통적 분화 및 지역별 군집 형성이 관찰되었으며, 1976년 경기도 동두천에서 분리된 HTNV 76-118 주를 기준으로 한 돌연변이 추적을 통해 계통별 분지 시점과 유전적 변이를 파악할 수 있었다. 본 플랫폼은 사용자 친화적인 웹 인터페이스를 제공하며, 연구자 및 방역 당국이 HTNV의 유전적 다양성과 전파 경로를 직관적으로 파악하고, 지역 감염원과의 역학적 연계를 도출하는 데 활용될 수 있다.

Activation of Toll-like receptor 2 is antiviral against Zika virus in microglia

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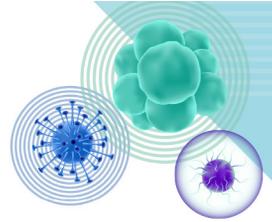
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Zika virus (ZIKV) poses a significant challenge due to its association with neurodevelopmental disorders such as congenital Zika syndrome. While the incidence of ZIKV is presently low, with the waning of the population immunity in the previously affected epidemic regions, it is possible for ZIKV to re-emerge and cause another major epidemic outbreak in the future. Brain-resident differentiated microglia serve neuroprotection, limiting infection and neuronal death. Toll-like receptors (TLRs) play an important role in innate immunity against invading pathogens. The function of TLR2 in ZIKV replication remains unknown, despite TLR signaling has been shown to shield cells from infection by a number of viruses.

In this work, we investigated the immunomodulatory role of TLR2 in microglial responses to ZIKV infection. We observed TLR2 expression increases in microglia during the early stages of infection. TLR2 knock-out or blockade using neutralizing antibodies enhanced viral replication in microglia. Conversely, stimulation with a TLR2 agonist led to suppression of viral replication. Mechanistically, TLR2 activation induced expression of antiviral genes, including ISG15, as well as downstream pro-inflammatory cytokines such as IL-8.

Furthermore, we detected an enrichment of ZIKV nonstructural protein 1 (NS1) in small extracellular vesicles (sEVs) released by infected microglia. Notably, treatment of neuronal progenitor cells (NPCs) with TLR2 knock-out microglia-derived sEVs resulted in elevated expression levels of ZIKV gene and titer, while promoting increased cell death in NPCs.

Altogether, activation of TLR2 provides antiviral activities against ZIKV in microglia and this research could pave the way for TLR2-targeted therapies or adjuvants in future ZIKV vaccines, especially as population immunity wanes and the risk of re-emergence grows.



울릉바이러스 발견 및 유전체 특성 분석

이재연^{1,2}, 박경민^{1,3}, 김종우^{1,2}, 김성규^{1,2}, 송동현⁴, 구세훈⁴, 이승호⁴, 이대상⁴, 김원근^{5,6}, 송진원^{1,2*}

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한타바이러스는 인수공통감염병을 유발하는 RNA 유전체 바이러스이다. 제주바이러스(Jeu virus, JJUV)는 작은땃쥐를 자연 숙주로 하는 한타바이러스의 일종으로, 2012년 제주도에서 처음 발견된 이후 제주도와 내륙지역에서도 확인된바 있다. 동아시아에 분포하는 땃쥐는 대표적으로 국내에는 우수리 땃쥐, 작은땃쥐 등이 서식하며, 울릉도에도 땃쥐가 서식하는 것으로 알려져 있다. 울릉도는 약 500만~250만 년 전에 형성된 화산섬으로, 한타바이러스에 대한 연구는 아직 미비한 실정이다. 본 연구에서는 울릉도에 서식하는 땃쥐로부터 새로운 한타바이러스 유전체를 확인하고, 이를 울릉바이러스(Ulleung virus, ULLEV)로 명명하였다. 2009년 울릉도에서 땃쥐를 채집하고, 분자생물학적 진단법인 역전사중합효소연쇄반응법(RT-PCR)을 통해 바이러스 진단을 하였다. 울릉바이러스의 바이러스 유전체 서열을 확보하기 위해 차세대 염기서열 분석(NGS)을 수행하였으며, 얻은 유전체를 기반으로 지리계통학적 분석을 하였다. 땃쥐의 유전적 특성을 분석을 위해 cytochrome *b* 유전자를 이용한 하플로타입 분석을 실시하였다. 총 62마리의 땃쥐 중 40마리(64.5%)에서 ULLEV RNA가 검출되었다. NGS를 통해 ULLEV의 전장 유전체 1주와 CDS 유전체 서열 3주를 확보하였다. 울릉바이러스 유전체 서열을 통한 계통학적 분석 결과, 제주바이러스와는 84-86%의 염기서열 유사성을 보였으며, 제주바이러스와 유전적으로 독립된 계통(subtype)으로 분류됨을 규명하였다. 또한 cytochrome *b* gene을 활용한 하플로타입 분석을 통해 울릉도의 땃쥐는 유전적 흐름 없이 유전적으로 독립되어 진화해 왔으며, 기존의 작은 땃쥐와는 유전적으로 구별되는 독립된 계통임을 밝혔다. 본 연구는 울릉도 고유의 땃쥐에서 독자적으로 진화한 울릉바이러스를 발견한 연구이며, 고립된 섬 생태계에서의 바이러스 다양성과 숙주-바이러스 공진화의 가능성을 강조한다.

Molecular identification of severe fever with thrombocytopenia syndrome virus in deer ked: Implications for disease transmission

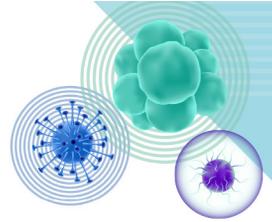
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Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV) is a highly pathogenic tick-borne virus that causes hemorrhagic fever in humans, with a mortality rate of up to 30 %. While ticks, particularly (*Haemaphysalis longicornis*, *Haemaphysalis flava*), are well-established as the primary vectors of SFTSV. A significant proportion of patients with confirmed SFTSV infection reported no history of tick bites, suggesting the existence of alternative vectors.

Here, we report the first detection of SFTSV RNA in deer ked (*Lipoptena fortisetosa*, family Hippoboscidae) using reverse transcription-PCR (RT-PCR) and in situ hybridization (ISH), marking the first identification of SFTSV within the class Insecta. Phylogenetic analysis revealed that the detected viral RNA belongs to Genotype B-3, the predominant strain in South Korea, and Genotype D. Although mere detection of viral RNA does not confirm transmission capability, in situ hybridization using RNAscope detected SFTSV-positive foci within the digestive tracts and in the male reproductive organs of the deer ked, indicating that these ectoparasites may not only harbor the virus but also support its replication, raising the possibility that they could act as biological vectors.

In conclusion, the detection of SFTSV in deer ked highlights the need for further investigation into their role in viral ecology and transmission dynamics. Determining whether deer ked serve as competent vectors or amplifiers of SFTSV requires continued surveillance and experimental studies. Given the potential public health implications, understanding their impact on SFTSV epidemiology in South Korea is critical for effective disease control and prevention strategies.



Coxsackievirus B3 mRNA vaccine against CVB3-induced myocarditis in mouse model

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Coxsackievirus B3 (CVB3) is the most common pathogen that causes human myocarditis and meningitis in children. However, a sufficient vaccine has not yet been developed due to the difficulty of creating a highly immunogenic antigen from the single-strand RNA genome. During the current COVID-19 pandemic, mRNA vaccines were developed and applied for pandemic-emergent conditions. To overcome the limitations of the previous vaccine system for CVB3, we developed a new mRNA vaccine using CVB3 VP1 and VP2 sequences to stimulate an immune response.

We designed an mRNA vaccine encoding the CVB3 capsid proteins VP1 and VP2. Protein expression was confirmed in HeLa cells by Western blot and immunofluorescence staining. Vaccine efficacy was evaluated in a mouse model of CVB3-induced acute myocarditis. Survival, tissue viral load, and inflammatory cytokines (TNF- α , IL-10) were confirmed using qPCR. Cellular immune responses (IFN- γ and IL-12-producing splenocytes) were examined by ELISpot. Neutralizing antibody production was tested in serum after vaccination. Vaccinated mice had improved survival and reduced viral replication in tissues. Reduced levels of inflammatory cytokines (TNF- α , IL-10) mRNA. Enhanced cellular immunity with significant increases in IFN- γ + and IL-12+ spleen cells (ELISpot). No detectable neutralizing antibodies were observed.

In this study, we observed the protective effect of a newly developed CVB3 mRNA vaccine. Further studies are needed to optimize immunogenicity and elucidate the mechanisms of immune protection of mRNA vaccines for CVB3 infection.

Cardiac-specific PDK4 deletion attenuates pyroptosis in CVB3-induced myocarditis model

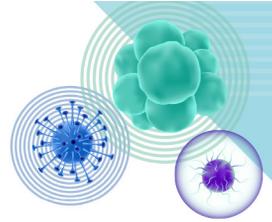
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Pyroptosis is a highly inflammatory form of lytic programmed cell death that typically occurs during infection with intracellular pathogens. Coxsackievirus B3 (CVB3) is one of the most common pathogens for acute myocarditis in humans. It may induce myocarditis and progress to dilated cardiomyopathy. Pyruvate dehydrogenase kinase 4 (PDK4) is a metabolic enzyme that regulates cell metabolism through mitochondrial function. PDK4 levels increased in the hearts of mice during CVB3 infection. We hypothesized that PDK4 inhibition may be an effective strategy to prevent pyroptosis in CVB3 infection.

Cardiac-specific conditional knockout (f/f) mice for PDK4 were generated using cardiac-specific modified estrogen-Cre mice. PDK4 knockout (KO) mice were injected intraperitoneally with tamoxifen (1mg/ml) for 5 days and then sacrificed 4 weeks later. Cardiomyocytes isolated from the heart were treated with 10^8 PFU of CVB3 for 1 hour. Heart protein and RNA were extracted and used for western blot and qPCR analysis. PDK4 protein and RNA were eliminated, and PDH phosphorylation was decreased in KO compared to wild-type (WT) cardiomyocytes. However, there was no change in mitochondrial oxidative phosphorylation (OXPHOS) complex proteins. Furthermore, the mitochondrial dynamics regulators (OPA1, MFN1, MFN2, DRP1) showed no significant difference between KO and WT cardiomyocytes. To investigate the inflammatory response induced by CVB3 infection, mice were injected with tamoxifen, and three weeks later, they were directly infected with 2×10^4 PFU of CVB3. Seven days after infection, RNA was extracted from the hearts of mice and used for qPCR. Innate immune response inflammation-related genes *Nlrp1*, *MyD88*, *Irf7*, *Slfn4*, and *SAA2* were significantly increased in KO mice compared to WT mice. In contrast, there was a notable decrease in the expression of cytokines associated with pyroptosis, including *IL-18*, *Caspase-1*, *Irgm1*, and *Gbp5*.

