

제24회 한·미·일 환태평양 국제컨퍼런스^{EID}

24th International Conference on Emerging Infectious Diseases in the Pacific Rim

Pandemic preparedness and the rapid emergence of pathogens caused by global environmental change



2024 International Symposium for
Infectious Diseases Research Institutes Cooperation

감염병연구기관 국제심포지엄

2024. 3. 8(금) 08:30~16:00 그랜드하얏트 인천

온-오프라인 동시 진행



질병관리청

국립보건연구원 국립감염병연구소

2024

감염병연구기관 국제심포지엄

International Symposium for Infectious Diseases Research Institutes Cooperation

Time(KST)	Program	
08:30~09:00	Registration	
09:00~09:15	Welcoming Remarks(KDCA)	Jee, Young-mee (Commissioner, Korea Disease Control and Prevention Agency)
	Opening Remarks(KNIH)	Park, Hyun-Young (Director, Korea National Institute of Health)
	Congratulatory Remarks(KNID)	Jang, Hee-Chang (Director, Korea National Institute of Infectious Diseases)
09:15~09:25	[Keynote speech 1] Development Strategies and Plans for the Therapeutics within 100/200 Days in Preparation for the Novel Infectious Disease Pandemic	Kim, Kyung-Chang (Director, KNIID Emerging Virus Research Center)
09:25~09:35	[Keynote speech 2] Development Strategies and Plans for the Vaccines within 100/200 Days in Preparation for the Novel Infectious Disease Pandemic	Lee, Yoo-Kyung (Director, KNIID Vaccine Research Center)
Session 1. Characteristics of Emerging Infectious Diseases and clinical studies		
Chair: Park, Man-Seong(Professor, Korea University)		
09:35~09:50	Age-depedent differential pathogenesis of SFTSV infections	Choi, Young-Ki (Director, Korea Virus Research Institute)
09:50~10:05	Deglycosylation of human influenza A virus (H3N2) hemagglutinine increases virulence in mice.	Choi, Jang-Hoon (Research officer, KNIID)
10:05~10:20	Clinical presentation and viral shedding in patients with Mpox in South Korea	Kim, Min-kyung (Professor, National Medical Center)
10:20~10:35	Long COVID Research Project in South Korea : What we've learned about long COVID	Lee, Ja-Cob (Professor, Hallym University)
10:35~10:45	Q&A	
10:45~11:00	Break	
Session 2. Current status and strategies for the development of therapeutics for Emerging Infectious Diseases		
Chair: Kim, Ki-Soon(Professor, Korea University)		
11:00~11:15	Platforms & Tools to Enable Rapid Pandemic Response	Dimitri Lavillette (Chief Scientific Officer, Institut Pasteur Korea)
11:15~11:30	Development of SARS-CoV-2 S2 Targeted Vaccines and Therapeutic Antibodies	Cho, Eun-Wie (Director, Korea Research Institute of Bioscience and Biotechnology)
11:30~11:45	Lessons from COVID-19 for the development of antiviral drugs	Han, Soo-Bong (Director, Korea Institute of Chemical Technology)
11:45~12:00	Acceleration of drug discovery with AI	Kim, Woo-Youn (Professor, Korea Advanced Institute of Science and Technology)
12:00~12:10	Q&A	
12:10~13:00	Lunch	

Time(KST)	Program	
Session 3. Outstanding Achievements in the Development of Vaccines for Emerging Infectious Diseases		
Chair: Seong, Baik-Rin(Professor, Yonsei University)		
13:00-13:15	Rapid screening of target antigenic sites for SARS-CoV-2 vaccine development using Fv-antibody library	Pyun, Jae-Chul (Professor, Yonsei University)
13:15-13:30	HAs-NAu strategy for the development of better influenza vaccines	Kim, Jin-Il (Professor, Korea University)
13:30-13:45	SFTS mRNA Vaccine Research and Development	Kim, Hyeon Guk (Research officer, KNIID)
13:45-14:00	Broad Spectrum Vaccine and mAbs for Sarbecoviruses	Wang Linfa (Professor, DUKE-NUS, Singapore Executive Director for the Programme for Research in Epidemic Preparedness and Response (PREPARE), Singapore)
14:00-14:10	Q&A	
14:10-14:25	Break	
Session 4. Current Status and Strategies in the Development of Vaccines for Emerging Infectious Diseases		
Chair: Hong, Kee-Jong(Professor, Gachon University)		
14:25-14:40	Vaccine adjuvant platform	Yeom, Jeong-Seon (CEO, CHA Vaccine Institute)
14:40-14:55	SKY mRNA Platform for Prophylactic Vaccine Development	Jinan Shin (Vice President, SK bioscience)
14:55-15:05	Research and Development Strategy for RSV Vaccine	Kim Seok-Kyu (Director, U Biologics)
15:05-15:15	Strategy to develop effective multivalent COVID-19 vaccines against emerging variants based on adenovirus vector platform	Kang, Chang-Yul (CEO, CELLID)
Panel Discussion		
Chair: Seong, Baik-Rin(Professor, Yonsei University)		
15:15-15:55	Q&A and Future Collaboration Prospects <Therapeutics> - Kim, Kyung-Chang, Dimitri Lavillette, Han, Soo-Bong, Kim, Woo-Yeon <Vaccines> - Lee, Yoo-Kyoung, Yeom, Jeong-Seon, Kim Seok-Kyu, Kang, Chang-Yul	
15:55-16:00	Closing Remarks(KNIID)	Jang, Hee-Chang (Director, Korea National Institute of Infectious Diseases)

Welcoming Remarks(KDCA)



Youngmee Jee

Commissioner

Korea Disease Control and Prevention Agency

🔍 EDUCATION:

Ph.D, Virology, University of London, United Kingdom, 1997

Diploma, Medical Microbiology, University of London, United Kingdom, 1988

MD, Seoul National University Medical School, Republic of Korea, 1986

🔍 WORK HISTORY:

○ Public Sector

Commissioner

Korea Disease Control and Prevention Agency

December 2022–Present

Director–General

Center for Infectious Disease Research, Korea Centers for Disease Control and Prevention,
Ministry of Health and Welfare

May 2017–October 2019

Director–General

Center for Immunology and Pathology, Korea Centers for Disease Control and Prevention,
Ministry of Health and Welfare

October 2014–May 2017

Regional Coordinator

Expanded Programme on Immunization, Western Pacific Regional Office,
World Health Organization (WHO)

August 2007–October 2014

Director

Hepatitis and Polio Viruses Team, National Institute of Health,
Ministry of Health and Welfare
October 2005–August 2007

Director

Division of Enteroviruses, Department of Virology, National Institute of Health,
Ministry of Health and Welfare
December 2003–October 2005

Deputy Scientific Director

Division of Enteroviruses, Department of Virology, National Institute of Health,
Ministry of Health and Welfare
July 1997–December 2003

○ Private Sector

Chief Executive Officer

Institute Pasteur Korea
January 2021–December 2022

President

Korean Society for Microbiology
January 2021– December 2021

Special Advisor to the Prime Minister

Health Affairs
November 2020–April 2021

Visiting Professor

Graduate School of Public Administration, Seoul National University
June 2020–May 2021

Special Representative for Health Diplomacy

Korea Foundation
April 2020–Present

Member

WHO International Health Regulation Emergency Committee on COVID-19
January 2020–Present

President

Korean Society of Infectious Diseases

December 2017–November 2019

Member

WHO Strategic Advisory Group of Experts for Immunization (SAGE)

April 2017–April 2020

Member

Board of Trustees of the International Vaccine Institute (IVI)

January 2016–December 2019

AWARDS:

President's Service Merit Medal

2017

Prime Minister's Commendation

in recognition of the contribution to infectious disease management projects

2005

Opening Remarks(KNIH)



Hyun-Young Park

- ✓ Director (Deputy Minister)
- ✓ Korea National Institute of Health

🔍 EDUCATION:

- 2000 Yonsei University College of Medicine (Ph.D.)
- 1995 Yonsei University College of Medicine (M.S.)
- 1990 Yonsei University College of Medicine (M.D.)

🔍 PROFESSIONAL EXPERIENCE:

- 2023 ~ Present Director, Korea National Institute of Health
- 2020 ~ 2023 Director, Department of Precision Medicine, KNIH
- 2018 ~ 2020 Director, Center for Genome Science, KNIH
- 2017 ~ 2018 Director, Division of Cardiovascular Diseases, KNIH, KCDC
- 2012 ~ 2023 PI, National Research Program for Women's Health
- 2011 ~ 2014 Team leader, National Center for Medical Information and Knowledge TF
- 2008 ~ 2014 Team leader, Clinical Research Coordination TF
- 2005 ~ 2017 Director, Division of Cardiovascular & Rare Diseases, KNIH, KCDC
- 2002 ~ 2003 Research Associate, Duke University Medical Center, USA
- 2004 ~ 2005 Assistant professor of Cardiology (Dept. of internal medicine)
- 2000 ~ 2002 Assistant professor of Cardiology (Dept. of internal medicine)
- 2000 ~ 2005 Assistant professor, Yonsei Cardiovascular Research Institute
- 1998 ~ 2000 Instructor, Yonsei Cardiovascular Research Institute, Yonsei University College of Medicine
- 1996 ~ 1998 Research Student, Department of Clinical Pathology, Shimane Medical University, Japan
- 1995 ~ 1996 Research fellow, Cardiology division, Yonsei Cardiovascular Center, Yonsei University College of Medicine
- 1990 ~ 1995 Resident, Department of Internal Medicine, Yongdong Severance Hospital

Congratulatory Remarks(KNID)



Hee-Chang Jang

- ✓ National Institute of Infectious Diseases (NIID), Korea
National Institute of Health (KNIH), Korea Disease
Control and Prevention Agency (KDCA)
- ✓ Director, National Institute of Infectious Diseases (NIID)

Q EDUCATION:

- 2017 Chonnam National University, Ph.D
- 2005 Seoul National University College of Medicine, M.M.Sc
- 2000 Seoul National University College of Medicine, M.D.

Q PROFESSIONAL EXPERIENCE:

- 2020 ~ Present Director, National Institute of Infectious Disease
- 2017 ~ 2019 Post-Doc/Research Fellow, Harvard Medical School / Massachusetts General Hospital
- 2009 ~ Present Professor (tenured), Infectious Disease, Chonnam National University & Chonnam National University Hospital
- 2008 ~ 2009 Fellow, Infectious Disease, Seoul National University Hospital
- 2000 ~ 2008 Volunteer Doctor, Korea International Cooperation Agency (KOICA)
- 2000 ~ 2015 Intern & Resident, Internal Medicine, Seoul National University Hospital

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DUKE-NUS, Singapore Executive Director for the Programme for Research in Epidemic Preparedness and Response Wang Linfa Professor

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기조강연 1.

신종감염병 대유행 대비 100/200일 치료제 개발전략 및 계획

Keynote speech 1



Kyung-Chang Kim

- ✔ Division of Emerging Virus & Vector Research
Center for Emerging Virus Research
Korea National Institutes of Infectious Diseases
- ✔ Director of Division

🔍 EDUCATION:

- 2000 B.Sc. (Molecular Biology), Pusan National University
- 2002 M.Sc. (Molecular Biology), Pusan National University
- 2011 Ph.D. (Molecular Biology), Korea University

🔍 PROFESSIONAL EXPERIENCE:

- 2020 ~ Present Division Director,
Division of Emerging Virus & Vector Research
National Institutes of Health, Korea DCA
- 2021 ~ Present Director of Therapeutics Research and Development Team,
Central Disease Control Headquarters Treatment and Vaccine Development Task Force
- 2018 ~ Present Board Member, Korean Society for AIDS (2018~)
Board Member, Korean Society for Virology (2022~)
- 2012 ~ 2015 Post.doc fellow, University of Northwestern, U.S
- 2004 ~ 2020 Senior Staff Scientist & Staff Scientist
Korea National Institutes of Health (KNIH)

🔍 Topic

R&D Strategies and Plan for 100/200 Days Therapeutics Development in Preparation and Response to Emerging Infectious Disease

🔍 Abstract

After entering the 21st century, various infectious diseases have been occurring almost every 1–2 years. With the advancement of transportation and the increase of international travelers, the inflow possibility of emerging infectious diseases is gradually increased. The COVID–19 pandemic has led to large–scale casualties, emphasizing the government's role in the development of treatments and vaccines around the globe. During a pandemic outbreak, treatment serves as the best means of protecting the population until vaccines are secured. To effectively responding future infectious disease outbreaks, proactive preparation and development strategies for therapeutics are urgently needed. Therefore, the KDCA has collaborated across ministries to plan a “Mid– to Long–Term Preparedness and Response Plan for Emerging Infectious Disease” and has devised concrete implementation measures. Through this plan for emerging infection, we introduce present development strategies for priority pathogens for next pandemic.