In this study, we successfully generated PDK4 knockout mice and provided strong evidence for the protective effects in CVB3 infection-induced pyroptosis. It will be valuable to investigate the mechanistic role of PDK4 in protecting mitochondrial function during virus-induced cardiac inflammation and cell death.



Evidence for G-Quadruplex-Mediated Transactivation by the Immediate-Early 2 Transactivator of Human Cytomegalovirus

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G-quadruplex (G4) formation in gene promoters regulates promoter activity either positively or negatively. Recent studies suggest that G4 can positively regulate promoter activation by acting as a structural element recruiting transcription factors. However, information on G4-mediated activation of viral promoters is limited. We recently showed that the 86-kDa immediate-early 2 (IE2) transactivator of human cytomegalovirus (HCMV) binds to a parallel G4 structure formed in the viral lytic replication origin, *oriLyt*, playing a critical role in initiating viral DNA replication. It was reported that the UL146 transcription is most significantly upregulated by IE2. Here, we present evidence that IE2 can transactivate the UL146 promoter by targeting G4. We found that the UL146 transcription was effectively suppressed by the treatment of a G4-binding ligand, NMM, during virus infection. A G4 motif was identified in the UL146 promoter. Circular dichroism spectroscopy and native gel electrophoresis analyses showed the stable formation of a parallel G4 by this motif. In G4 pull-down assays, IE2 bound to the G4, and NMM inhibited the IE2's G4 binding. In reporter assays, the G4 motif was essential for the UL146 promoter activity, and NMM treatment suppressed the IE2-mediated activation of the UL146 promoter. Furthermore, a recombinant virus containing G4-disrupting mutations showed significantly reduced transcription of UL146. Our results demonstrate that IE2 can transactivate the UL146-UL132 genes by binding G4s in the promoter during HCMV infection, suggesting that G4 may be a therapeutic target for controlling IE2-mediated transactivation during viral infection.

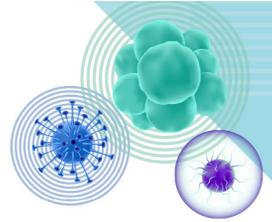
ZNF451 Promotes HSV-1 Replication Under ICP0-Deficient Conditions

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Herpes simplex virus type 1 (HSV-1) evades host antiviral defenses at the onset of infection by deploying its E3 ubiquitin ligase ICP0, which targets host restriction factors for proteasomal degradation. The cellular SUMO E3/E4 ligase ZNF451 catalyzes the poly-SUMOylation of antiviral proteins such as PML and RNF168. Since ICP0 predominantly recognizes and degrades poly-SUMOylated substrates, we hypothesized that ZNF451 may influence ICP0 target recognition and thereby modulate HSV-1 replication.

We found that ZNF451 protein levels decline during wild-type HSV-1 infection, but remain stable in cells infected with an ICP0-deficient mutant. Proteasome inhibition with MG132 blocked ZNF451 degradation, demonstrating that ZNF451 is targeted for proteasomal degradation during wild-type HSV-1 infection. In a doxycycline-inducible ZNF451 HaCaT cell line, overexpression of either wild-type ZNF451 or a SUMO-interaction motif mutant (L48A/V49A) did not affect wild-type virus yields, but significantly enhanced replication of the ICP0-deficient virus. Conversely, ZNF451 knockdown reduced replication of the ICP0-deficient virus. Immunofluorescence analysis revealed colocalization of ZNF451 and ICP0 in nuclear foci during infection, and co-immunoprecipitation confirmed a strong interaction with an ICP0-FXE mutant. These findings reveal a SUMOylation-independent role for ZNF451 in promoting HSV-1 replication in the absence of ICP0, providing mechanistic insight into host-virus interactions and highlighting the ZNF451-ICP0 axis as a potential target for modulating viral replication. [Grant: RS-2023-00270936]



HSV-1 UL36 stabilizes ICP0 Independent of its Deubiquitinase Activity

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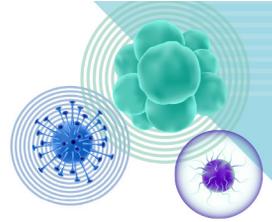
Herpes simplex virus type 1 (HSV-1) employs multiple strategies to evade host antiviral defenses and ensure efficient replication. In this study, we investigated the role of the viral deubiquitinase (DUB) UL36 in regulating the protein stability of ICP0, a key viral E3 ubiquitin ligase, during the early phase of infection. To this end, we engineered a recombinant HSV-1 in which UL36 expression is driven by the cytomegalovirus (CMV) promoter, enabling earlier expression compared to the wild-type virus. This early expression of UL36 resulted in more than a 10-fold increase in viral replication. Immunoblot analysis showed an increase in the expression of multiple viral proteins, including ICP0, in cells infected with the E.UL36 virus. Co-transfection assays demonstrated that UL36USP enhances the protein stability of ICP0 by reducing its auto-ubiquitination. Consistent with these findings, infection with the UL36-recombinant virus led to accelerated degradation of established ICP0 substrates such as PML, DNA-PKcs, and SLFN5. Interestingly, we also observed that UL36 could enhance ICP0 stability even in the absence of its DUB activity, suggesting a potential additional mechanism. Collectively, our findings suggest that UL36 contributes to HSV-1 replication not only through its deubiquitinating function but also by stabilizing ICP0, thereby supporting viral immune evasion and propagation. [Grant: RS-2023-00270936]

HP1BP3 is a histone-like G-quadruplex-binding protein that promotes Varicella-Zoster virus glycoprotein C expression and cell-free virion production

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G-quadruplexes (G4s) are non-canonical nucleic acid structures involved in various cellular processes. In the Varicella-Zoster virus (VZV) genome, G4 formation in ORF14, which encodes glycoprotein C (gC), suppresses gC expression at the transcriptional level, promoting viral cell-to-cell spread. However, whether this G4-mediated gC suppression is regulated remains unknown. Here, using G4 pull-down assays coupled with spectrometry analysis, we identified heterochromatin protein 1 binding protein 3 (HP1BP3) as a novel histone-related protein that binds to ORF14 G4s. HP1BP3 increased transcription of ORF14 but not its G4-disrupted mutant (G4m). HP1BP3 reduced G4 formation in ORF14. An HP1BP3 mutant defective in HP1 α binding retained its ability to bind G4s and upregulate gC transcription, indicating HP1 α -independent activity. HP1BP3 knockdown increased viral gene expression and production of progeny virions, indicating an overall negative role of HP1BP3 in viral growth, but decreased the ORF14(gC)/ORF68(gE) mRNA ratio, demonstrating its requirement for efficient gC transcription. This effect of HP1BP3 knockdown was mitigated in ORF14(G4m) virus infection, further supporting that HP1BP3 regulates gC expression by targeting G4s. Moreover, HP1BP3 levels in different cell types correlated with cell-free virion production. Our results uncover a novel G4-binding and -unwinding activity of HP1BP3 that upregulates gC expression and promotes cell-free virion production during VZV infection.



CRISPR-Cas9-Mediated Integration of the Auxin-Inducible Degron System into VZV ORF61 for Controlled Protein Degradation

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Varicella-zoster virus (VZV) is an alphaherpesvirus with a double-stranded DNA genome that establishes latency in sensory nerve cells. The cell-associated nature, strict host specificity, and slow replication of VZV make clinical isolation and genetic manipulation challenging, imposing significant constraints on research. Conventional bacterial artificial chromosome (BAC)-based cloning methods have several limitations, including time-consuming cloning and recovery processes, low replication efficiency in cells, and an inability to accurately reflect the genetic diversity of clinical isolates. To overcome these limitations, more precise and efficient genetic engineering tools are required. Here, we introduce a system that combines CRISPR-Cas9 genome editing and auxin-inducible degron (AID)-mediated temporal protein regulation to address the challenges of genetic manipulation in cell-associated VZV. We performed whole-genome sequencing of clinical VZV isolates from patient samples and applied CRISPR-Cas9 together with the AID system to precisely investigate viral gene functions. CRISPR-Cas9 technology enables the targeted integration of a degron system into the genome of a clinical VZV isolate in less than two weeks, without the need for extensive viral rescue procedures. The AID system allows accurate temporal control of viral protein expression, facilitating targeted protein degradation at defined experimental time points. Additionally, we integrated a fusion protein composed of an AID tag, a self-cleaving P2A peptide, and GFP (AID-P2A-GFP) into the viral genome of clinical isolates, enabling fluorescent tracking and inducible protein degradation. This study establishes a robust platform for the functional characterization of essential VZV genes and detailed mechanistic studies of viral pathogenesis. This platform also provides a foundation for future studies aimed at exploring therapeutic strategies and developing attenuated strains suitable for clinical investigation. This platform also provides a foundation for future studies aimed at exploring therapeutic strategies and developing attenuated strains suitable for clinical investigation. [RS2023-00270936]

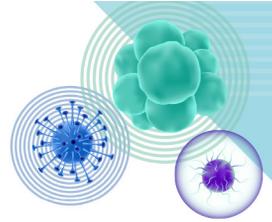
A comprehensive analysis of human microglial models to evaluate the pathogenesis of Varicella Zoster Virus

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Varicella zoster virus (VZV) is a human neurotropic virus that can establish latency in sensory neurons. Microglia play a complex role in the neuropathogenesis of viral infections; however, their role during VZV infection remains to be determined. In the present study, we explored the role of VZV-induced alterations in the morphodynamics and function of microglia in triggering neuroinflammation. We prepared cell-free VZV and compared the replication efficiencies of wild-type (YC01) and attenuated (MAV) using various microglial cell lines as well as embryonic stem cell derived human microglia to comprehensively analyze microglial gene signatures, phenotype and function. Bulk RNA sequencing was used to assess the molecular signatures of microglia following VZV infection in ESC-MG cells, and cytokine profiles were determined to further investigate neuroinflammation. VZV effectively replicated in the microglia and increased their phagocytic activity by upregulating the expression of several phagocytic receptors. Notably, transcriptomic analysis of YC01-infected microglia revealed the upregulation of differentially expressed genes linked to neuroinflammation, including interleukin-6 and -8. In this study, we show for the first time that multiple human microglia cell culture can be directly infected by VZV and VZV infection in microglia induces structural and functional shifts in microglia, which may contribute to sustained neuroinflammatory states and long-term neuronal dysfunction.

The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.



First Report and Genomic Characterization of Parahenipavirus Langya virus in *Crocidura lasiura*, Republic of Korea

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Within the genus *Parahenipavirus*, the only species reported to be zoonotic is Langya virus (LayV). Since its discovery, no additional LayV detections have been reported outside of China. In the Republic of Korea, the presence of *Parahenipavirus* species has been indicated by the identification of Gamak virus and Daeryeong virus in shrews. Virus surveillance of shrew populations was conducted to uncover other *Parahenipavirus* species.

We reanalyzed the metagenomic raw reads from our previous study in 2017. We then performed RT-PCR for paramyxovirus screening on RNA extracted from kidney tissue of *Crocidura lasiura* collected in 2023. Positive samples proceeded to partial genome sequencing. The complete viral sequences obtained from *de novo* assembly and reference-based mapping of metagenomic data were used as templates for designing an amplicon-based primer set. The positive RNA from 2023 was processed with tiled PCR and sequenced using Oxford Nanopore Technology. The amplicon-based sequencing raw reads were then mapped to the complete genome sequence obtained from the previous metagenomic analysis. Complete genomes were further characterized by phylogenetic analysis and amino acid similarity.

Analysis of the 2017 metagenomic data resulted in two complete paramyxovirus genomes, exhibiting approximately 80% and 95.5% homology at the nucleotide and amino acid levels, respectively, with LayV. Paramyxovirus screening of the 2023 samples showed a 62.5% positivity rate, and three out of fifteen partial sequences were closely related to LayV. Subsequently, tiled PCR generated three additional partial complete viral genomes. Phylogenetic analysis demonstrated a close evolutionary relationship between LayV strains from the Republic of Korea and China.

This is the first report of LayV outside China, highlighting the cross-border circulation of emerging *Parahenipavirus*.

In Vitro and AI-based Antiviral Study of Tabamide A Derivative TA25 Using Lung Organoid Model for Human Rhinovirus

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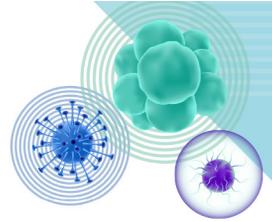
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Human rhinovirus (HRV), a common cause of the common cold, was first isolated in 1956. However, there are no FDA-approved anti-viral or anti-inflammation drugs against for HRV. HRV causes mild symptoms, but also causes severe respiratory disease such as asthma, chronic obstructive pulmonary disease (COPD) and pneumonia. TA25 is a phenolic amide isolated from the leaves of *Nicotiana tabacum*. In this study, the antiviral and anti-inflammatory activities of TA25 were evaluated against HRV. The reduction of viral amplification was confirmed in TA25-treated cells by virus genome strand-specific RT-qPCR. Additionally, the interaction of HRV 2B protein and TA25 was computationally examined by AI-driven structure-based analysis. Moreover, TA25 showed the broad-spectrum antiviral activity against multiple viruses, including HRV-1A, Zika virus, Dengue virus, Influenza B virus, and Vaccinia virus. Lung organoids (LOs) from embryonic stem cells were developed with expression of alveolar genes. Additionally, optimal condition of HRV-B14 infection was confirmed in LOs. In conclusion, TA25 demonstrated antiviral and anti-inflammation activities against HRV. This study provides insights into a potential candidate of TA25 for antiviral therapeutics against human rhinovirus as well as zoonotic viruses.



Development of pan-coronavirus novel SARS-CoV-2 antiviral using phenotypic high-throughput screening

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The Coronavirus disease (COVID-19), caused by the SARS-CoV-2 virus, has resulted in over 778 million confirmed cases and more than 7 million deaths worldwide since its emergence in China in December 2019. In light of the global COVID-19 pandemic, several small-molecule antiviral drugs, such as Paxlovid, Remdesivir, and Molnupiravir, have been introduced as responses to this crisis. However, the continuous evolution of coronaviruses and the increasing resistance to clinically used drugs underscores the need for novel small-molecule therapeutics.

In this work, we performed a phenotypic high-throughput screening campaign of our medicinal chemistry's proprietary library and identified several thiazoleamide derivatives exhibiting moderate antiviral activity against ancestral SARS-CoV-2 in Vero E6 cells. This research presents our ongoing efforts to develop a pan-coronavirus small molecule drug. To elucidate potential target proteins, we utilized the Hyper Lab program from HITS to calculate binding energies to predict candidate target proteins involved in the RNA virus life cycle.

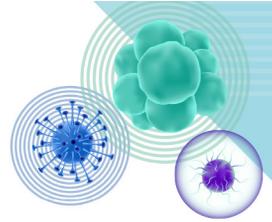
Based on the findings, the thiazoleamide derivatives demonstrate the strongest binding affinity for the 3CLpro protein, highlighting it as a promising primary target. Our ultimate goal is to advance these lead candidates by optimizing their drug-like properties as a potential oral drug.

Analysis of SARS-CoV-2 spike mutations in immunocompromised patients: canonical and non-canonical immune escape mechanisms

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Immunocompromised patients with persistent SARS-CoV-2 infections serve as reservoirs for viral evolution due to prolonged selective immune pressure. Accumulating evidence suggests that viral mutations arising in these hosts contribute to the emergence of immune-evasive variants and provide valuable insights into viral adaptation and therapeutic susceptibility. We previously performed whole genome sequencing on SARS-CoV-2 samples from 13 immunocompromised patients infected with BA.1, BA.2, or BA.5 lineages, identifying multiple spike mutations not commonly observed in circulating strains. To evaluate their functional impact, we generated recombinant SARS-CoV-2 variants encoding patients-derived spike mutations using a BA.1 reverse genetics system. We assessed the neutralization sensitivity of these engineered variants against five monoclonal antibodies-Adintrevimab (ADI), Bectelovimab (BEB), Cilgavimab (CIL), Romlusevimab (ROM), Sipavibart (SIP)-which are known to retain activity against the BA.1 wild type. The recombinant viruses exhibited both canonical and non-canonical escape phenotypes. Notably, we observed strong resistance to some therapeutics-ADI, BEB, CIL, and ROM, while Sipavibart retained partial activity. Our findings emphasize the role of prolonged infections in shaping diverse antibody resistance profiles and highlight the need to monitor non-circulating variants, particularly those arising in immunocompromised hosts. Incorporating both epitope-dependent and epitope-independent pathways into antibody surveillance and design may enhance preparedness against future therapeutic failures.



호흡기 5

The DPP4-utilizing MERS-related bat coronavirus B20-180 may potentially exhibit enhanced cell entry through recombination and modification of the furin cleavage site

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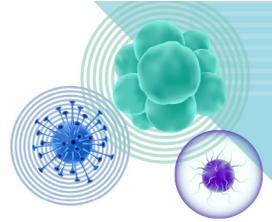
In the early 21st century, three major pandemics—SARS, MERS, and COVID-19—were caused by zoonotic betacoronaviruses likely originating from bats. Understanding how these viruses adapt to human hosts is essential for predicting and preventing future outbreaks. In this study, we characterized two MERS-related bat coronaviruses: B20-180, identified in *Rhinolophus ferrumequinum*, and B24-268G, a newly discovered HKU5-like strain from *Pipistrellus abramus* in Korea. Using biochemical binding assays and pseudovirus-based entry models, we found that B20-180 can utilize both bat and human DPP4 receptors for cell entry, with its infectivity enhanced through recombination in the receptor-binding domain and acquisition of a furin cleavage site (FCS). Although B24-268G did not bind to DPP4 and ACE2, the presence of multiple FCSs (S1/S2 and S2') suggests a potential for recombination with B20-180. While no serological evidence of human exposure to B20-180 has been found among cave-exposed individuals in Korea to date, multiple FCSs of B24-268G highlight the importance of continued surveillance for possible recombination events between these viruses.

국내 영아 폐렴 환자에서 확인된 신종 인간 코로나바이러스

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코로나바이러스(Coronaviruses, CoVs)는 다양한 임상 증상과 경과를 유발하며, 공중보건에 중대한 위협이 되고 있다. 일부 인간 코로나바이러스(Human CoVs, HCoVs)는 세계적 유행을 초래한 바 있으며, 그 외에도 HCoVs는 호흡기 감염 환자에서 빈번히 검출된다. 그러나 알파코로나바이러스는 상대적으로 낮은 유병률과 치명률로 인해 지금까지는 제한적인 관심을 받아왔다. 본 연구에서는 폐렴 증상을 보인 영아 환자로부터 비인두도말 및 혈청 검체를 수집하고, 역학조사를 수행하였다. 환아는 2022년 12월 15일, 발열, 기침, 가래, 콧물 등의 증상으로 입원하였고, 입원 당시 인간 파라인플루엔자바이러스 1형(human parainfluenza virus 1)과 라이노바이러스(rhinovirus) 동시 감염이 확인되었다. 입원 4일째, AST 및 ALT 수치가 각각 462 IU/L와 350 IU/L로 상승하여 일시적인 간기능 이상이 동반되었으며, 이는 호흡기 바이러스 외의 다른 병원체와의 연관 가능성을 시사하였다. 이후 메타게놈 차세대 염기서열분석법(metagenomic next-generation sequencing, mNGS)을 통해 해당 환자의 비인두도말 및 혈청 시료에서 새로운 인간 알파코로나바이러스(HCoV KUMC22-3)가 동정되었다. 이에 따라 2018년부터 2022년까지 국내에서 포획된 설치류 880개체를 대상으로 코로나바이러스의 분자 유병률을 조사하고, 계통유전학적 분석을 실시하였다. 그 결과, 새롭게 확인된 HCoV는 대한민국 및 중국에서 *Apodemus* spp.로부터 검출된 알파코로나바이러스들과 높은 유전적 유사성을 나타냈다. 이 사례는 mNGS 기반 분석이 신종 병원체 탐지에 효과적인 도구임을 보여주며, 새롭게 발견된 HCoV가 간기능 이상과 같은 비호흡기계 증상과 연관될 가능성을 제기한다. 본 바이러스의 임상적 의미, 유행역학적 특성 및 인수공통감염 가능성을 규명하기 위한 후속 연구가 필요하다.