신종바이러스연구센터 조직도



신종바이러스연구센터 추진방향

비전 국가 바이러스 감염병 대응 연구 선도 및 전주기 지원

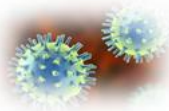
목표 바이러스 감염병 제어를 위한 핵심기술 및 연구역량 고도화

추진 전략

- 1) 바이러스 감염병 대응 핵심기술 고도화
- 2) 치료제 비임상 파이프라인 강화
- 3) 감염병 임상연구체계 강화
- 4) 국내·외 협력 및 인프라 강화

글로벌 감염병 위기 지속

√ 21세기 바이러스성
감염병 이슈



√ 미해결,
신변종바이러스 위협
상존

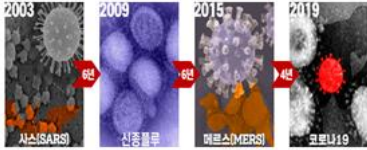


글로벌 시대, 감염병 안전지대는 없다.

코로나19로 인한 전세계 경제손실 → 13.8조 달러 (IMF, 2022년)

신종감염병 대유행 대비 중장기 계획 발표(23.5)

발생 주기는 짧아지고, 피해는 커지는 팬데믹 위험 상존



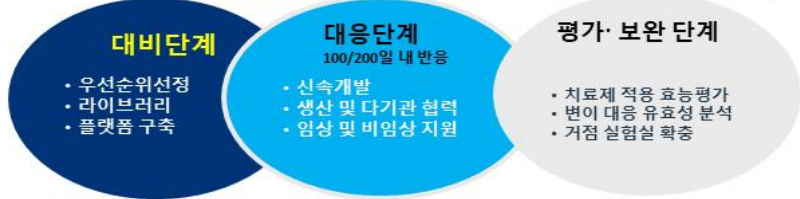
- 코로나19 다음 대유행 감염병 후보는 조류인플루엔자(AI) 인체감염증
한 US CDC director, 글로벌 바이오포럼 2021, '21.11
- Disease X로 인한 재난적 감염병 유형은 고 병독성 RNA 바이러스의 인수공통 전파로 인해 발생할 것
란셋, '20.5월
- 앞으로 20년 이내 또 다른 팬데믹 발생 가능
빌 게이츠



[신종감염병 대유행 대비 중장기계획 10대 핵심과제]

감시·예방	① 감염병 조기경보를 위한 통합 감시체계 구축 ② 글로벌 보건정보 선도 및 국제협력체계 강화
대비·대응	③ 세계에서 인정받은 초기 대응역량 지속 발전 ④ 日 확진자 100만명 대응가능한 의료체계 구축 ⑤ 대규모&장기 유행에 흔들리지 않는 필수인력 확보 ⑥ 감염에 취약한 시설·집단을 안전하게 보호
기반	⑦ 협력적·효율적 위기대응을 위한 튼튼한 기반 조성 ⑧ 고도화된 정보시스템 및 빅데이터 플랫폼 구축
회복	⑨ 피해완화와 조기 회복을 위한 두터운 지원체계
연구개발	⑩ 백신·치료제 개발 가속화를 위한 R&D 지원체계를 혁신

- 🏠 (필요성) 빠른 치료제 개발 및 공급으로 감염병 위험과 사회·경제적 충격 최소화
- 🏠 (목표) 신종감염병 발생 100/200일 이내 치료제 개발 및 공급 가능한 대비, 대응, 평가 체계 구축



글로벌 팬데믹 대비 감염병 치료제 확보 프로젝트



프로젝트	신종감염병 대유행 대비 중장기계획(23.5)	100 day mission (21.11)	프로젝트 NextGen (23.8)	팬데믹 대비 계획 PPP(21.12) + PANDEMIC PREPAREDNESS PLAN
목표	팬데믹 위기 시 100/200일 초고속 치료제 개발	WHO 비상사태(PHEIC) 선언 후 100일 이내 치료제 확보	미래 팬데믹 발생 대비 미국 정부의 백신 및 치료제 개발	팬데믹 우려 RNA 바이러스과 항바이러스제 표적약물 발굴 플랫폼
우선순위 병원체	6개 바이러스 과 (8종 바이러스) 라싸, SFTS, 코로나19, MERS, 뎅기, 니파, 조류인플루, RSV	25개 바이러스 과 호흡기바이러스과 대상 저분자항바이러스제 25개 후보 확보 (임상 1상 완료)	코로나19 변이주 또는 미래 팬데믹 감염병 흡입형(점막형), long-lasting 백신 또는 항체치료제	7개 바이러스 과 Bunyaviridae, Coronaviridae, Filoviridae, Flaviviridae, Paramyxoviridae, Picornaviridae, Togaviridae

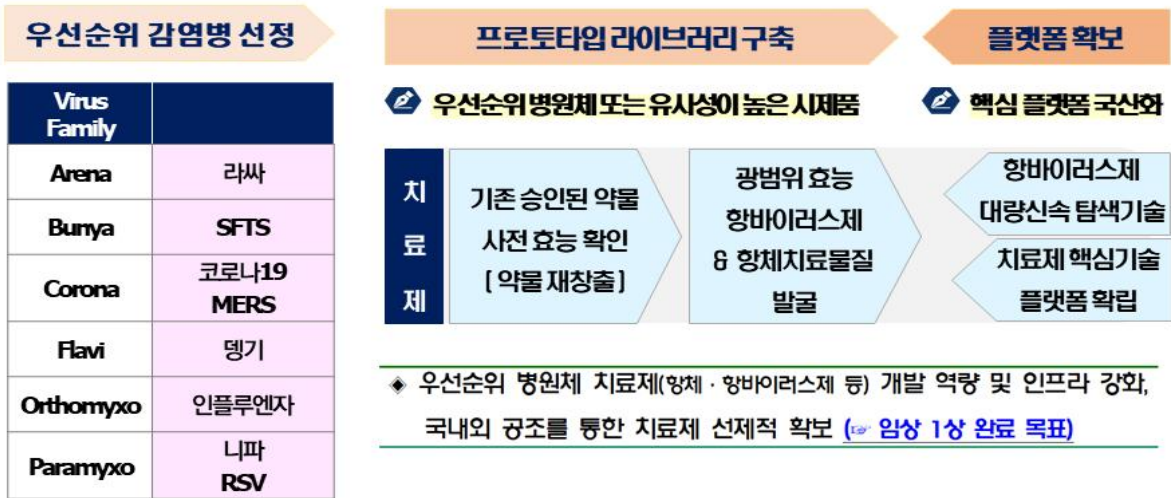
Korea National Institute of Infectious Diseases / Novel Virus Research Institute

신종감염병 치료제 개발 전략

신종감염병 발생 시 우선순위 병원체(8종) 중심 100일/200일내 치료제 신속 개발 추진



대비: 팬데믹 발생 전 신속개발 체계 구축



목표 : 후보물질 발굴 → 임상1상 완료

대응: 팬데믹 발생시 신속 개발

100일 (Track 1) 타겟 병원체에 대한 임상1/2상 정도의 안전성과 용량이 확인된 **시제품 기 확보 시**

200일 (Track 2) 타겟 병원체와 유사성이 높은 **시제품 기 확보 시** (예시: SARS-CoV-3)

적합 플랫폼	구분	후보물질	임상 단계			허가 및 심사
			비임상 생산	임상 1/2상	임상 3상	
(치료제) 항바이러스제 항체치료제 등	T1(100일)	시제품 확보	30일 (대량생산)	생략	70일	
	T2(200일)	유사 시제품 확보	40일 (대량생산, 평가)	60일 (임상1/2상 동시진행)	100일	
렉키로나주 개발	코로나19 (330일)	90일	120일	120일 (조건부허가)	-	

목표 : 100/200일 내 치료제 확보

평가 · 보완: 면역원성 및 치료임상 효능 평가 등

효능평가

- ▶ 치료제 적용 후 임상효능평가
- ▶ 변이 발생 시 유효성 분석 등 사후평가



민간 지원

- ▶ 항바이러스제 약효평가 실험실 운영
- ▶ 약효평가거점실험실 확충



시설 · 자원

- ▶ 신종바이러스연구센터 [B2/3]
- ▶ 국가병원체자원은행
- ▶ 질병청 B4 시설활용 활성화



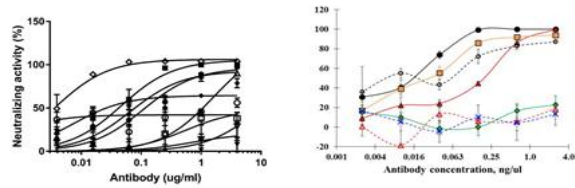
목표 : 치료제 효능에 대한 과학적·정책적 근거 마련

메르스 단클론 항체 개발 플랫폼 구축

- ▶ 메르스 지속발생 및 재유입대비
- 국가차원의 긴급대응 연구를 통한 사회적 불안감 해소

국내 메르스 회복 환자 PBMC로부터 MERS 특이항체 보유 B세포 분리 핵심 기술

미국 NIH와 "정밀 의료와 메르스 치료제 개발 협력" 추진(2015-10-18)하에 핵심 기술 연수



[특허 등록, '18.9.10]

특허명: MERS-CoV 특이항체...
출원번호: 10-2017-01111111

[특허기술 가치평가, '19.12]

특허기술 가치평가서...
평가기관: KIPDA

[기술 이전]

기술이전 계약서...
계약번호: 2019-00000000

(기술명) 메르스바이러스 스카이크 51 단백질에 대한 단클론항체 및 이의 용도
계10-1895228호

국유특허 통상실시계약(20.7) - 단원생명과학

- ✓ 메르스 항체 미국 NIH 공동 및 자체 개발
- ✓ 단클론 항체 개발 플랫폼 구축

코로나19 항체치료제 후보물질 발굴

a Microbial surface display

Human antibody library → COVID-19 patients (B cell mRNA) → PCR for V_H & V_L and cloning → Display phmAbs fragments → Phage library 확보

Library selection: Ag binding → SARS-CoV-2 RBD Probes → Elution → Screening → Cloning → 항체분질(scFv-Fc) screening

확보된 Phage 중 RBP 반응성 phage 선별

수백 개의 항체분질(scFv-Fc) → 바이러스 중화능 평가 → full IgG 후보 선별 → 생산성(동물세포) 고려 최종 후보 항체 선정

Flowchart: 최적 환자 혈액 샘플 채취 → 항체 후보 유전자 집합체 구축 → 지퍼 항체 후보 선별 → 중화능 테스트 최종 항체 선별 → 최종 선정

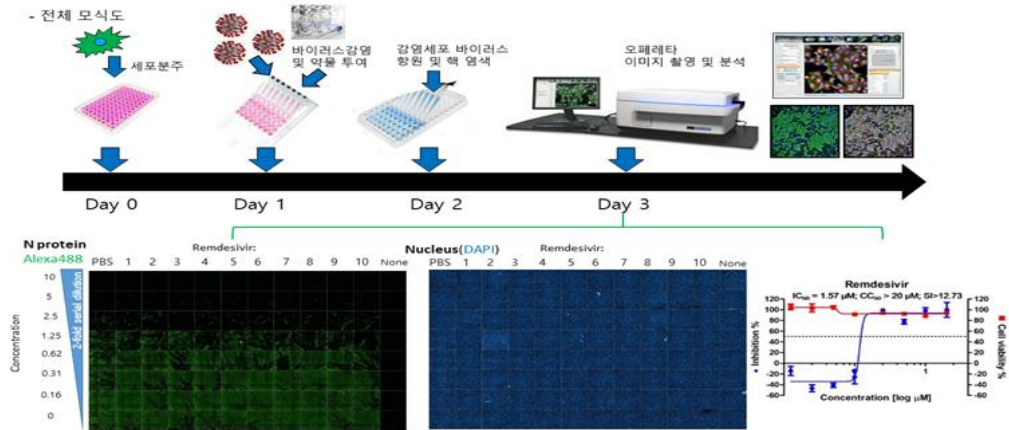
scFv

Human IgG

Int. J. Biol. Sci. 2020, 16(10):1895-1905

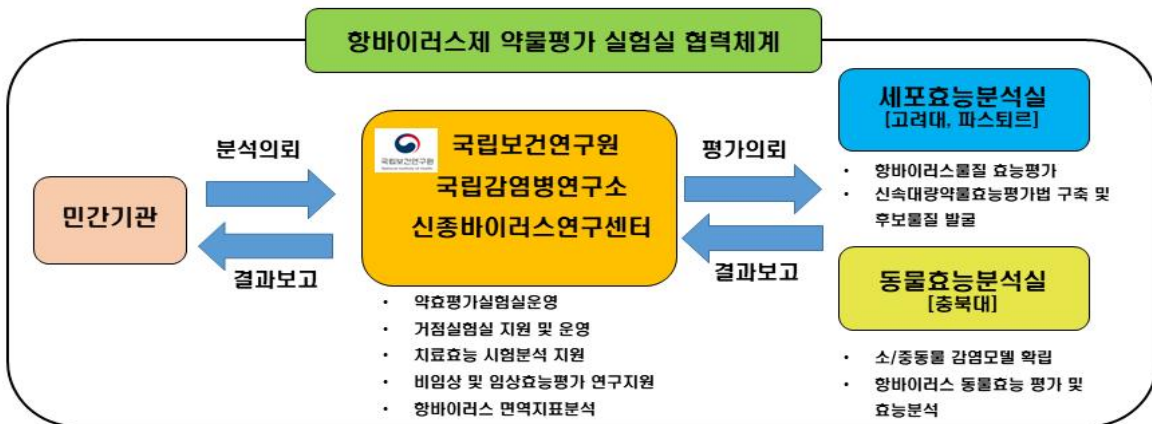
HTS 기반 치료제 신속 효능평가 플랫폼 확보

- ▶ “Solidarity” WHO 주도 국제적 약물 재창출 임상시험 진행
- ▶ “렘데시비르” 한·미·일 등에서 코로나19 치료제 최초 승인 [에볼라치료제]
- ▶ 신변증바이러스 대비 신속 대량 약물 선별법 구축 필요