Antisense Oligonucleotide Targeting Nipah Virus and Efficacy Evaluation Using a Fluorescent Reporter Cell System

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Nipah virus (NiV; species *Henipavirus nipahense*) is a highly pathogenic, zoonotic paramyxovirus that causes severe respiratory illness and fatal encephalitis in humans. With a high case-fatality rate and potential for human-to-human transmission, NiV is classified by the World Health Organization as a priority pathogen with pandemic potential. Despite this threat, no approved antiviral therapies or vaccines currently exist, underscoring the urgent need for innovative antiviral strategies. Antisense oligonucleotides (ASOs) are short strands of DNA, RNA, or chemically modified nucleotides that bind target RNA via Watson-Crick base pairing to modulate gene expression. Among them, Gapmer ASOs recruit RNase H upon hybridization, resulting in cleavage and degradation of the target RNA. ASO-based approaches have shown therapeutic potential in targeting viral RNA, including in SARS-CoV-2. In this study, we designed and synthesized Gapmer ASOs targeting NiV RNA using solid-phase synthesis. To assess their efficacy against NiV RNA, we developed a fluorescent reporter system by inserting NiV RNA fragments into a reporter construct and generating a stable A549 cell line expressing the system. This model enables both monitoring and screening of candidate ASOs' activity. RT-qPCR and flow cytometry analyses confirmed that the designed ASOs effectively bind and degrade the NiV RNA fragments in cells. The selected ASOs warrant further validation and safety assessment as potential therapeutics. Moreover, the ASO design and reporter platform established in this study may provide a foundation for developing ASO-based antiviral therapies targeting NiV and other emerging respiratory viruses.

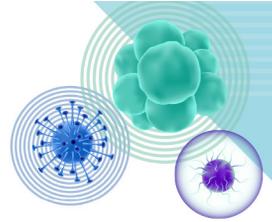
This research was supported by the National Institute of Health(NIH) research project(project No.2024-ER1605-00 and 2025-ER1607-00)

Distinct Gene Expression Profiles Associated with Respiratory Syncytial Virus (RSV) Infection in Humans

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Respiratory syncytial virus (RSV) causes severe respiratory illness in infants, the elderly, and those with chronic lung disease. Although vaccines and preventive antibodies are now available, effective treatments for established infection remain limited. RSV infection begins in the respiratory tract, primarily targeting airway epithelial cells that serve as the first line of defense against pathogens. As the virus spreads from the nasal passages to the lower respiratory tract, it replicates within both upper and lower airway epithelial cells, leading to inflammation, epithelial damage, mucus overproduction, impaired ciliary function, and ultimately exacerbated disease severity. Systems biology approaches, including transcriptomic profiling, have provided valuable insights into virus-specific molecular pathways and host responses. In particular, age-specific transcriptional analysis is critical for understanding RSV pathogenesis, as gene expression and signaling dynamics vary across age groups. To further investigate this, we analyzed publicly available transcriptional profiling datasets from RSV-infected patients across different age groups. Through this analysis, we identified age-specific upregulated gene targets and further extracted commonly elevated genes shared across age groups. In infants and children, MMP8, IFI27, STAT1, CXCL10, DEFA1, DEFA3, ARG1, OLFM4, and CD177 were commonly upregulated; in children and adults, MMP9 and RSAD2; and in infants and adults, GBP-1 and MPO. We then examined the correlations among these shared genes and validated their relevance by applying viral replication inhibitors during infection. This integrative analysis, grounded in patient-derived transcriptomic data, identified conserved antiviral gene signatures, offering potential targets for the development of broadly applicable RSV therapeutic strategies.



Development of a Broad-Spectrum DNA Vaccine Against Influenza A Viruses Using Baculoviral Gene Delivery System

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Influenza viruses continue to pose a persistent global health threat due to their rapid antigenic variation, which can lead to the emergence of new pandemics. Currently available egg- and cell-based influenza vaccines are reformulated annually based on predictions of circulating strains. However, these vaccines exhibit limited cross-reactivity, resulting in reduced effectiveness against novel influenza viruses and often failing to provide sufficient protection during emerging pandemics. To overcome these limitations, various research fields are actively developing new vaccine platforms and universal influenza vaccines.

In this study, we developed a novel DNA vaccine, AcHERV-H5-ConA, which encodes the hemagglutinin (HA) of H5N1, three matrix-2 (M2) regions derived from H1N1, three conserved HA2 domains, and nucleoprotein (NP) antigens. This recombinant baculovirus is enveloped with a human endogenous retrovirus (HERV) membrane to enhance cellular entry and DNA delivery efficiency. After confirming efficient intracellular delivery and antigen-specific expression of AcHERV-H5-ConA, BALB/c mice were intramuscularly immunized with 6×10^7 FFU.

Sera from immunized mice exhibited strong humoral immune responses and antibody-dependent cellular cytotoxicity (ADCC) against H1N1, H3N2, and H5N2 influenza viruses. In addition, splenocytes from vaccinated mice secreted high levels of interferon-gamma, indicating robust cellular immune responses. In viral challenge experiments evaluating protective efficacy, vaccinated mice showed significantly increased survival rates and reduced lung viral titers compared to the control group.

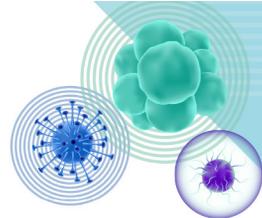
These findings demonstrate that AcHERV-H5-ConA effectively delivers antigenic DNA and elicited strong and broad-spectrum immune responses against influenza A viruses.

Potential of Avian Paramyxovirus Type 14 as a Viral Vector

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One of the main challenges with the viral vector platform is pre-existing antibodies against the vector virus itself. Avian Paramyxoviruses (APMVs) are primarily detected in wild birds and rarely infect humans, with the exception of APMV type 1, the Newcastle disease virus, which can occasionally infect humans. The use of different avian paramyxovirus types may provide a strategy to circumvent pre-existing antibodies that may impair viral vector efficacy, owing to their ability to infect diverse host cells by utilizing sialic acid-containing receptors. We isolated an APMV type 14 and passed it 60 times in embryonated eggs. The egg-adapted APMV-14 replicated to a high titer in eggs but caused minimal weight loss in mice compared to the wild type APMV-14. We constructed an infectious clone of the egg-adapted APMV-14 and inserted a GFP reporter gene into the N-P intergenic site to evaluate its potential as a viral vector. The ability of APMV-14 to deliver external proteins was confirmed through GFP expression in Vero cell, and the signal was further enhanced by including the viral UTR sequences flanking the GFP gene. In mice, we confirmed that the recombinant APMV-14 can efficiently deliver a transgene (luciferase gene) and that inclusion of flanking UTR sequences enhances more sustained reporter expression. Further studies are required to evaluate its efficacy as a viral vector for vaccines, including assessments of immunogenicity and protective efficacy.



Codon Optimization Strategies and Immunogenicity Comparative Study for Optimal mRNA Vaccine Candidate Discovery Against SARS-CoV-2 Omicron KP.2 Variant

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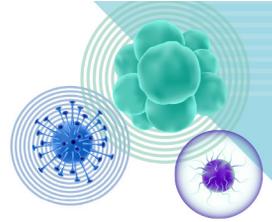
The KP.2 strain, a descendant of SARS-CoV-2 JN.1, was designated as a Variant Under Monitoring (VUM) by the WHO in 2024 owing to its enhanced transmissibility, infectivity, and immune evasion capabilities. The mRNA vaccine platform has garnered significant attention as a rapid and effective countermeasure against continuously evolving viral variants. The mRNA vaccine technology enables the expeditious development of enhanced-efficacy vaccines against diverse antigens through codon optimization as a pivotal strategy. This study aimed to compare codon optimization strategies developed to enhance spike protein immunogenicity and identify optimal vaccine candidates against the KP.2 variant. We designed and evaluated three mRNA vaccine candidates based on the KP.2 spike protein: 2P incorporating two proline substitutions, 2P-2 with additional structural stabilization modifications applied to the 2P construct and 6P featuring six proline substitutions. Immunological evaluation in preclinical models demonstrated that all three candidates elicited significantly enhanced antibody responses and antigen-specific cellular immunity compared to the wild-type construct. These findings indicate that strategic codon optimization of the spike protein can augment mRNA vaccine efficacy, and such mRNA platform-based codon optimization strategies may facilitate rapid responses to emerging variants, enabling optimal antigen selection for future vaccine development.

Simulating Evolution of Coronavirus Spike Gene with Random Mutation and Similarity-Based Selection

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Viruses evolve rapidly through random mutations and selective pressures, driving adaptation and cross-species transmission. We present a graphical user interface (GUI)-based simulation framework that models the stepwise evolution of a viral sequence toward a predefined target using random mutation and similarity-based selection. In each replication cycle, the framework generates multiple mutated replicates and selects the top-N amino acid sequences with the highest similarity to advance to the next cycle. Simulations of SARS-CoV-2 Wuhan-Hu-1 toward the Omicron variant (BA.1) revealed plateau-like similarity trends, with higher substitution rates accelerating progression toward the plateau. The resulting intermediate spike sequences reflected real-world evolutionary patterns, with many classified into historical lineages such as B, B.1.2, B.1.160, B.1.398, B.1.1.529, and BA.1. The same approach reproduced distinct evolutionary pathways of experimentally passaged porcine epidemic diarrhea virus (PEDV) under trypsin-treated and untreated conditions. This accessible, GUI-based tool enables the exploration of plausible evolutionary trajectories and the identification of potential intermediate forms, offering insights into viral adaptation and zoonotic emergence. Planned enhancements—including recombination modeling, population dynamics, and additional biological constraints—will further expand its predictive capabilities.



Isolation of a SARS-CoV-2 strain from pediatric patients in South Korea: Biologic and genetic characterization

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A SARS-CoV-2, N15 strain was successfully isolated from the nasal swab of a pediatric patient after five blind passages in Vero cells. The biological properties of this isolate were investigated extensively. Cytopathic effects (CPE) were observed within 48 hours post-infection, characterized by aggregates of dead cells. The N15 isolate demonstrated the ability to replicate across various human-derived cell lines with different growth kinetics. Genetic analyses revealed that the strain belongs to the 19B lineage of SARS-CoV-2, showing 99.9% similarity to the original Wuhan 1 strain. Importantly, the N15 strain possessed rare mutations N709S in the spike protein and T11M in the E protein. Drug testing indicated that Remdesivir, Molnupiravir, and Nirmatrelvir effectively inhibited this isolate at varying concentrations. The N15 isolate may serve as a valuable material for comparative studies with currently circulating SARS-CoV-2 variants.

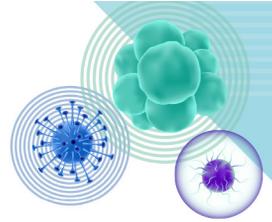
This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant (No. 2020R1I1A1A01054539) and by the Korea Research Foundation Grant funded by the Korean Government (NFR-2019R1A6A1A03032869).

Regulation of ISG15 secretion by the SARS-CoV-2 proteins through the LC3-derived secretory pathway

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The ISG15 protein encoded by *Interferon-Stimulated Gene 15* is a ubiquitin-like protein that can be covalently conjugated to a target protein. ISG15 modification of proteins (ISGylation) plays a role in host defense. ISG15 is also secreted outside of cells and acts as a cytokine. During severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, ISGylation is largely limited due to the deISGylating activity of the virus-encoded papain-like protease (PLpro). PLpro has been shown to increase the accumulation of free ISG15 within the cell, promoting its secretion out of the cell. However, whether other viral proteins directly regulate ISG15 secretion is not known. In this study, the SARS-CoV-2 proteins that regulate ISG15 secretion were identified. As in interferon- β -treated Calu-3 and A549 cells, ISG15-overexpressing 293T cells secreted ISG15. Co-transfection assays performed in 293T cells with ISG15 and 26 viral proteins indicated that seven viral proteins, such as NSP2, NSP6, ORF3a, ORF3b, membrane (M), ORF7a, and ORF7b upregulate ISG15 secretion, while three viral proteins, such as NSP13, NSP14, and ORF6, downregulate it. ISG15 is secreted in SARS-CoV-2-infected macrophages via an unconventional, LC3-derived secretory pathway. Among these ten viral proteins screened, NSP6, ORF3a, M, and ORF7a increased the accumulation of LC3B-II within the cell, while NSP14 reduced it, suggesting that these viral proteins act on the early steps in the LC3-derived secretory pathway. LC3B depletion with small hairpin RNAs diminished the ISG15 secretion-promoting activity of NSP2, NSP6, ORF3a, ORF3b, M, and ORF7a but not ORF7b, suggesting that NSP2 and ORF3b may act on the other steps of the LC3-derived secretory pathway and that ORF7b may promote the ISG15 secretion by an as-yet-unknown mechanism. In summary, these results demonstrate that the ISG15 secretion is regulated by the SARS-CoV-2 proteins primarily through the LC3-derived secretory pathway.



Unmodified UTP mRNA Vaccine Provides Rapid and Superior Protection Against Canine H3N2 Influenza

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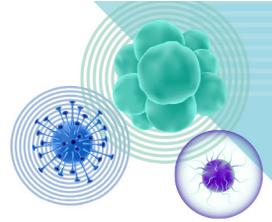
mRNA vaccines represent a versatile platform for both cancer immunotherapy and the prevention of infectious diseases. While modified nucleosides such as N1-methyl- pseudouridine (m1 ψ) are conventionally employed to mitigate innate immune recognition of exogenous mRNA, we devised a codon optimization strategy that enables robust antigen expression and antigen-specific immune responses using unmodified UTP-based mRNA, thereby eliminating the need for nucleotide modification. We engineered coding sequences for E7 of HPV16 and OVA according to four criteria. Based on these sequences, we produced mRNA and analyzed it in various ways. Interestingly, Two of them exhibited differential RNA secondary structures, transcriptional efficiencies, antigen expression levels and immunogenicity. Subsequently, we applied this codon optimization strategy to develop a unmodified mRNA vaccine encoding hemagglutinin (HA) from the H3N2 subtype of Canine Influenza Virus. This vaccine induced a strong cellular immune response and excellent protective efficacy in mice, and in particular, it caused faster virus clearance compared to commercial inactivated vaccines. The excellent immunogenicity of this vaccine was further demonstrated in a dog model. Collectively, our findings demonstrate that rational codon optimization of unmodified mRNA can substantially improve immunogenicity and protective performance, offering a cost-efficient and immunologically effective strategy for the development of next-generation mRNA vaccines.

Diverse bat organoids provide pathophysiological models for zoonotic viruses

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Bats are well-recognized natural reservoirs of diverse zoonotic viruses, yet in vitro models to study bat-virus interactions remain scarce. To address this limitation, we established a comprehensive organoid platform derived from the trachea, lung, small intestine, and kidney tissues of five insectivorous bat species. These organoids faithfully recapitulated the cellular composition and architecture of their tissues of origin, as demonstrated by multiplexed immunohistochemistry and single-cell RNA sequencing analyses. Infection of these organoids with representative zoonotic viruses including coronaviruses, influenza viruses, and paramyxoviruses allowed us to evaluate viral tropism and host responses, revealing distinct species- and tissue-specific patterns of viral replication and innate immune responses. Furthermore, we successfully isolated and characterized a novel mammalian orthoreovirus from bat fecal samples using this platform. The platform also facilitated rapid antiviral drug screening. Altogether, our bat organoid system provides a reliable in vitro model for investigating host-virus interactions and for the isolation and characterization of zoonotic viruses.



Persistent Immune Imbalance in Post-Acute Sequelae of SARS-CoV-2: Neutrophil-Driven Pathology and Therapeutic Strategies from a *P. roborovskii* Hamster Model

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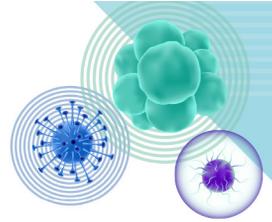
Post-acute sequelae of SARS-CoV-2 (PASC), characterized by long-term symptoms such as fatigue, respiratory dysfunction, and cognitive impairment, affects at least 10% of COVID-19 patients. However, its underlying pathophysiology remains poorly understood. To investigate the long-term effects of SARS-CoV-2 infection, we employed the *Phodopus roborovskii* hamster as an animal model, comparing outcomes following infection with SARS-CoV-2 and H1N1 influenza A virus (IAV). Among SARS-CoV-2-infected survivors, 13.75% exhibited delayed recovery, pronounced pulmonary injury, and persistent weight loss, and were designated as the PASC group. Single-cell transcriptomic profiling of bronchoalveolar lavage fluid, lung, and spleen tissues at 30 days post-infection (dpi) revealed PASC-associated gene signatures specifically enriched in the PASC group. Notably, the PASC group displayed pronounced neutrophil infiltration alongside reduced macrophage populations, indicative of skewed myeloid cell differentiation. Immunohistochemical analysis confirmed persistent SARS-CoV-2 spike S1 antigen in the lungs of PASC hamsters at 30 dpi, co-localizing with dense neutrophilic infiltrates. Neutrophils from the PASC group showed prolonged expression of inflammatory genes such as *FPR2*, *MMP9*, and *S100A9*, linked to neutrophil degranulation and extracellular trap formation. Targeted inhibition of neutrophil-associated pathways, particularly with the neutrophil elastase inhibitor Sivelestat, effectively reduced neutrophilic inflammation, PASC incidence, and mortality. Our findings implicate persistent neutrophil activation as a key driver of PASC pathogenesis and suggest neutrophil-targeted therapies as promising strategies to alleviate chronic complications following SARS-CoV-2 infection.

Liquid-liquid phase separation mediated immune evasion of respiratory syncytial virus against oligoadenylate synthetase-RNase L pathway

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Respiratory syncytial virus (RSV) infection is the major cause of severe respiratory illnesses in infants and older adults. RSV forms phase-separated biomolecular condensates called inclusion bodies (IBs), which serve as hubs for viral replication. However, the contribution of IBs to host immune response evasion remains elusive. We report that RSV IBs protect viral RNA from the 2'-5' oligoadenylate synthetase (OAS)-RNase L pathway, a critical antiviral defense mechanism that cleaves viral and cellular RNAs. RSV infection did not activate the OAS-RNase L pathway, and ectopically activated RNase L did not suppress viral replication. In RSV-infected cells, double-stranded RNA (dsRNA) was efficiently sequestered within liquid-liquid phase separation (LLPS)-mediated IBs, rendering its detection challenging. LLPS perturbation caused dsRNA release from IBs into the cytosol. dsRNA extracted from infected cells, which lacked LLPS shielding, triggered OAS-RNase L pathway activation. Thus, LLPS-driven IBs structurally sequester viral RNA, facilitating RSV to evade RNase-dependent genomic RNA degradation mediated by the OAS-RNase L antiviral pathway.



Dose-Dependent Modulation of mRNA Vaccine Expression and Immune Response by dsRNA Contamination

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Double-stranded RNA (dsRNA), a primary contaminant in in vitro transcription (IVT) mRNA production, can compromise the safety and efficacy of mRNA vaccines by inducing unintended immune responses. This study investigates the impact of dsRNA contamination on mRNA expression and immunogenicity to emphasize the importance of dsRNA purification in vaccine development. mRNA was synthesized via IVT using uridine and N1-methyl-pseudouridine nucleosides, followed by cellulose purification to assess residual dsRNA levels. To systematically evaluate the effects of dsRNA contamination, purified mRNA was supplemented with increasing concentrations of dsRNA. In vivo studies in mice revealed that higher dsRNA concentrations correlated with enhanced innate immune responses, characterized by elevated pro-inflammatory cytokine production and decreased mRNA expression, regardless of the nucleoside composition used in IVT mRNA synthesis. Dosing-dependent dsRNA gradients were incorporated into mRNA encoding influenza hemagglutinin (HA) antigen to distinguish between expression-related and specific immune responses. Results showed a decline in antibody titers and T cell-mediated immunity as dsRNA concentrations in HA mRNA increased, further highlighting the detrimental impact of dsRNA contamination on mRNA vaccine efficacy. This study underscores the critical importance of minimizing dsRNA impurities in IVT mRNA to ensure controlled immune responses and develop safer, more effective mRNA treatments. By systematically evaluating the dose-dependent effects of dsRNA contamination on mRNA expression and immune responses, this research provides valuable benchmarks for optimizing mRNA production and purification strategies, potentially advancing the field of mRNA vaccine development.