민관협력 항바이러스제 약효평가 거점실험실 구축

- ▶ 국가 공중보건 위기대응 연구역량 상시 강화
- ▶ 코로나19 등 바이러스 감염병 제어를 위한 치료제 후보물질 발굴 및 개발
- ▶ 약물의 항바이러스 효능 비임상(세포 및 동물) 평가 및 지원
- ▶ 항바이러스제 약물평가 거점실험실 지정·운영을 통한 협력 네트워크 구축



국내외 치료제 개발 네트워크 공조 강화

[국내]

국가핵심 항체전문 연구소 스크립스코리아
연구협력의향서('22.4.)

감염완치자 항체라이브리 개발

[국외]

한국화학연구원
연구협력의향서('22.11.)

신변종 감염병 핵심기술개발

최신 기술 및 연구 자원확보를 통한
신변종 감염병 선제적 대응 연구역량 강화

국가	기관	내용	비고
미국	NIAID	SFTSV 항체치료제	수행 중 ('22~)
라이베리아	라이베리아감염병연구소	출혈열, 호흡기 바이러스 자원	수행 중 ('23~)
탄자니아	남동아프리카감염병연구소		
말레이시아	열대감염병연구 및 교육센터	SFTSV, 니파 연구자원 등	
호주	피터도허티	치료제 개발 기술 교류	진행 예정 ('24~)
남아공	국립전염병연구소	출혈열 바이러스 치료제 개발	수행 중 ('23~)
칠레/호주/독일	칠레-오스트랄 대학교, 퀸즈대학교, BNMH, RZ, UKE	라싸열 바이러스 치료제 개발	수행 중 ('24~)

Korea National Institute of Infectious Diseases / Novel Virus Research Institute

개발 단계별 역할 및 지원 - [예] 항체치료제 개발

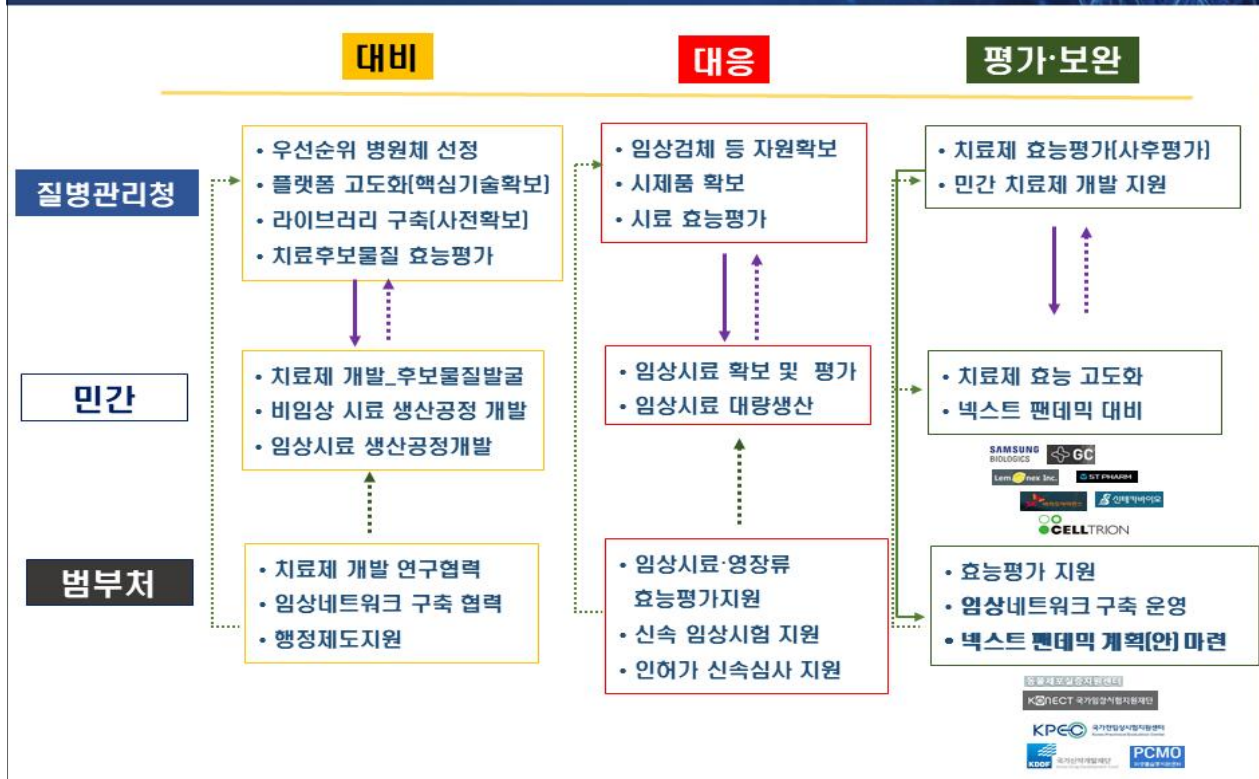
START

상용화

개발 단계	시료 확보	항체발굴	후보항체 선별	비임상	시료생산 및 평가	임상	인허가
장애 요인	회복기 환자 혈액수집, 항원확보	항체 중화능 평가	후보항체 중화능 및 동물효능 검증	영장류 효능평가	비임상 및 임상시료 생산, 효능평가	임상환자 모집, 예산지원, 임상검체분석, 임상허가심사	신속 심사
주요 협력 기관	질병청/ 병원/ 기업/ 연구기관 복지부	질병청/ 연구기관/기업	질병청/ 연구기관/기업	과기부, 교육부 (국가전임상 지원센터)	질병청/ 기업 /산자부	질병청/ 기업/복지부/ 식약처/ 임상시험재단 검체분석기관	식약처

Korea National Institute of Infectious Diseases / Novel Virus Research Institute

단계별 상호 역할 및 지원



고려사항

- ▶ 치료제 개발을 위한 전주기 민-관 협의체 구성 필요
 - 평시/ 위기 시 상황에 따른 유연한 민관협력 체계 구축
 - 치료제 개발을 위한 범정부 컨소시엄 혹은 사업단 마련
- ▶ 임상시험 관련 인허가 등 규제 간소화
- ▶ AI 활용 등 치료제 개발 데이터베이스 구축 및 운영
- ▶ 지속적 투자를 위한 출연금 등 신규 예산 확보 필요

향후 계획

- ▶ 「신종감염병 대유행 대비 중장기 계획」 이행 추진전략 및 로드맵 수립
- ▶ 신기술 기반 치료물질 개발 플랫폼 고도화
 - ✓ AI, Nanobody, mRNA 치료제 등 첨단기술 도입
- ▶ 국내외 네트워크 및 인프라 확대
 - ✓ [국내] 복지부, 과기부, 식약처 등 관계부처 협력
 - ✓ [국외] 미국 NIAID, 호주 피터-도허티연구소 등 협력확대
- ▶ 치료제 개발 고시 운영을 통한 민간지원 활성화

감사합니다

기조강연 2.

신종감염병 대유행 대비 100/200일 백신 개발전략 및 계획

Keynote speech 2



Yoo-Kyoung Lee

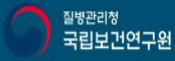
- ✔ Korea Disease Control and Prevention Agency, National Institute of Health)
- ✔ Division Director

🔍 EDUCATION:

- 2004 D.V.M., Seoul National University School of Veterinary Medicine
- 1998 Master's Degree, Seoul National University School of Veterinary Medicine
- 1994 ABD(all but dissertation), Seoul National University School of Public Health

🔍 PROFESSIONAL EXPERIENCE:

- 2021 ~ Present Division Director, Korea Disease Control and Prevention Agency, Division of Vaccine Development Coordination
- 1998 ~ 2021 Senior Staff Scientist, Ministry of Food and Drug Safety



신종감염병 대유행 대비 100/200일 백신 개발전략 및 계획

2024. 3. 8.
공공백신개발지원센터



신종감염병 대유행 대비 중장기 계획(23.5.22)

백신개발전략 / 질병관리청 국립보건연구원

국가 백신 관련 정책(22)

- “윤석열 정부 120대 중점 과제”
▷ (포스트 코로나) 감염병 등 보건안보 관련 과제와 희귀난치 질환 등 국가적 해결 필요과제에 대한 **혁신적 연구개발 체계** 구축(한국형 Arpa-H)

	과제 목표	주요 내용
감염병 대응 체계 고도화	팬데믹 대비 과학적 근거 기반 신진적 감염병 대응 체계 구축	• 재유행 대비 백신 추가 접종 및 백신 이상 반응 국민 입증 부담 완화
바이오디지털 헬스 글로벌 중심 국가 도약	보건안보전략기술 집중 투자와 글로벌 협력 강화로 백신·치료제 강국 도약	• 혁신적 연구개발 체계 구축 - 초고속 백신·치료제 개발 전략
예방적 건강관리 강화	국가예방접종 지원 백신 및 대상 확대로 예방 가능한 감염병 대비	• 국가 필수 예방 접종 확대 및 백신 안전관리 체계 구축

- 범정부 차원의 감염병 위기 대응 상황 대비를 위한 중장기 계획 수립
✓ 제3차 국가 감염병 위기대응 기술개발 추진 전략(22~26)

백신 국산화 기술 확보	2021년 50%	2026년 70%
국가 예방 접종	피내용 BCG 성인용 디프테리아-파상풍-백일해(TdaP) 디프테리아-파상풍-백일해(DTaP)	자궁경부암(HPV)
기타 예방 접종	소아장염(Rotavirus) 수막구균성 수막염(MCV)	
대유행, 대테러 대비		탄저



[신종감염병 대유행 대비 중장기계획 10대 핵심과제]

감시·예방	① 감염병 조기경보를 위한 통합 감시체계 구축 ② 글로벌 보건안보 선도 및 국제협력체계 강화
대비·대응	③ 세계에서 인정받은 초기 대응역량 지속 발전 ④ 100만명 100일 대응 가능한 의료체계 구축 ⑤ 대규모&장기 유행에 흔들리지 않는 필수인력 확보 ⑥ 감염에 취약한 시설·집단을 안전하게 보호
기반	⑦ 협력적·효율적 위기대응 위한 튼튼한 기반 조성 ⑧ 고도화된 정보시스템 및 빅데이터 플랫폼 구축
회복	⑨ 피해완화와 조기 회복을 위한 두터운 지원체계
연구개발	⑩ 백신·치료제 개발 가속화를 위한 R&D 지원체계를 혁신

- 신종감염병 대유행 대비 백신개발 전략

2024년 질병관리청 주요 정책계획 ('24.2.19)

2024. 2.



2024 비전	새로운 위기에는 신속하게 일상속 위험에는 단단하게
정책목표	보건안보 강국, 건강사회 실현을 위한 하루 100만명 감염병 환자 대응 전략 마련 대유행 100-200일 내 백신·치료제 신속개발 기반 구축 100세 시대 생애주기별 건강한 일상 보호
핵심과제	<p>1. 새로운 감염병 유행에 대한 선제적 대비·대응</p> <ul style="list-style-type: none"> ① 출중한 감시, 정밀한 위기예측 ② 신속한 진단, 고도화된 역학조사 ③ 빅데이터 기반 방역, 탄력적 의료대응 ④ 新팬데믹 대비체계 마련 <p>2. 상시 감염병 위험요인 관리 및 퇴치</p> <ul style="list-style-type: none"> ① 국가예방접종 확대 및 운영 고도화 ② 감염병 전파의 잠재 위험요인 관리 ③ 감진·예방 강화로 주요 감염병 퇴치 ④ 의료관련 감염 및 항생제 내성 관리기반 강화 <p>3. 초고령사회 질병 대비 및 건강취약계층 보호</p> <ul style="list-style-type: none"> ① 지역사회 만성질환 예방관리 강화 ② 지속가능한 생애주기 건강조사체계 ③ 거주지 중심 두터운 화귀질환자 지원 ④ 손상건강위해 예방 안전망 공고화 <p>4. 국가 보건으로 연구역량 제고</p> <ul style="list-style-type: none"> ① 백신·치료제 신속개발 및 지원체계 강화 ② 건강격차 해소를 위한 만성질환 연구 ③ 보건으로 연구 데이터 확보·개발 <p>5. 공중보건 글로벌 협력 선도</p> <ul style="list-style-type: none"> ① 글로벌 보건안보 역량네트워크 강화 ② 공중보건 정책 및 기술 연계 강화

4. 국가 보건으로 연구역량 제고

- ◆ 신종감염병 대유행 시 백신·치료제를 신속 개발할 수 있는 기반을 만들겠습니다.
- ◆ 국내·외 연구 협력으로 미래질 감염병, 만성질환을 극복하겠습니다.

1. 신종감염병 대비 백신·치료제 신속개발 및 지원체계 강화

- (백신) 국가 백신 R&D 핵심기관으로서, 국내·외 민·관과 전략적 연계·협력으로 백신 신세 개발 및 국산화로 백신주권 확보
- (전략) 신종감염병 대유행 위기 시 신속한 백신 개발을 위해 우선 순위 병원체(病院體) 중심 투트랙 전략 추진(신세개발, 글로벌 공동)
 - * 코로나19 신종인플루엔자, 니파, 라바, 중기, SFTS, 지문구니아 신종중요병원체(중요한) 연구
- (국산화) 생물대리 등 공공안보 감염병 백신 개발, mRNA 핵심 기술 확보 등 국가 주도의 백신 개발로 보건안보 강화
 - * 한제백신 공동개발(식약처, 동국대, 진정) * 백신전문기업(LNP용), 정온형 백신(VT) 기술
- (인프라) “국가원단백신개발센터” 운영으로 인공지능 활용 백신 형원 설계, 디지털(m-silico) 비임상, 백신 항원 라이브러리 등 인프라 구축

신종감염병 백신 개발 전략

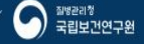
■ (팬데믹 발생전) 체계 구축 → (팬데믹 발생시) 100/200일 이내 신속 개발 추진



‘대비 단계: 팬데믹 발생전 신속개발 체계 구축’이 필수적

1단계 : 대비(최대한 준비)

3 백신개발전략



(1단계) 대비 : 팬데믹 발생 전 신속 개발 체계 구축



1단계: 우선순위 백신 개발 계획

3 백신개발전략



- 우선순위 병원체(9종) 중심으로 단계적 개발
- (two-track 전략) 국내 자체개발, 글로벌 개발 공조

개발전략

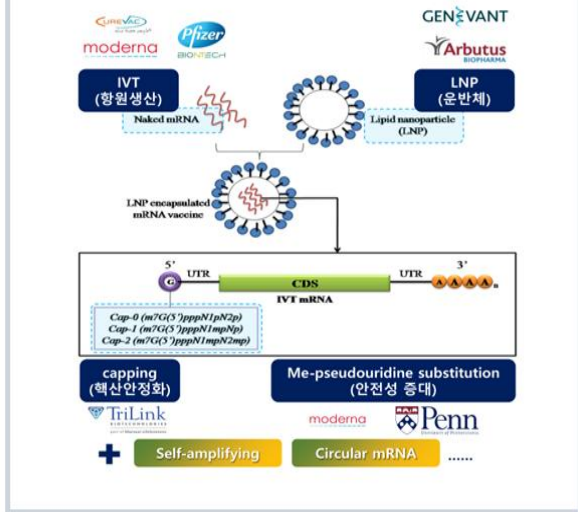
전략	병원체	현 개발단계 (국내)	실용화 목표
국내 자체 개발	신종인플루엔자	비임상	품목허가
	코로나19	임상1상	품목허가
	RSV	비임상	품목허가
	SFTS	비임상	품목허가
	신중후군출혈열(한탄)	후보물질 개발	품목허가
글로벌 공조	라싸	비임상	임상1상
	니파	후보물질 개발	임상1상
	댕기	비임상	임상1상
	치쿤구니아	후보물질 개발	임상1상

1단계; mRNA 백신 플랫폼 등 핵심기술 확보

3 백신개발전략



mRNA 백신 플랫폼 핵심기술요소



개발 현황

- 일부기술 도입을 통한 mRNA 백신신속 개발 추진 중
- mRNA 백신 후보물질 질병청 자체 연구개발 중
 - * 차세대 결핵, SFTS, 일본뇌염, 다가형코로나 및 엡폭스
- 산학연 대상 핵심기술개발 및 (비)임상 시험 연구과제 지원
 - * 신변종감염병 mRNA백신 사업단(질병청/복지부): 팬코로나, 지카, 라싸열 등

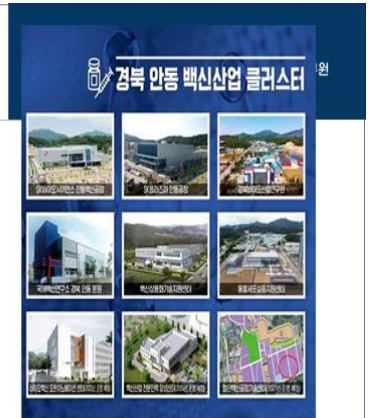
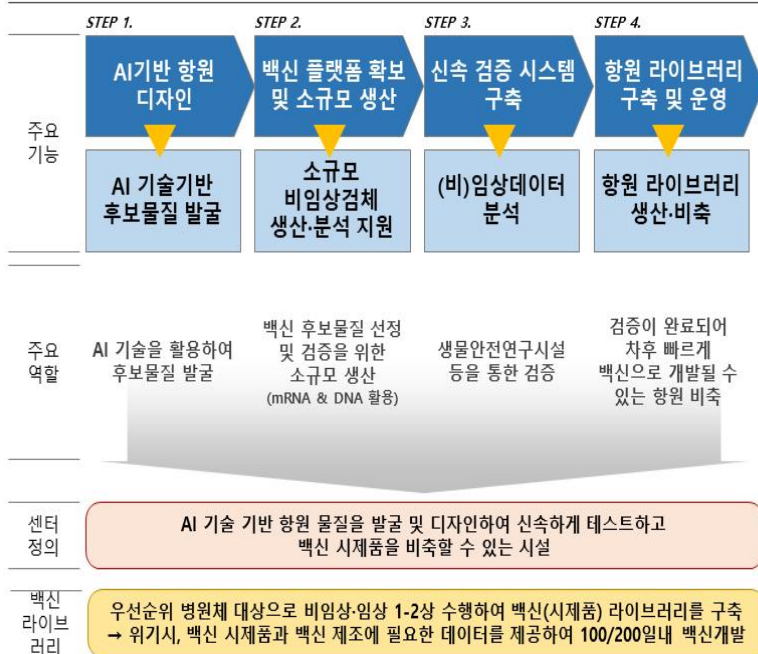
향후 계획

- 특허회피 가능 mRNA백신 핵심요소 기술 개발 지속 지원
 - * 생산벡터, 고효능 원형 mRNA 벡터, LNP대량 생산 및 개선 등
- 한국형 mRNA백신 플랫폼 구축 (**28~30**)
 - * 특허회피 가능 mRNA 백신기술 고도화를 통한 한국형 플랫폼 구축

1단계; 백신 라이브러리 구축

국가첨단백신개발센터 사업내용

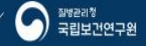
(재)국가첨단백신개발센터 사업 내용



위치 및 사업기간	<ul style="list-style-type: none"> • 위치: 경북 안동시 경북바이오산업단지 일원 • 사업기간: '23년 ~ '27년 (5년)
규모	<ul style="list-style-type: none"> • 부지 약 10,000㎡, 건축 약 5,000㎡(연구시설, 1개동)
총사업비	<ul style="list-style-type: none"> • 총 사업비(1단계): 95억 원(국비[건축비, AI·빅데이터구축비] + 95억 원(지방비[부지·연구장비])) • 예산확보: '23년 10억, '24년 22억

2단계: 대응 (즉각적반응)

백신개발전략

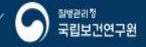


(2단계) 대응 : 팬데믹 발생 시 신속 개발 추진



2단계: 대응 (즉각적 반응)

백신개발전략



100일 (Track 1)

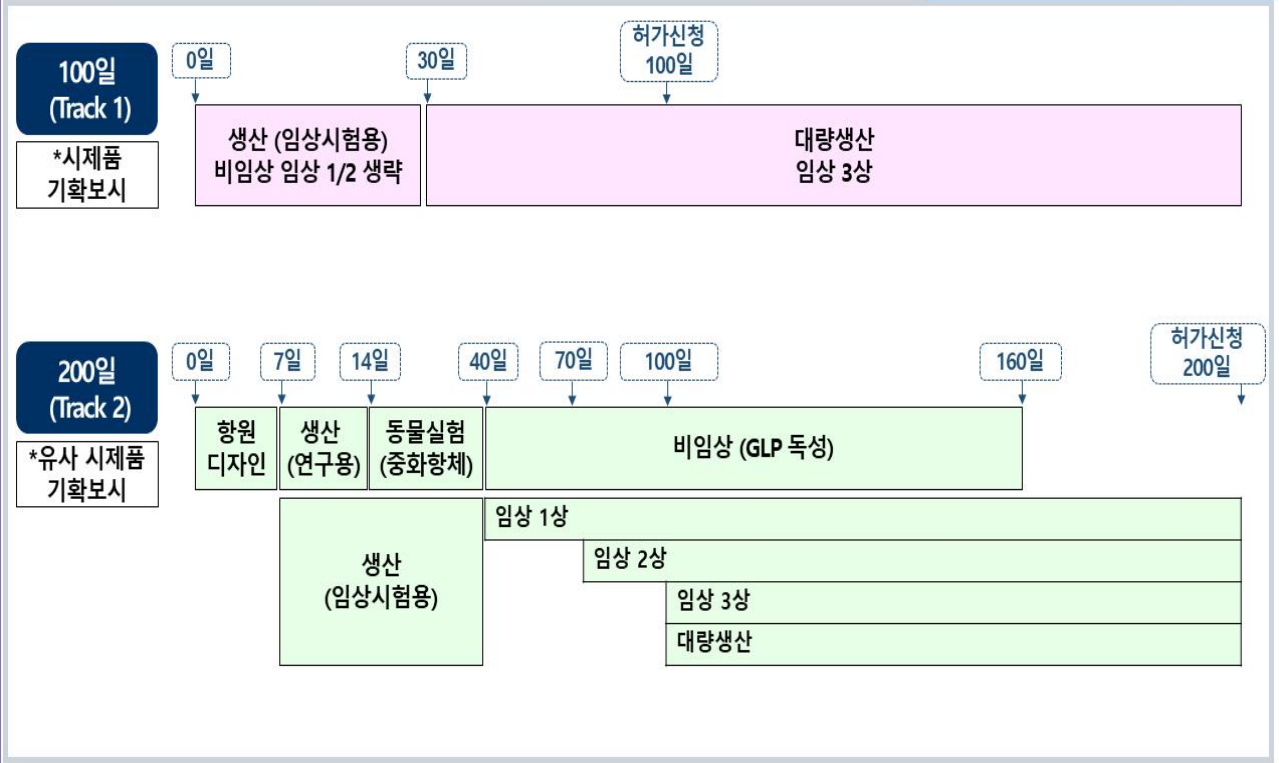
[임상 1/2상] 해당 수준의 안전성과 용량 데이터가 확보된 타겟 병원체 프로토타입 활용 가능 시 생략

200일 (Track 2)

임상 1/2상 단계에서 타겟 병원체와 유사성이 높은 프로토타입을 미리 확보한 경우 수행 가능 (예: SARS-CoV-3 프로토타입)

2단계(대응): 100/200일 개발 일정 시나리오(안)