Cholesterol Sulfate Restricts SARS-CoV-2 Infection by Modulating Intracellular Cholesterol Trafficking and Autolysosome Formation

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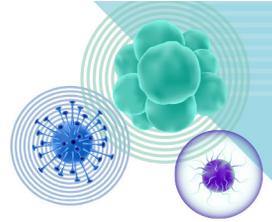
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Emerging SARS-CoV-2 variants challenge the efficacy of vaccines and neutralizing antibodies, highlighting the need for host-targeted antiviral strategies. Genome-wide CRISPR screens have identified cholesterol metabolism as a critical host pathway required for viral infection. Cholesterol-rich membranes facilitate multiple stages of the viral life cycle, including entry, replication, and egress.

Cholesterol sulfate (CS), a naturally occurring sterol sulfate, has been suggested to negatively regulate intracellular cholesterol. Patients with X-linked ichthyosis (XLI), a disorder caused by steroid sulfatase (STS) deficiency, exhibit elevated plasma CS levels. We show that CS displays broad antiviral activity against SARS-CoV-2 in vitro and in K18-hACE2 transgenic mice. CS disrupts intracellular cholesterol trafficking, leading to cholesterol accumulation in lysosomes and inhibition of SREBP2 activation. These changes reduce total and plasma membrane cholesterol levels, impairing viral entry and replication.

In addition, CS promotes autolysosome formation by reversing SARS-CoV-2-induced blockade of autolysosome maturation, a process shown to be essential for viral egress via the lysosomal exocytosis pathway. Furthermore, Irosustat, an STS inhibitor that elevates circulating CS levels, enhances the antiviral effect of CS.

These findings identify cholesterol sulfate as a host-directed antiviral agent that impairs both cholesterol-dependent viral entry and lysosome-mediated viral egress, offering a promising therapeutic strategy against SARS-CoV-2.



Development of a Broad-Lineage, REASSURED-Compliant Rapid Diagnostic Test for Lassa Virus Using Optimized Monoclonal Antibody Pairs

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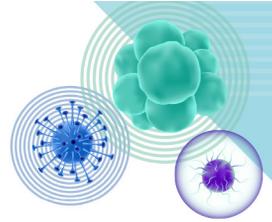
Lassa fever is a severe viral hemorrhagic disease endemic to West Africa, where rapid and accurate diagnosis is essential for controlling outbreaks. Current diagnostic tools often show inconsistent performance and limited sensitivity, underscoring the need for improved Lassa virus detection methods. In this study, we developed a lateral flow-based rapid diagnostic test (RDT) targeting the Lassa virus nucleoprotein (NP) using newly generated monoclonal antibodies. Candidate antibodies were assessed for binding affinity, epitope specificity, and assay performance, leading to the selection of the optimal pair, 1P-44-7/9B-28, for RDT construction. The assay's analytical performance was evaluated with human serum and plasma samples, inactivated viral strains, and benchmarked against existing commercial assays. The finalized RDT achieved a limit of detection of 0.98 ng/mL and demonstrated 100% specificity in a panel of 60 human samples. It detected all five major Lassa virus lineages, although analytical sensitivity varied by lineage. The Josiah strain was consistently identified at Ct values of 17–18, while other lineages—Togo, NJ2015, NGR, and SLE Niahun—were detected at clinically relevant titers. No cross-reactivity was observed with other hemorrhagic fever viruses or common blood interferents. When compared to the ReLASV® Pan-Lassa Antigen Rapid Test, the newly developed assay showed an 8- to 32-fold improvement in sensitivity. Meeting WHO's REASSURED criteria, the RDT enables rapid visual interpretation, remains stable at ambient temperature, and is well suited for field deployment. These results support its applicability for broad-lineage Lassa virus detection and highlight its potential role in surveillance and outbreak control in resource-limited settings.

Genomic Surveillance of Monkeypox Virus Reveals the Evolutionary Framework and Transmission Dynamics in South Korea

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The 2022 global mpox outbreak was characterized by the rapid accumulation of APOBEC3 (A3)-mediated mutations via sustained human-to-human transmission, closely associated with distinct behavioral and epidemiological factors. To elucidate the genomic and epidemiological features of mpox in South Korea, we analyzed whole-genome sequences from 146 clinical samples collected between 2022 and 2025, prepared using probe-capture hybridization. In 2022, four imported cases, including one in a healthcare worker, were identified and classified into sub-lineages B.1.1 and A.2.1. A sharp increase in cases occurred in 2023 (~150 cases), predominantly linked to epidemiological connections with Japan. The index case for 2023 was assigned to clade IIb sub-lineage C.1 and harbored an L16F mutation shared with strains from Japan, Taiwan, and Belgium, but absent in those from Germany, the USA, and Canada. Subsequent local transmission continued for approximately six months, with all cases exhibiting the L16F mutation; >80% involved close contact with anonymous partners, often facilitated by social media and sauna visits, thereby complicating contact tracing and amplifying superspreading potential. Genomic analyses indicated the dominance of a single viral lineage from 2023 to 2025 and identified eight mutation-defined sub-clusters, primarily reflecting A3 deaminase activity. These mutations were enriched in structural components, including ankyrin repeat/F-box proteins, and appeared to restrict cell-free spread while enhancing contact-dependent transmission, facilitating localized viral persistence under minimal adaptive cost. These findings highlight the critical need for continuous genomic surveillance coupled with behavioral epidemiology to refine public health interventions and inform coordinated global mpox response strategies.



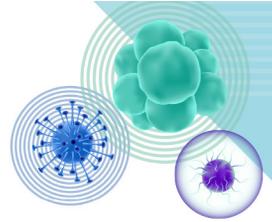
Prolonged MPXV shedding and emergence of Tecovirimat resistance in an immunocompromised person living with HIV: Evidence from genomic surveillance in South Korea.

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Mpox, historically a sporadic zoonotic infection confined to Central and West Africa, has undergone a significant shift in its epidemiological pattern since May 2022. Multiple countries have reported a rapid increase in cases predominantly among young males without recent travel history to endemic areas. Unlike previous outbreaks limited to endemic regions, the 2022 global outbreak is characterized by sustained human-to-human transmission through highly connected sexual networks exhibiting heavy-tailed contact distributions. This outbreak was driven by Clade IIb MPXV and was accompanied by a notable accumulation of APOBEC3-mediated mutations. Since 2024, a distinct lineage of Clade I MPXV, genetically divergent from those previously circulating in traditional endemic zones, has caused localized outbreaks in Africa. Sporadic cases of this lineage have also been identified in non-endemic countries, mainly among travelers returning from affected areas. In response to this resurgence and geographic expansion, the World Health Organization (WHO) declared mpox a Public Health Emergency of International Concern (PHEIC) in August 2024, a status that remains in effect. Globally disseminated Clade IIb MPXV infections typically present with characteristic clinical features such as skin lesions. Immunocompromised individuals, particularly those with uncontrolled HIV infection, may experience more severe disease manifestations. Tecovirimat, initially approved by the U.S. FDA for the treatment of smallpox and subsequently authorized in Europe for orthopoxvirus infections including mpox, has been used therapeutically. Although its safety profile in humans is well established, clinical efficacy data remain variable. In South Korea, a case of mpox concurrent with uncontrolled HIV infection was identified. Despite over three months of systematic treatment—including symptomatic management and tecovirimat administration—viral clearance was not achieved. The patient's immunodeficient status was considered a contributing factor to prolonged viral shedding, highlighting the challenges in managing mpox in immunocompromised hosts. To investigate viral dynamics, retrospective whole-genome sequencing was performed on multiple clinical specimens collected over time using a hybridization probe-capture method. Phylogenetic analysis confirmed that the infection belonged to the locally circulating MPXV lineage C.1. On day 23 of tecovirimat treatment, a dominant viral population

carrying the A290V mutation in the VP37 protein was detected at an allele frequency of 99.7%. This mutation is rarely observed in untreated cases and has been associated with reduced susceptibility to tecovirimat, with reported EC50 values increasing 10- to 2500-fold. At the same time, an additional VP37 mutation, A288P, was identified in a lesion sample from the pubic area, with wild-type and mutant alleles coexisting (64.1% C and 34.7% G). By day 41, the A288P mutation became fixed (allele frequency 100%), indicating within-host selection under drug pressure. This case highlights the risk of resistance development during prolonged tecovirimat therapy in immunocompromised hosts and emphasizes the importance of genomic surveillance to detect emerging resistance mutations. Notably, this study provides important scientific evidence amid ongoing debates regarding the efficacy of tecovirimat as a treatment for mpox.



Kinetically activating nanovaccine mimicking multidimensional immunomodulation of natural infection for broad protection against heterologous viruses in animal models

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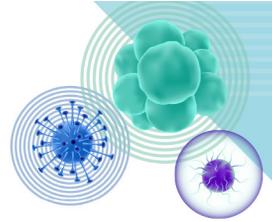
Vaccination can substantially improve human health by reducing disease severity and preventing infection by heterologous viruses. However, the protective efficacy of current vaccines often remains inferior to that achieved by natural infection. Here, we develop a kinetically engineered vaccine (KE-VAC) designed to mimic the multidimensional immune modulation induced during natural infection. KE-VAC achieves dynamic and sustained activation of antigen-presenting cells (APCs) through a masked TLR7/8 agonist, enhancing antigen uptake and migration of APCs to draining lymph nodes, leading to robust T follicular helper (Tfh) cell responses and germinal center formation in vaccinated mice. Compared with Alum-adjuvanted and mRNA vaccines, KE-VAC exhibits superior immunogenicity, providing complete protection through the induction of high-titer neutralizing antibodies and polyfunctional CD8⁺ T cells against multiple SARS-CoV-2 variants. Furthermore, KE-VAC elicits broad and durable immune responses that protect against diverse strains of influenza viruses. Notably, in aged ferrets, KE-VAC conferred complete protection against severe fever with thrombocytopenia syndrome virus (SFTSV), achieving viral clearance in target organs. These findings demonstrate that KE-VAC induces broad, potent, and long-lasting immunity against a spectrum of RNA viruses, underscoring its potential as a universal vaccine platform for emerging infectious diseases.