백신개발전략



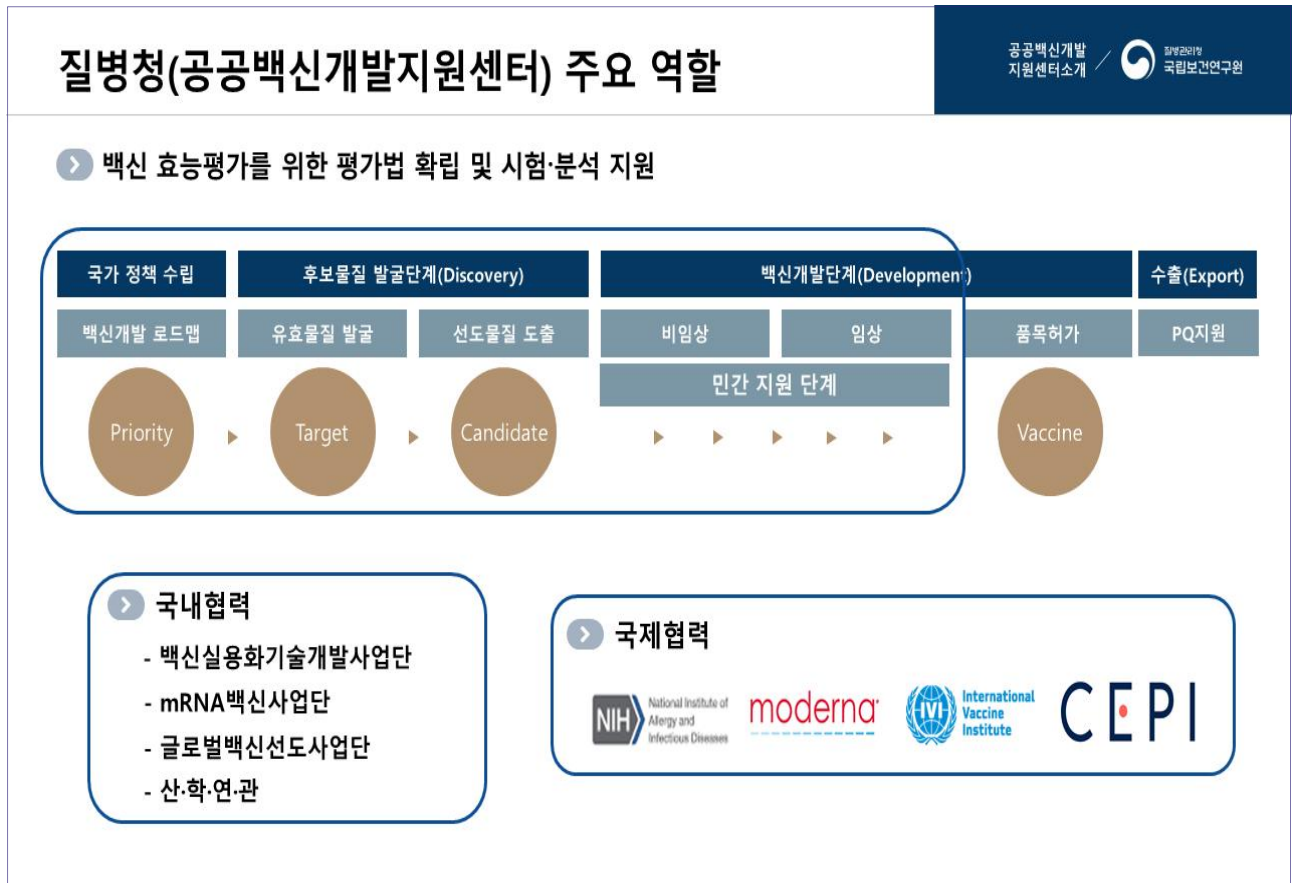
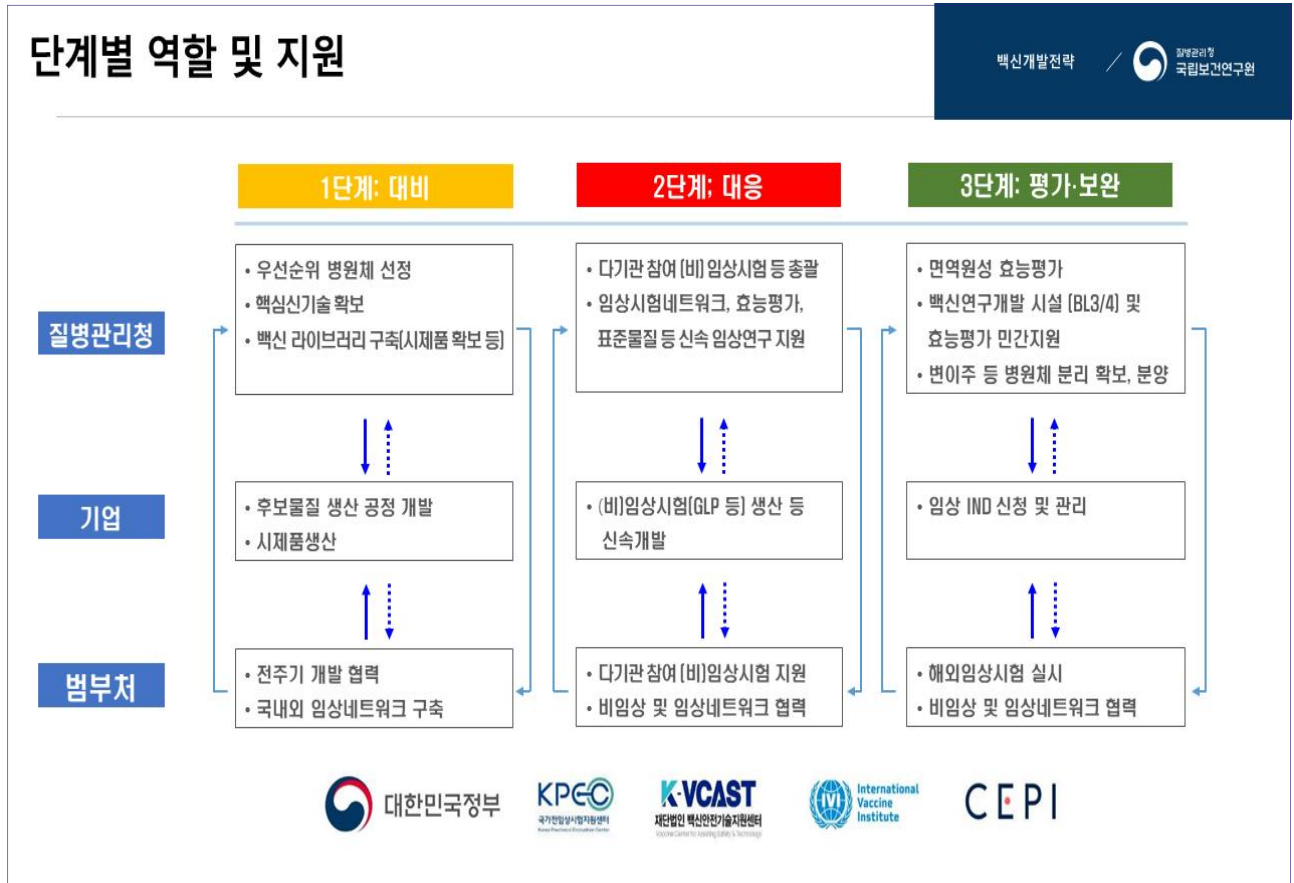
3단계: 평가보완

백신개발전략



(3단계) 대응 : 팬데믹 발생 후 평가보완





질병청(공공백신개발지원센터) 국산 백신 개발 역량

백신개발현황 및 성과 / 질병관리청 국립보건연구원

코로나19 백신개발

SKB 허가/국내 접종(22년), WHO PQ인증(23년)

mRNA 코로나19 백신 임상(2개) 진입 성과

* 신변증 mRNA백신사업단 지원(아이진, 에스티팜)

(비)임상검체 분석 지원

플랫폼	기업	백신	임상			비고
			1상	2상	3상	
합성형원	SK바이오사이언스	GBP510-AS03	80	240	9,962	3상
DNA	진원생명과학	GLS-5310	45	126		1/2a상
RNA	큐라티스	QTP104 (repRNA)	36			1상
RNA	에스티팜	STP2104 (mRNA)	30			1상

질병청 개발 백신

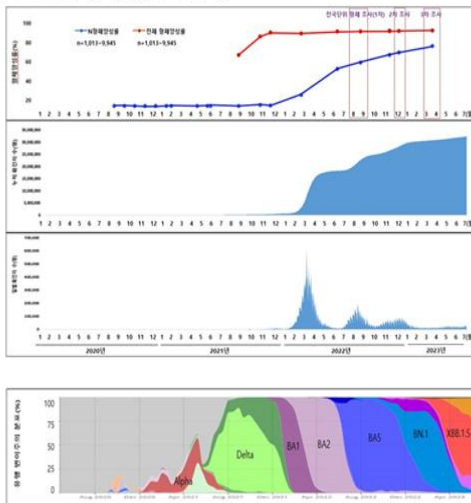
백신	플랫폼	진행현황	향후계획
차세대결핵	재조합	마우스모델에서 효능 평가	비임상 연구추진 ('24~)
아데노55형	불활화	생산공정 개발 및 비임상(독성 및 효력) 수행 중	영장류 효능평가 (~'24) 및 임상연구 추진('25~)
3세대두창	약독화	생산공정 확립 및 비임상(독성 및 약리) 수행 중	임상시험 추진('24~)
탄저	재조합	비임상 및 임상 완료	품목허가신청 ('23.10월)

질병청(공공백신개발지원센터)의 과학적 근거 제공

코로나19 백신개발현황 및 성과 / 질병관리청 국립보건연구원

코로나19 항체양성을 조사

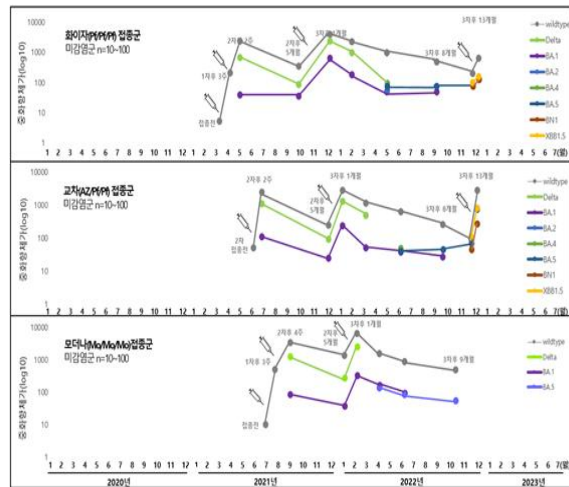
신종 및 법정 감염병 돌발 유행에 대비하여 감염취약집단 확인 및 유행위험 평가를 위해 전국단위 혈청역학 감시체계 구축운영
- 대표성 강한 국가 통계 산출을 위한 지역 대표 표본 1만명만 5세 이상에 대한 주기적 코로나19 항체양성률 조사수행



백신 면역원성 장기 추적조사

국내 도입 백신 접종자의 면역원성 장기 추적조사를 위한 코호트 구축 및 운영

- 국내 도입 코로나19 백신 5종 및 2가 백신 접종자에 대한 코호트 구축 후 주기적 검체 수집 및 중화항체 분석 실시



향후 계획

3 백신개발전략



- 신속 백신개발을 위한 mRNA 등 핵심기술 및 플랫폼 고도화
→ AI(인공지능) 기반 백신 후보물질 발굴 등 첨단기술 도입, 백신 라이브러리 구축 등
- 국내·외 연구협력 네트워크 확대
 - (국내) 백신안전기술센터(식약처 재단법인)
국가전임상기술센터(과기부 출연연)
 - (국외) 국제백신연구소(IVI), WHO, CEPI
등 백신 공동연구
- 고시 제정('24.1월), BL3/4 시설, 병원체자원은행 활성화를
통한 민간지원 사업 활성화



세션 1.

신종감염병 특성 및 임상연구

2024

감염병연구기관 국제심포지엄

International Symposium for Infectious Diseases Research Institutes Cooperation

Chair



Man-Seong Park

- ✔ Department of Microbiology, Institute of Viral Disease, College of Medicine, Korea University
- ✔ Professor

🔍 EDUCATION:

- 1999 Korea University Graduate School, Ph.D.
- 1996 Korea University Graduate School, M.S.
- 1994 Korea University, College of Science, B.S.