Organ-Specific Delivery of Ionizable Lipid Nanoparticles to the Spleen Enhances mRNA Expression and Immunity

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Lipid nanoparticles (LNPs) have emerged as a promising platform for mRNA delivery in both infectious disease and cancer immunotherapy. Nevertheless, most clinically evaluated LNPs predominantly accumulate in the liver, regardless of the route of administration. The spleen—a crucial secondary lymphoid organ—presents a valuable target for enhancing immune responses through localized delivery. In this study, we investigated differences in mRNA expression and immune activation following intravenous (IV) and intramuscular (IM) administration of novel ionizable lipid-based LNP designed for spleen-targeted delivery. Biodistribution studies using firefly luciferase (F/L) mRNA-encapsulated LNPs revealed that this spleen-targeting LNP (sLNP) was distributed primarily to the spleen, in contrast to a conventional LNP that mainly localized to the liver. To evaluate immune responses, hemagglutinin (HA) mRNA-encapsulated LNPs were administered to mice. ELISpot and flow cytometric analyses demonstrated that the sLNP elicited similar IFN- γ responses, as well as higher germinal center B cell and memory B cell populations, compared with the conventional LNP. In the HI assay, the sLNP induced lower neutralizing antibody levels than the control LNP in the IM group, whereas in the IV group, sLNP elicited higher neutralizing antibody levels compared to the control LNP. However, these differences were not statistically significant. Overall, these findings underscore the importance of the administration route in determining LNP biodistribution and subsequent immunological outcomes. By leveraging sLNP, it may be possible to enhance vaccine efficacy and therapeutic interventions for spleen-related disorders. Ongoing studies aim to elucidate the mechanisms underlying the administration-dependent differences observed in immune responses.



Unmodified UTP is not always best friend for mRNA Cancer Vaccines: Prove from IL-12 mRNA in mEER tumor mice model

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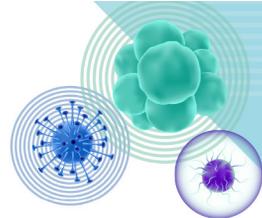
mRNA technology gained prominence during the COVID-19 pandemic and is now being widely explored for applications including cancer immunotherapy and protein replacement strategies. A widely held view in the field suggests that mRNA cancer vaccines should be generated using unmodified UTP to stimulate type I interferon production, thereby enhancing anti-tumor immune responses. However, in combination regimens involving multiple mRNAs, unmodified UTP may impair protein synthesis due to interferon-mediated degradation of mRNA transcripts. This raises concerns that the expression of therapeutic proteins, such as cytokines, could be significantly diminished when co-delivered with antigen-encoding mRNA transcribed using unmodified UTP. To test this hypothesis, we initially screened a panel of cytokines with established anti-tumor activity in the mEER head and neck cancer mouse model and identified IL-12 as the most potent candidate. Subsequently, we assessed the anti-cancer efficacy and immunological responses of two mRNA combination strategies: (1) antigen mRNA produced with unmodified UTP co-administered with IL-12 mRNA synthesized using modified UTP, and (2) both antigen and IL-12 mRNAs transcribed with modified UTP. Our findings revealed that using modified UTP for both mRNAs resulted in significantly improved tumor suppression and stronger immune responses, compared to the combination utilizing unmodified UTP for the antigen mRNA. In summary, unmodified UTP is not universally advantageous for mRNA-based cancer immunotherapy, particularly in co-formulations with cytokine-expressing mRNAs. The type I interferon response induced by unmodified UTP may accelerate degradation of co-delivered mRNAs, thereby limiting the expression of critical effector proteins and undermining therapeutic efficacy.

Development of Neutralization-Based Serological Standards Using Gardasil 9 Clinical Samples in Korea

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Cervical cancer, primarily caused by human papillomavirus (HPV), is one of the most common cancers among women worldwide. In Korea, as of 2025, the national immunization program provides free HPV vaccination for 12-year-old girls, with either the bivalent vaccine (Cervarix) or the quadrivalent vaccine (Gardasil 4). However, these vaccines do not provide protection against HPV types 52 and 58—two high-risk strains that are particularly prevalent in Korea. Gardasil 9, which offers coverage against these types, provides broader protection and may therefore be more suitable for the Korean population. In this study, we produced pseudoviruses representing all nine HPV types covered by Gardasil 9 and developed an optimized pseudovirus-based neutralization assay (PBNA). Using plasma samples collected from participants at Hallym University Kangnam Sacred Heart Hospital, Ewha Womans University Mokdong Hospital, and Seoul St. Mary's Hospital, we measured neutralizing antibody activity and analyzed the results based on the number of Gardasil 9 doses received. For samples collected after the third dose, we categorized them into high-, medium-, and low-titer groups and pooled them accordingly. These pooled samples were then analyzed in parallel with WHO standards to compare ND_{50} values, thereby contributing to the standardization of antibody testing following HPV vaccination and vaccine development.



Eighteen-Month Persistence of Neutralizing Antibodies Following Mpox Infection in South Korea: A Longitudinal Analysis

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Mpox was first reported in South Korea in June 2022, with a cumulative total of 175 confirmed cases by April 2025. The incidence peaked in May 2023 and has since been occurring sporadically. All cases have been identified as Clade 2b based on viral genotyping.

In this study, we conducted a longitudinal analysis of neutralizing antibody persistence in individuals 18 months post-Mpox infection. Most patients retained Mpox-specific neutralizing antibody titers at this time point. While a statistically significant change in antibody titers over time was observed ($P = 0.039$), no significant difference was found between people living with HIV (PLWH) and non-HIV-infected individuals.

Although individuals with hybrid immunity (prior smallpox vaccination and Mpox infection) tended to show higher antibody titers, the difference did not reach statistical significance ($P = 0.065$). Furthermore, comparison of the duration of viral DNA detection in skin lesions revealed that individuals with lower antibody titers had shorter durations of viral DNA detectability.

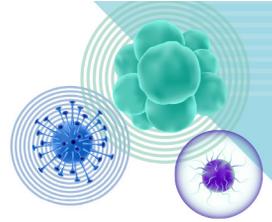
These findings suggest long-term persistence of neutralizing antibodies following Mpox infection. Future studies will aim to elucidate the functional differences in both humoral and cellular immunity between individuals with prior smallpox vaccination and those with natural Mpox infection.

TLR7/8 Agonist-Integrated Lipid Nanoparticles Enhance Immune Responses of N1-Methyl- Ψ -Modified mRNA Vaccines for Preventive and Therapeutic Applications

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Messenger RNA (mRNA) therapeutic vaccines often employ unmodified mRNA to leverage innate immune signaling pathways, including Toll-like receptor (TLR) 7/8 activation. While N1-methyl-pseudouridine (m1 Ψ)-modified mRNA can offer enhanced safety, its reduced capacity to induce innate immunity remains a challenge. In this study, we sought to improve both the expression and immunostimulatory potential of m1 Ψ -modified mRNA by incorporating TLR7/8 agonists into lipid nanoparticle (LNP) formulations. Various TLR7/8 agonists were evaluated at different concentrations, and mRNA expression efficiency was assessed using renilla luciferase (R/L) and firefly luciferase (F/L) reporters. Following intradermal, intramuscular, and intravenous administration, an optimized LNP formulation containing TLR7/8 agonist (AD03-LNP) was selected for further investigation. When mRNA encoding human papillomavirus (HPV) type 16 E7 and type 18 E6 antigens was delivered using AD03-LNP, significant increases in HPV-specific CD8⁺ T-cell responses and cytokine production were observed compared to conventional LNPs (Con-LNP). In the analysis using hemagglutinin (HA) mRNA, both antigen-specific CD8⁺ T cell responses and humoral immunity were enhanced, and a significant increase in immunoglobulin G2a (IgG2a) levels was observed when analyzing SARS-CoV-2 Omicron spike protein mRNA, reflecting a T helper type 1 (Th1)-biased immune response. AD03-LNP induced higher T cell responses than Con-LNPs, while showing comparable neutralizing activity. These findings highlight the role of TLR7/8 agonist-loaded LNPs in modulating mRNA expression and enhancing immune responses, offering a promising formulation strategy to improve the immunogenicity of mRNA-LNP vaccines. This strategy may contribute to the development of mRNA-based immunotherapies and prophylactic vaccines requiring robust T cell activation.



Development of HPV mRNA Vaccine and Evaluation Indicators

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HPV (Human Papillomavirus) has over 150 genotypes, among which 30-40 types cause genital infections. In particular, types 16 and 18 are classified as high-risk types, and these high-risk types account for approximately 70% of cervical cancer cases. Currently, HPV preventive vaccines developed by Merck (Gardasil – quadrivalent and nonavalent) and GlaxoSmithKline (Cervarix – bivalent) have been approved and are in use. However, due to the monopoly of foreign pharmaceutical companies, supply instability, and high vaccination costs, the domestic vaccination rate remains significantly low. To overcome this issue, our study aimed to design an mRNA-based HPV vaccine. Additionally, we aimed to develop evaluation indicators to assess the efficacy of this vaccine.

To establish evaluation indicators, we produced HPV PsV (Pseudovirus) and VLP (Virus-Like Particle) for 9 genotypes. Using these, we aimed to establish VLP ELISA, PBNA (Pseudovirus-Based Neutralization Assay), and a PsV infection model. Using anti-Gardasil mouse serum and NIBSC standard serum, we performed VLP ELISA and PBNA, successfully establishing detection limits and quantification methods for binding and neutralizing antibodies. Additionally, after vaginal infection with PsV, luciferase activity was confirmed using IVIS imaging. Luminescence was observed only in mice infected with PsV, allowing us to establish a PsV infection mouse model. Using the established evaluation methods, we measured the binding and neutralizing antibody titers at concentrations where protection efficacy of Gardasil 9 is observed, in order to propose evaluation indicators.

We collected human blood samples from 30 individuals vaccinated with Gardasil 9 and isolated serum. These clinical samples were applied to the established assays to measure binding and neutralizing antibody titers, demonstrating the potential clinical applicability of the evaluation methods.

To assess the applicability of the established evaluation methods for mRNA vaccine, we produced and purified an mRNA vaccine using HPV16 and 18 L1 antigens and confirmed antigen expression. We then evaluated how immune responses varied by formulation and how these changes were reflected in the evaluation indicators.

Baculovirus-Delivered DNA Vaccine Platform for Broad Protection Against Novel JEV Genotypes

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Japanese encephalitis virus (JEV) remains a major cause of viral encephalitis across Asia, with mortality rates reaching up to 30% after clinical onset. Recent shifts in the predominant circulating strains—from genotype 3 (G3) to genotype 1 (G1), along with the emergence of genotype 5 (G5)—highlight the urgent need for vaccines that provide broader and updated protection.

In this study, we established a novel DNA vaccine platform based on a recombinant baculovirus vector (AcherV), which displays human endogenous retrovirus (HERV) envelope proteins to facilitate efficient gene delivery into human cells. A codon-optimized prM-E gene cassette derived from JEV G1 was inserted into the AcherV vector under control of a CMV promoter, generating the AcherV-JEVG1 construct.