🔍 PROFESSIONAL EXPERIENCE:

- 2022 ~ Present Member, Committee for Infectious diseases, PRESIDENTIAL ADVISORY COUNCIL ON SCIENCE & TECHNOLOGY,
- 2007 ~ 2014 Assistant/Associate Professor, Dept of Microbiology, College of Medicine, Hallym University
- 2014 ~ Present Assistant/Associate Professor, Dept of Microbiology, College of Medicine, Korea University
- 2005 ~ 2007 Instructor, Dept of Microbiology, Icahn School of Medicine at Mount Sinai, USA
- 1999 ~ 2004 Post-doctoral fellow, Dept of Microbiology, Icahn School of Medicine at Mount Sinai, USA
- 2022 ~ Present Board member, Government-wide R&D Fund for Infectious Disease Research (GFID), Korea

01

SFTSV 감염 연령에 따른 병인 기전

최영기 소장
한국바이러스기초연구소



Speaker



Young-Ki Choi

- ✓ Korea Virus Research Institute, IBS
- ✓ Managing Director

🔍 EDUCATION:

- 2002 Ph.D, University of Minnesota, College of Veterinary Medicine (USA)
- 1999 MS, Chungnam National University, College of Veterinary medicine
- 1996 DVM, Chungnam National University, College of Veterinary medicine

🔍 PROFESSIONAL EXPERIENCE:

- 2021 ~ Present Managing Director, Korea Virus Research Institute, IBS (Korea)
- 2023 ~ 2024 Chungbuk National University, College Medicine,
(Assistant professor – Professor)
- 2023 ~ 2024 Post-Doc Fellow, St. Jude Children's Research Hospital (USA)

🔍 Topic

Age-dependent differential pathogenesis of SFTSV infections

🔍 Abstract

Dabie bandavirus (severe fever with thrombocytopenia syndrome virus [SFTSV]) induces an immunopathogenic disease with a high fatality rate; however, the mechanisms underlying its clinical manifestations are largely unknown. In this study, we applied targeted proteomics and single-cell transcriptomics to examine the differential immune landscape in SFTS patient blood. Serum immunoprofiling identified low-risk and high-risk clusters of SFTS patients based on inflammatory cytokine levels, which corresponded to disease severity. Single-cell transcriptomic analysis of SFTS patient peripheral blood mononuclear cells (PBMCs) at different infection stages showed pronounced expansion of B cells with alterations in B-cell subsets in fatal cases. Furthermore, plasma cells in which the interferon (IFN) pathway is downregulated were identified as the primary reservoir of SFTSV replication. This study identified not only the molecular signatures of serum inflammatory cytokines and B-cell lineage populations in SFTSV-induced fatalities but also plasma cells as the viral reservoir. Thus, this suggests that altered B-cell function is linked to lethality in SFTSV infections.

02

마우스 모델에서의 인간 인플루엔자 A바이러스 헤마글루틴인의 탈당쇄화에 따른 병원성 증가

최장훈 연구관

국립감염병연구소 급성바이러스연구과



Speaker



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🔍 EDUCATION:

- 2011 Hanyang University Graduate School, Ph.D.
- 2004 Korea University graduate School, M.S.
- 2001 Hanyang University College of Science, B.S.

🔍 PROFESSIONAL EXPERIENCE:

- 2020 ~ Present Deputy Scientific Director, Division of Acute Viral Disease Research, Center for Emerging Virus Research, National Institute of Infectious Diseases, KNIH
- 2016 ~ 2020 Staff Scientist, Division of Viral Disease Research, Center for Infectious Diseases, KNIH
- 2016 ~ 2016 Visiting scientist, VRC, NIAID, NIH
- 2014 ~ 2016 Visiting fellow, NIAID, NIH
- 2007 ~ 2014 Staff Scientist, Div. of Influenza virus, Center for Infectious Diseases, Korea National Institute of Health

Q Topic

Deglycosylation of seasonal influenza virus (A/H3N2) hemagglutinine confers infectivity and pathogenicity during mouse adaptation

Q Abstract

Pandemic Influenza A viruses (IAVs) occasionally cross the species barrier through either host adaptation or genetic reassortment. Understanding the viral genetics that underlie virulence and cross-species transmission is critical for designing durable vaccines and therapeutics. In our previous work, we successfully established a mouse adapted strain (maSW293) from seasonal influenza A/H3N2 virus (A/Switzerland/9715293/2013). Unlike the parental strain, maSW293 exhibits infectivity and pathogenicity in mice. Pathogenicity analysis using recombinant viruses revealed that hemagglutinin (HA) plays a pivotal role in infection and mortality in mice. Notably, three identified mutations (N160D, T183A, N262T) within the HA sequence have the potential to induce deglycosylation in the globular head domain.

The analysis of mouse pathogenicity using recombinant viruses revealed the significant contribution of HA mutations to both infection and mortality in mice. Each virus carrying the deglycosylation mutation exhibited infectivity in mice. Notably, mice infected with the triple mutant virus exhibited a significantly reduced survival rate compared to the wild-type virus. Consequently, infection with the mutant viruses led to severe lung pathology and elevated induction of inflammatory cytokine and chemokine. Interestingly, the triple mutant virus exhibited not only enhanced α -2,6pism. Additionally, mutant viruses carrying the T183A and N262T mutations showed reduced NA activity, suggesting a potential contribution to viral fitness during host adaptation.

Collectively, the finding from this study suggest that the deglycosylation of the globular head of the HA can enhance pathogenicity and facilitate cross-species adaptability in mice. This is likely achieved through alterations in receptor binding affinity and NA activity.

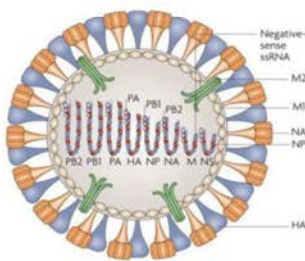
Deglycosylation of human influenza A virus (H3N2) hemagglutinin increases virulence in mice

Jang-Hoon Choi

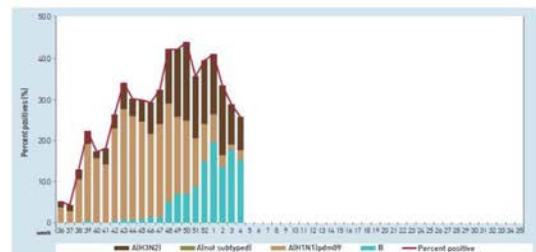
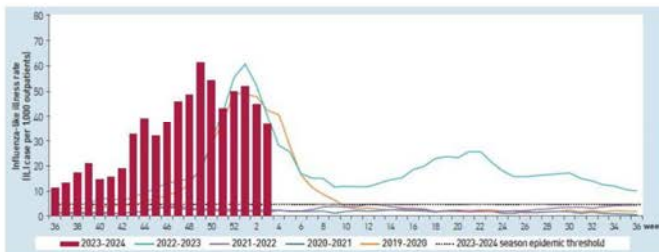
Center for Emerging Virus Research, National Institute of Infectious Diseases,
Korea National Institute of Health



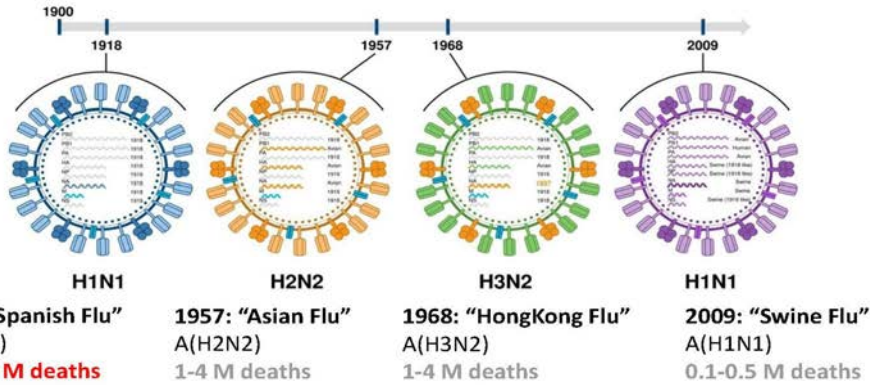
Influenza virus



- *Orthomyxoviridae* family
- (-)ssRNA virus, 8 segmented RNA
- Current seasonal influenza viruses: A(H3N2, H1N1), B(Vic/Yam)
- Infects up to 20% of the population each year



Pandemic Influenza viruses



Credit: US National Museum of Health and Medicine



Walter N. Harrington et al., *EMM*, 2021

Risk Assessment Tools

IRAT (CDC, 2011)

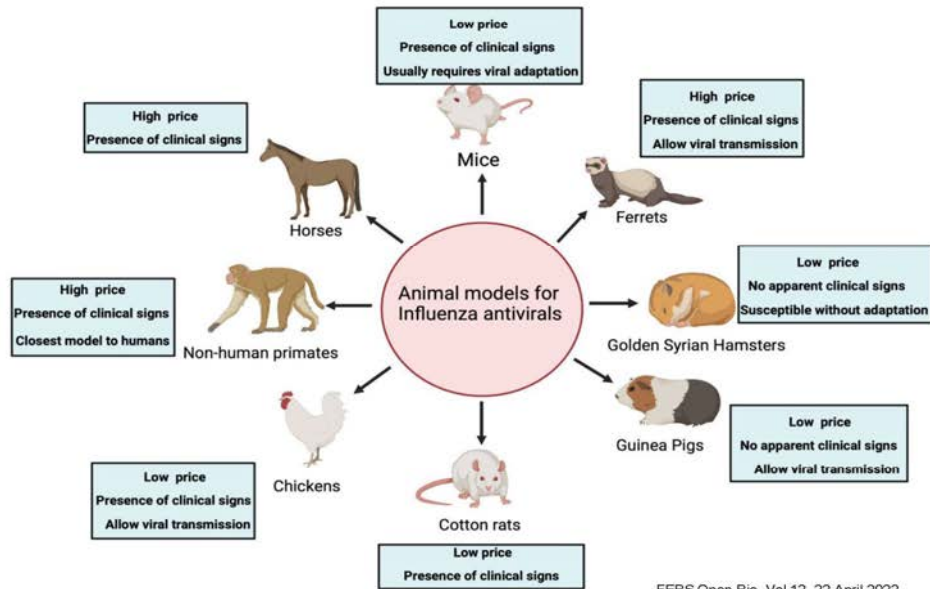
Virus	<ul style="list-style-type: none"> • Genomic variation • Receptor binding • Transmission in lab animals • Antivirals and treatment options
Population	<ul style="list-style-type: none"> • Existing population immunity • Disease severity and pathogenicity • Antigenic relationship to vaccine candidates
Ecology	<ul style="list-style-type: none"> • Global geographic distribution • Infections in animals • Human infections and transmission

TIPRA (WHO, 2016)

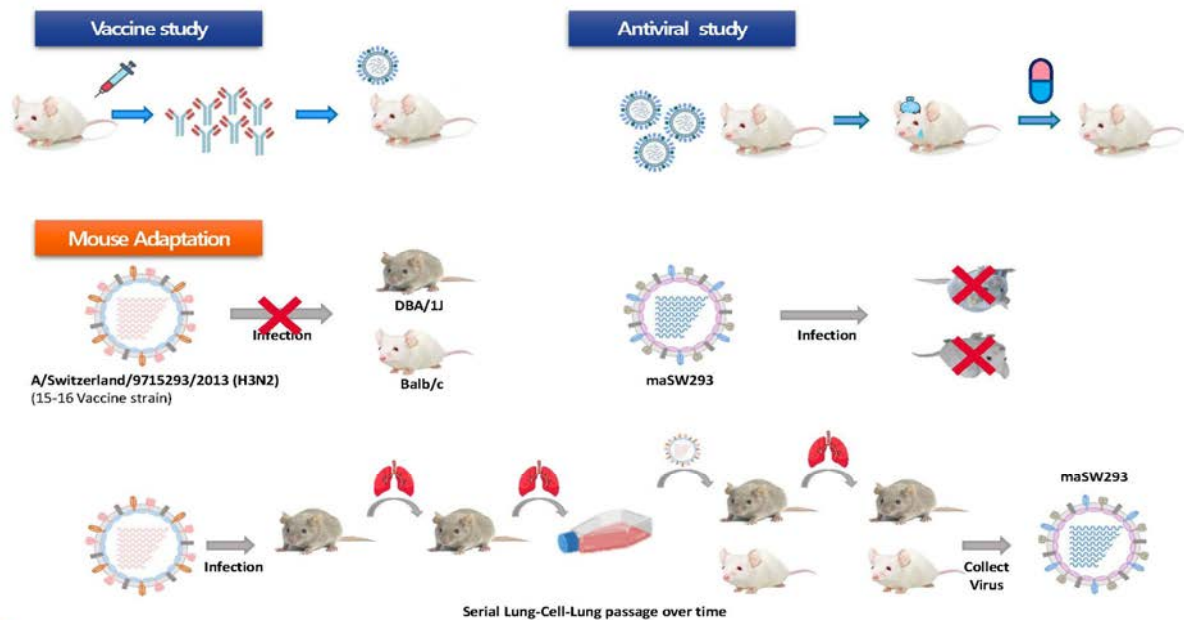
Virology	<ul style="list-style-type: none"> • Genomic characteristics • Receptor binding properties • Transmission in animal model • Susceptibility to antiviral treatment
Public Health	<ul style="list-style-type: none"> • Population immunity • Disease severity • Human infection
Animal Health	<ul style="list-style-type: none"> • Geographic distribution in animals • Infections in animals

IRAT: Influenza Risk Assessment Tool
TIPRA: Tool for Influenza Pandemic Risk Assessment

Animal models for influenza study

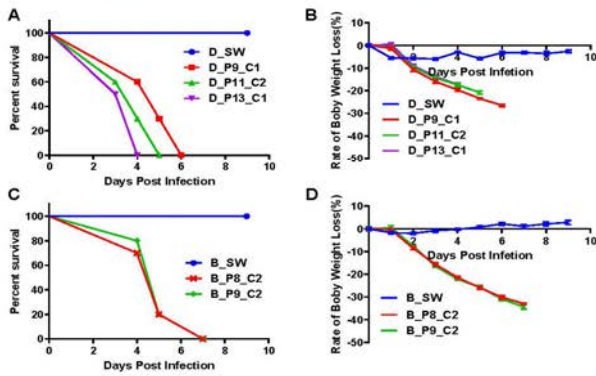


Experimental mouse adaptation



Generation of mouse adapted(MA) H3N2 virus

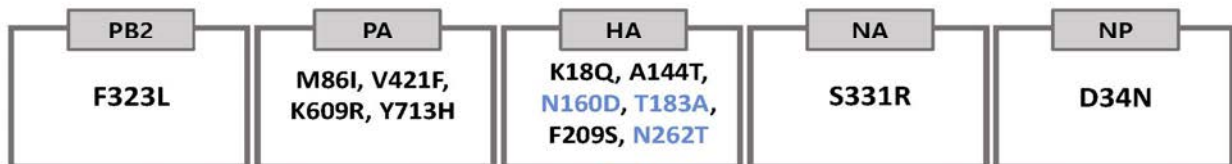
Virulence of H3N2 MA strains



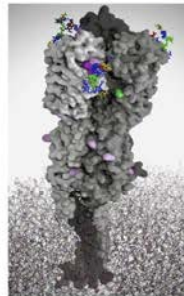
Amino acid substitutions identified in H3N2 MA strains

Name	HA					NA			NP			PA			PB2						
	18	144	160	183	209	262	522	331	369	463	34	189	354	86	356	421	609	713	323	355	
A/Switzerland/9/15/293/2013	K	A	N	T	F	N	E	S	T	D	D	M	G	M	E	V	K	Y	F	R	
DBA/11_P9_C1	K	T	N	A	S	T	E	S	M	D	D	M	G	M	E	V	K	Y	L	R	
DBA/11_P11_C2	K	T	N	A	S	T	E	S	A	N	D	M	R	I	E	V	R	H	L	R	
DBA/11_P13_C1	K	T	N	A	S	T	E	S	K	D	D	I	R	I	E	V	R	H	L	R	
Hall/c_P8_C2	Q	T	D	A	S	T	E	R	T	D	N	M	G	I	E	F	R	H	L	R	
Dalb/c_P9_C2	Q	T	D	A	S	T	E	R	T	D	N	M	G	I	K	F	R	I	L	R	

Amino acid substitutions of maH3N2 virus



HA mutation



Hemagglutinin glycosylation

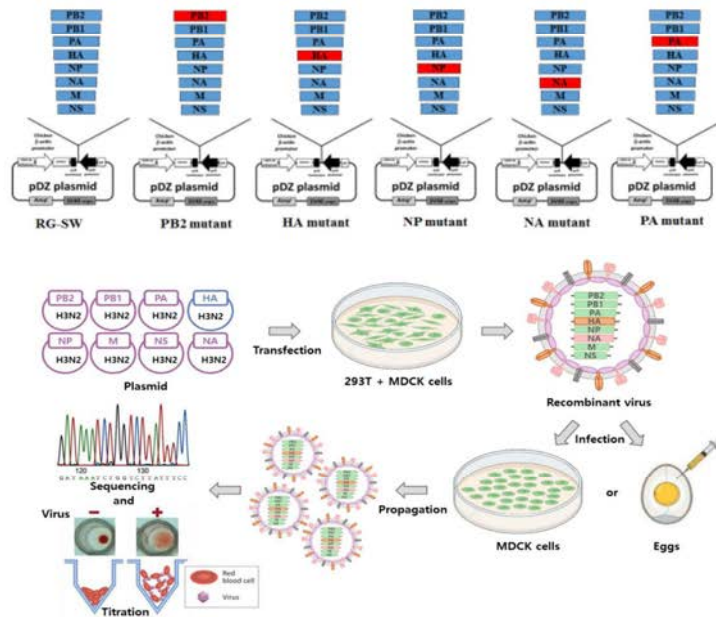
1) HA Immunogenicity

Escape Humoral Immunity (Abs Shielding)
Protein folding

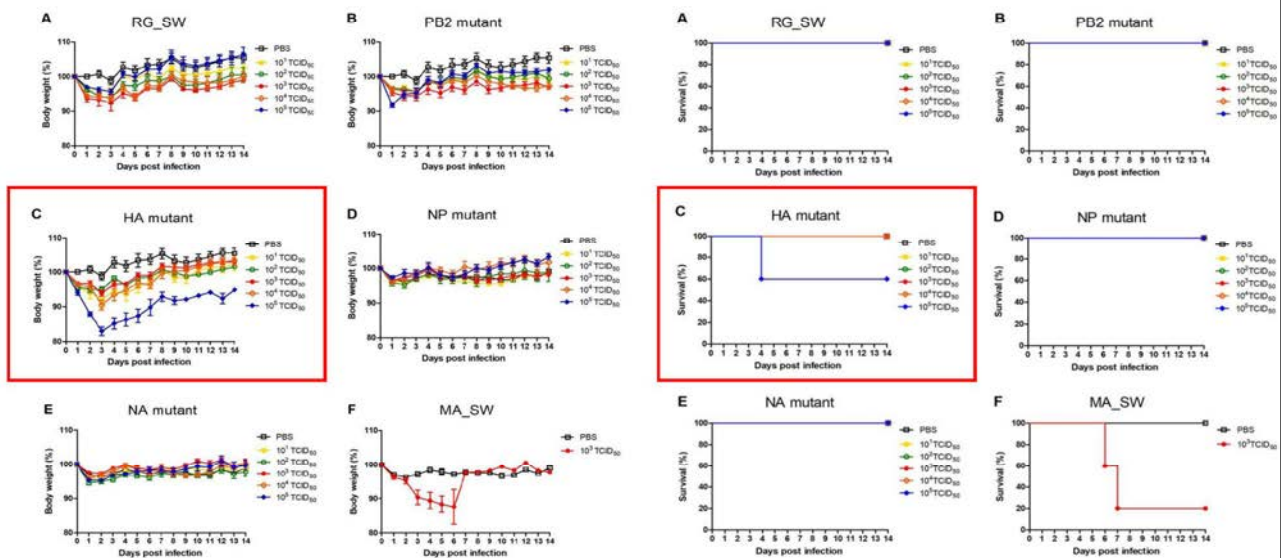
2) Viral Virulence

Receptor binding
Avoid Innate immune response (C-type Lectin)

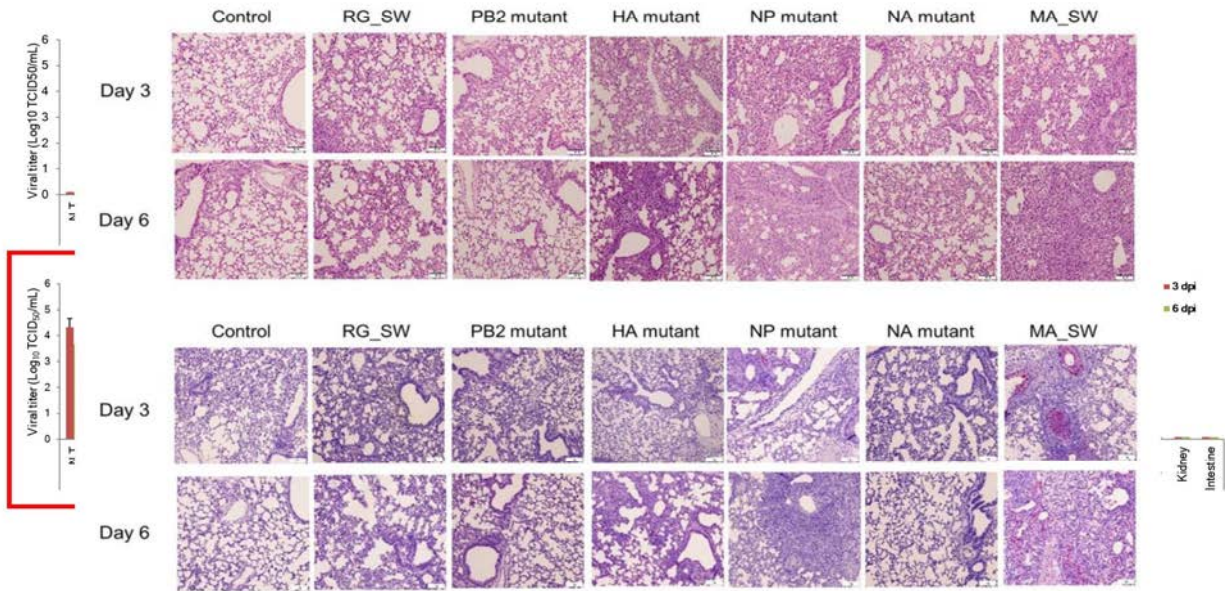
Generation of mutant viruses (Reverse-Genetics)



Pathogenesis of recombinant maH3N2 viruses

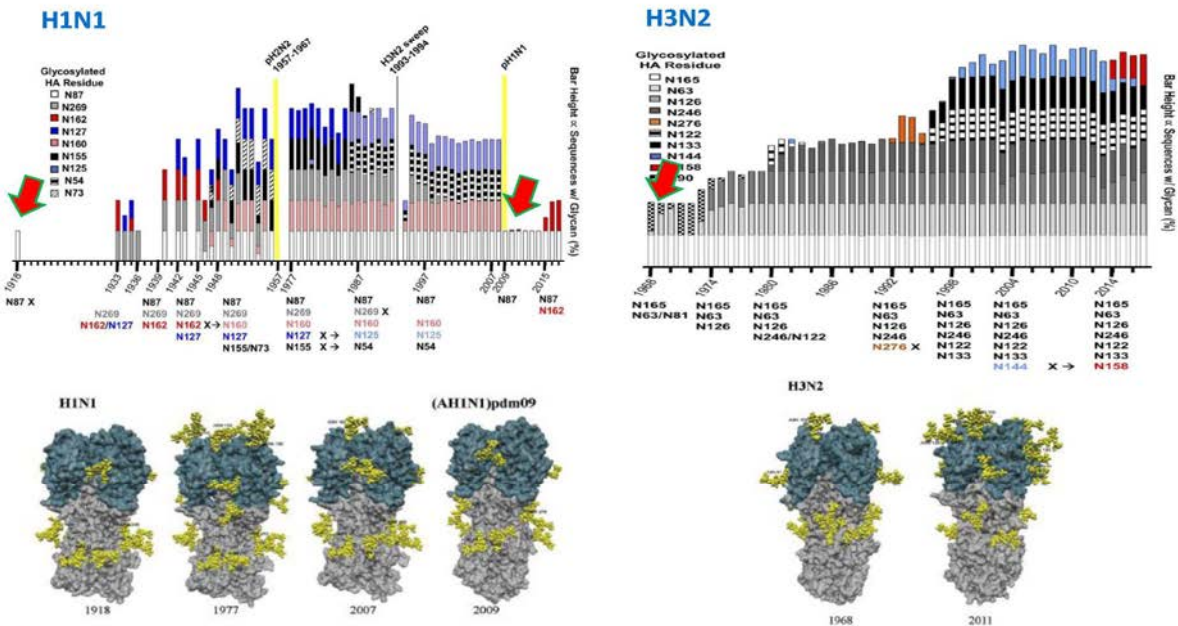


Pathogenesis of recombinant maH3N2 viruses



National Institute of Health
Republic of Korea

Pandemic and HA glycosylation



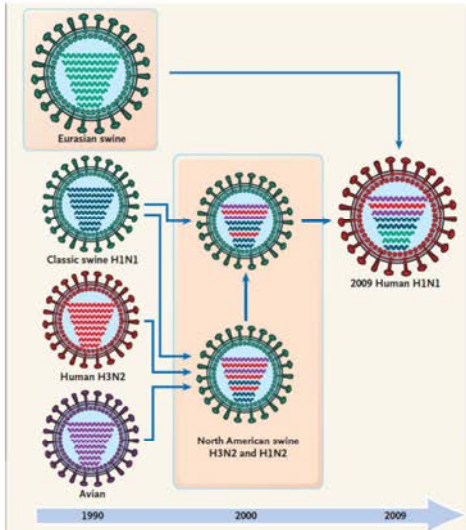
National Institute of Health
Republic of Korea