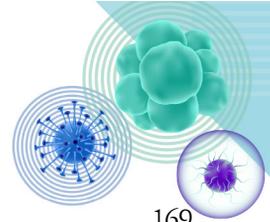
The JEV antigens were robustly expressed both *in vitro* and *in vivo*. In mouse models challenged intracerebrally with wild-type JEV G1, G3, or G5 strains, the AcherV-JEVG1 vaccine exhibited superior cross-genotype protection compared to currently licensed inactivated and live-attenuated vaccines. Immunized animals developed strong JEV-specific IgG responses and sustained protective immunity for at least six months post-boost, with a 66.7% survival rate observed in long-term G1 challenge studies.

These findings support the potential of AcherV-JEVG1 as a broadly protective and adaptable next-generation vaccine candidate for Japanese encephalitis, with implications for application against other emerging viral threats.

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Keywords Index

MEMO



A

AcHERV platform	188
adenovirus	47
Aging	72
AI	44
Alphacoronavirus/Betacoronavirus	127
Androgen receptor	67
animal model	123
antibody-dependent enhancement	56
Antibody-resistance	160
Antimicrobial Resistance	135
anti-prion agents	136
Antisense oligonucleotide	163
Antiviral peptide	19
antiviral therapy	176
Antiviral	108
Antivirals	109
Antivirals	110
APyV	121
Assembly compartment	70
Astrocytosis	138
Attitudes	117
Autophagy	138
Avian influenza	133
Avian Paramyxovirus 14	166

B

Bacillus subtilis	38
Baculovirus vector	114
Baculovirus vector	188
Baculovirus	165
Bardoxolone-Methyl	107
Bat adenovirus	132
Bat astrovirus (BtAstV)	131
Bat coronaviruses	127
Bat pestivirus	126
Bat	172
Bats	119
Bayesian structural time series model	135

biology	169
Biosecurity	117
Brain	32
Bunyavirus	12

C

Canine H3N2 Influenza virus	171
cap-based platform	130
Cattle	117
CD109	72
cell model	56
Cholesterol sulfate	176
Codon Optimization Strategies	167
collective interaction	82
Combination therapy	112
Competing Endogenous RNA	111
Complete genome	126
Coronavirus	81
COVID-19	59
COVID-19	79
COVID-19	81
Coxsackievirus B3	37
Coxsackievirus B3	149
Coxsackievirus B3	150
CRISPR	153
Cross-protection	61
Cross-reactivity	78
CVB3	39
Cytokine Storm	59

D

deep learning	82
Dengue virus	56
Diagnostic performance	120
Dihydrotestosterone	67
distemper	47
DIVA Vaccine	46
DNA methylation	67
DNA vaccine	165

DNA vaccine	188
domestic poultry	133
DPP4 receptor	161
Drug development	44
Drug screening	172
dsRNA	175
DUB	153
Duplex qPCR	121

E

E3 ligase	152
E3 ligase	153
Early detection	124
Elastase	81
Entecavir (ETV)	112
Epidemiology	121
Epstein-Barr virus	67
Escherichia coli	38
Etiological agent	57
Evaluation Indicators	187
Evaluation	120
Evolutionary trajectory	168

F

FASTA	122
FASTQ	122
Fever of unknown origin	57
FMD	48
Foot-and-Mouth Disease (FMD)	46
Foot-and-Mouth Disease Virus(FMDV)	130
Foot-and-Mouth Disease	48
Freedom From Disease Model	48
Furin cleavage site (FCS)	161

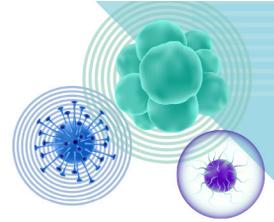
G

Gardasil	184
Gastric cancer	67
genetic characterization	169

Genetic diversity	131
genetic fusion	139
genetic fusion	31
Genomic characterization	119
Genotyping	128
G-quadruplex	154
G-quadruplex	151
GUI based tool	122

H

H5N1	80
H9N2	133
Hantavirus	61
HBV core protein	112
HBV	108
Head and Neck cancer	183
Hepatitis B virus (HBV)	112
Hepatitis B Virus	106
Hepatitis B Virus	107
Hepatitis B Virus	111
Hepatocellular Carcinoma	107
Hepatocellular Carcinoma	111
HepG2.2.15	112
HIV-1 Gag VLPs	31
HIV-1 Gag VLPs	139
HIV	185
HNFs	108
HP1BP3	154
HPAI	80
HPV	183
HSFX1	108
HSV-1	152
HTNV	59
Human adenovirus C (HAdV-C)	132
Human cytomegalovirus	70
Human intestinal enteroids (HIEs)	113
Human norovirus (HNoV)	113
Human norovirus	114
Human Papillomavirus	184
Human Papillomavirus	187



humoral immune response 130

I

ICP0 152
 ICP0 153
 IE2 151
 IL-10 59
 Immune escape 160
 Immune evasion 174
 Immune response 67
 Immunocompromised patients 160
 immunogenicity 114
 Immunotherapy 183
 In Silico Sequence Mining(ISSM) 122
 inactivated vaccine 171
 inclusion bodies 174
 Incursion of Emerging disease 124
 Infectious clone 166
 Inflammasome activation 113
 Inflammation 149
 inflammation 79
 inflammatory cell death 79
 Influenza A virus 173
 influenza A virus 82
 influenza virus 181
 Influenza 165
 innate immunity 79
 interferon receptor 56
 Interrupted time series analysis 135
 Interspecies transmission 119
 Interspecies transmission 126
 IRES-based platform 130
 ISG15 secretion 170
 ISG15 170

J

Japanese encephalitis virus (JEV) 188
 Javanicin 112

K

Kaposi's sarcoma-associated herpesvirus 72
 KE-VAC 181
 Knowledge 117
 KSHV 72

L

LC3-derived secretory pathway 170
 Lipid nanoparticles 182
 lipid nanoparticles 186
 liquid-liquid phase separation 174
 Live Attenuated Vaccine (LAV) 46
 Long COVID 17
 Long Non-Coding RNA 111
 Lumpy Skin Disease 117
 Lumpy Skin Disease 124

M

macrophages 56
 Mamastrovirus 131
 Mathematical Modeling 124
 MazF 38
 MERS-related bat coronaviruses 161
 Metagenomic next-generation sequencing (mNGS) 43
 MICA 67
 Microglia 17
 microglia 146
 Microglia 156
 Molecular detection 128
 Molecular diagnostics 121
 Mosaic Antigen 61
 Mpox 185
 mRNA delivery 182
 mRNA interferase 38
 mRNA therapeutics 142
 mRNA vaccine technology 130
 mRNA vaccine 61

mRNA vaccine	149
mRNA Vaccine	167
mRNA vaccine	171
mRNA vaccine	175
mRNA vaccine	186
mRNA vaccine	187
mRNA	142
mRNA	183
Multiplex real-time RT-PCR	120
Myocarditis	37
Myocarditis	149
Myocarditis	150

N

Neural stem cells	33
Neural stem cells	137
Neuroinflammation	156
Neurological pathogenesis	17
Neutralizing Antibodies	185
Neutralizing Antibody Activity	184
Neutrophil	81
Neutrophil	173
Newcastle disease virus	78
Next-generation sequencing	57
Next-generation sequencing (NGS)	126
Next-generation sequencing (NGS)	127
Next-generation sequencing (NGS)	131
NGS	122
Nipah virus	163
NiRAN	109
NiV	123
NLRP6	113
NLRP12	79
Novel platform	33
Novel platform	137
Novel virus discovery	43
Novel zoonotic viruses	57
NS1	146
NS7 protein	113
NSP12-NSP8 interface	19

nucleocapsid protein	31
nucleocapsid protein	139
Nucleoside analog	109
Nucleus Accumbens - Associated Protein 2	106

O

OAS-RNase L pathway	174
Ocular manifestation	17
Oligonucleotide therapeutics	163
One Health approach	135
One Health	43
ORF14 (gC)	154
Organoid	172

P

P53	106
PAD2	32
PAD2	138
PAFA	136
parainfluenza virus	47
Parvovirus surveillance	118
parvovirus	47
Pathogenesis	12
PBFDV	121
PCV2	120
pediatric patient	169
Pet parrot	128
Pharmaco-Net	44
Phodopus roborovskii	173
Phylogenetic analysis	78
phylogenetic analysis	133
phylogenetics	80
PIKfyve	110
PIP5K1C	110
Post-Acute Sequelae of SARS-CoV-2 (PASC)	173
Pp28	70
Prion disease	33
Prion disease	137
Prion disease	138

Ultrastructural analysis	138
Ungulate tetraparvovirus 1	118
UNI418	110

V

Vaccination	184
Vaccine Development	46
Vaccine	12
vaccine	47
Vaccine	114
Varicella zoster virus	156
Veterinary prescription policy	135
Vietnam	118
Viperin	70
Viral hemorrhagic fever	12
Viral reactivation	67
Viral vector vaccine	78
Viral vector	166
Virome analysis	132
Virome sequencing	127
Virome	43
Virus evolution	168
Virus isolation	172

W

Water buffalo	118
---------------	-----

Z

ZIKV	146
ZNF451	152
zoonosis	80
zoonosis	82
Zoonotic potential	119
Zoonotic potential	126
Zoonotic potential	127
Zoonotic potential	131
Zoonotic potential	132
Zoonotic viruses	43

22L scrapie	32
3D modeling	137
3D modeling	33

공진화	147
나노포어 시퀀싱	144
나노포어 염기서열분석법	141
넥스트스트레인	145
마이크로니들(Microneedle Array Patch)	15
메신저 리보핵산 백신(mRNA Vaccine)	15
무주바이러스	141
바이러스 재편성	144
분자 진화	141
설치류 감시	162
시공간 유전자 감시	145
신증후군출혈열	11
심근염	39
올도맛쥐	147
올롱도	147
올롱바이러스	147
유전체 감시	144
유전체 특성화	147
이호왕	11
인간 코로나바이러스	162
인수공통 바이러스	162
인수공통감염 평가	141
입자형 백신(Powder Vaccine)	15
차세대염기서열분석법	144
차세대염기서열분석법	162
폐렴	162
푸말라바이러스	141
한타바이러스	11
한타바이러스	147
한타바이러스페증후군	11
한탄바이러스	144
한탄바이러스	145
항바이러스	39

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