Tate et al., *Viruses*, 2014

Altman et al., *mBio*, 2019

Pandemic and HA glycosylation

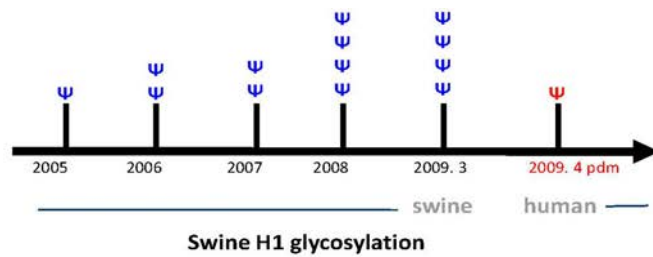
Origin of 2009 pandemic H1N1 virus



Trifonov et al., NEJM, 2009

Swine/North American/H1N2/2005-2009.03 HA Glycosylation number

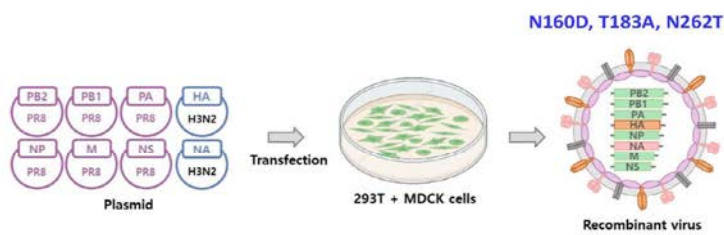
No. GLY	2005	2006	2007	2008	2009 (01-03)
Max	1	2	2	4	4
Min	1	1	1	2	3
Avg	1	1.5	1.6	3.2	3.3



Decreased glycosylation when it cross to new host

Generation of mutant viruses

Recombinant viruses by Reverse Genetics

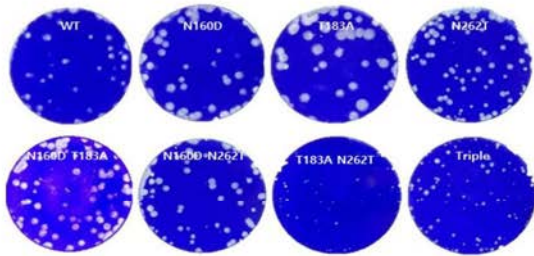


바이러스	역가 (TCID ₅₀ /ml)	내부 유전자	HA	NA
SW-WT:PRB	2.47 x 10 ⁶	PRB	SW-HA	SW-NA
SW-N160D:PRB	3.98 x 10 ⁶		SW-HA N160D	SW-NA
SW-T183A:PRB	2.7 x 10 ⁶		SW-HA T183A	SW-NA
SW-N262T:PRB	1.37 x 10 ⁷		SW-HA N262T	SW-NA
SW-N160D T183A:PRB	3.98 x 10 ⁶		SW-HA N160D T183A	SW-NA
SW-N160D N262T:PRB	1.17 x 10 ⁷		SW-HA N160D N262T	SW-NA
SW-T183A N262T:PRB	5.62 x 10 ⁶		SW-HA T183A N262T	SW-NA
SW-Triple ¹⁾ :PRB	1.83 x 10 ⁷		SW-HA Triple ¹⁾	SW-NA

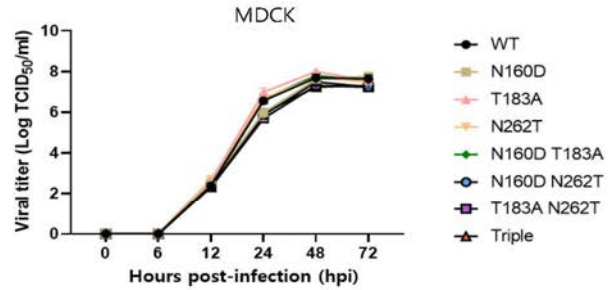
1) N160D/T183A/N262T

Biological characterization of Deglycosylated mutant H3N2 viruses

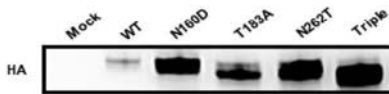
Plaque morphology



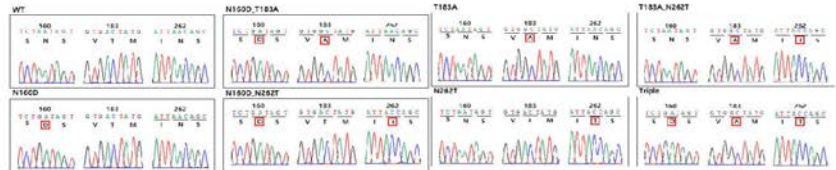
Growth curve analysis



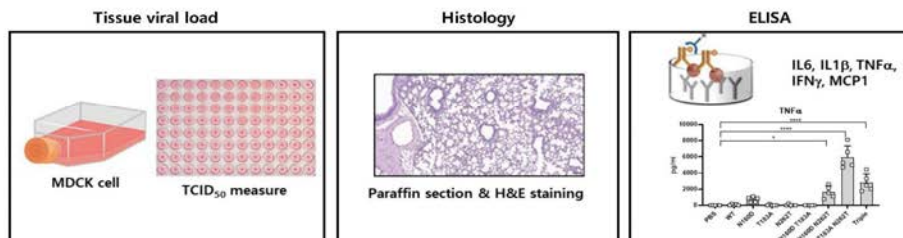
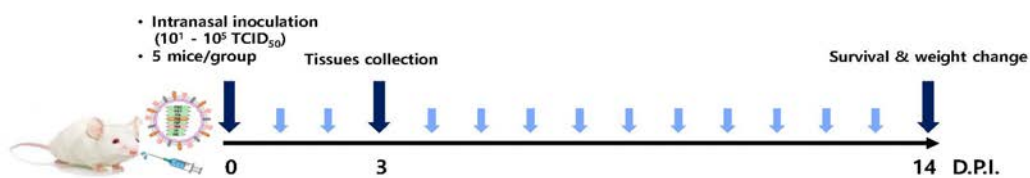
Gel mobility shifts



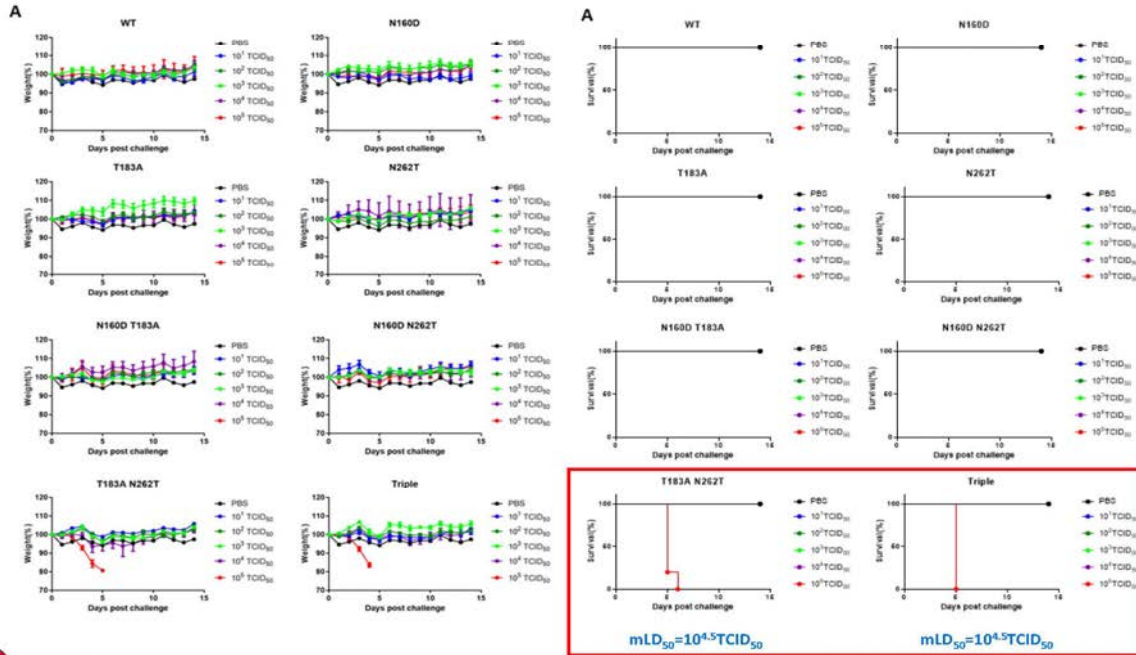
Genetic stability



Mouse pathogenesis of mutant viruses

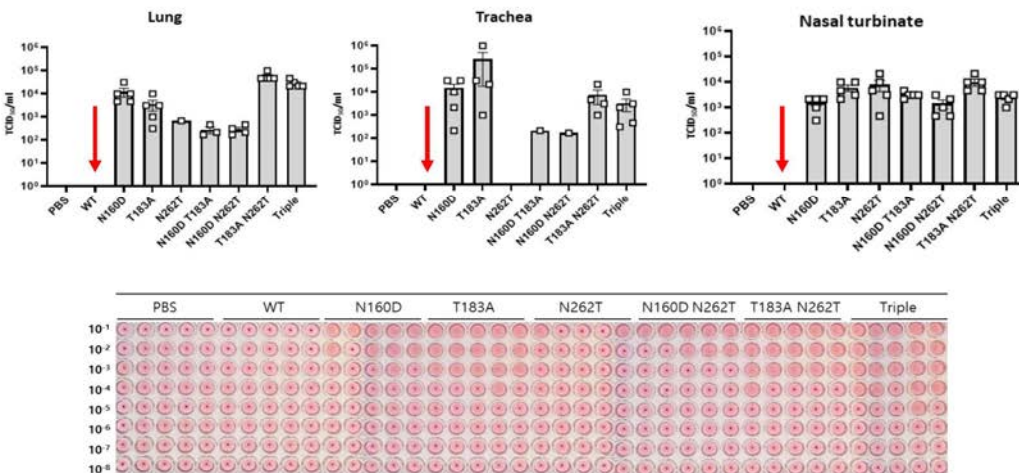


Pathogenesis of mutant H3N2 viruses in Balb/c mice

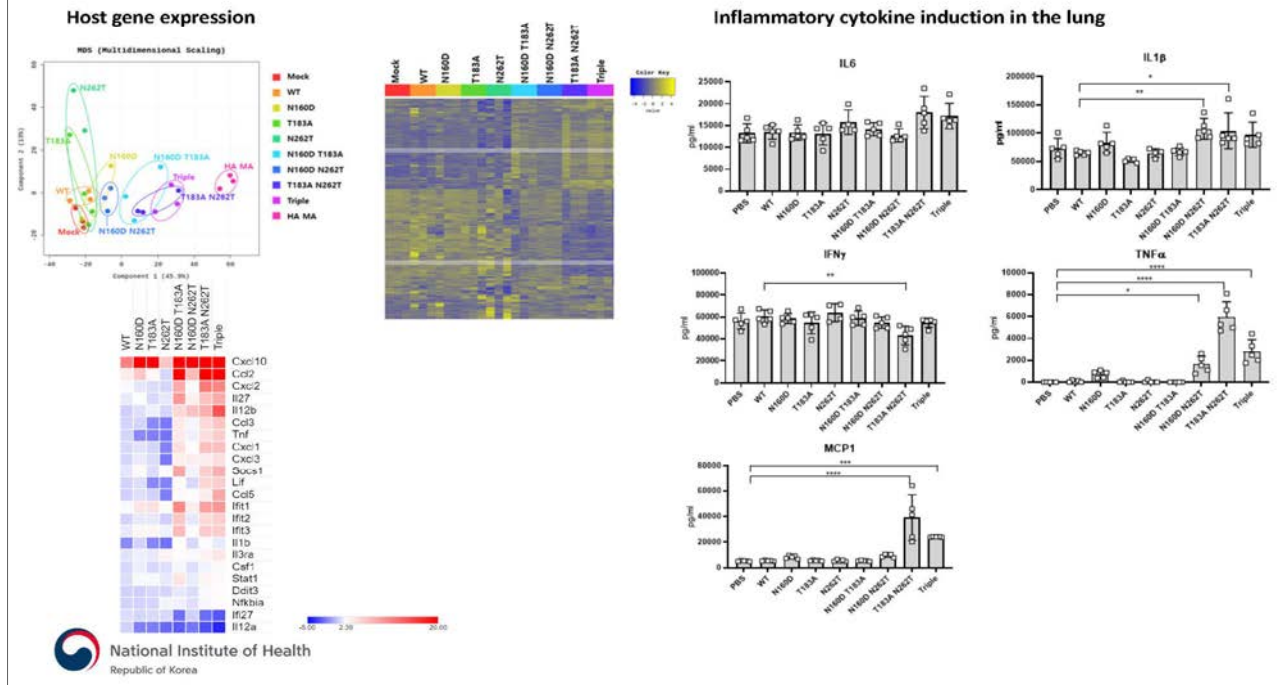


Pathogenesis of mutant H3N2 viruses in Balb/c mice

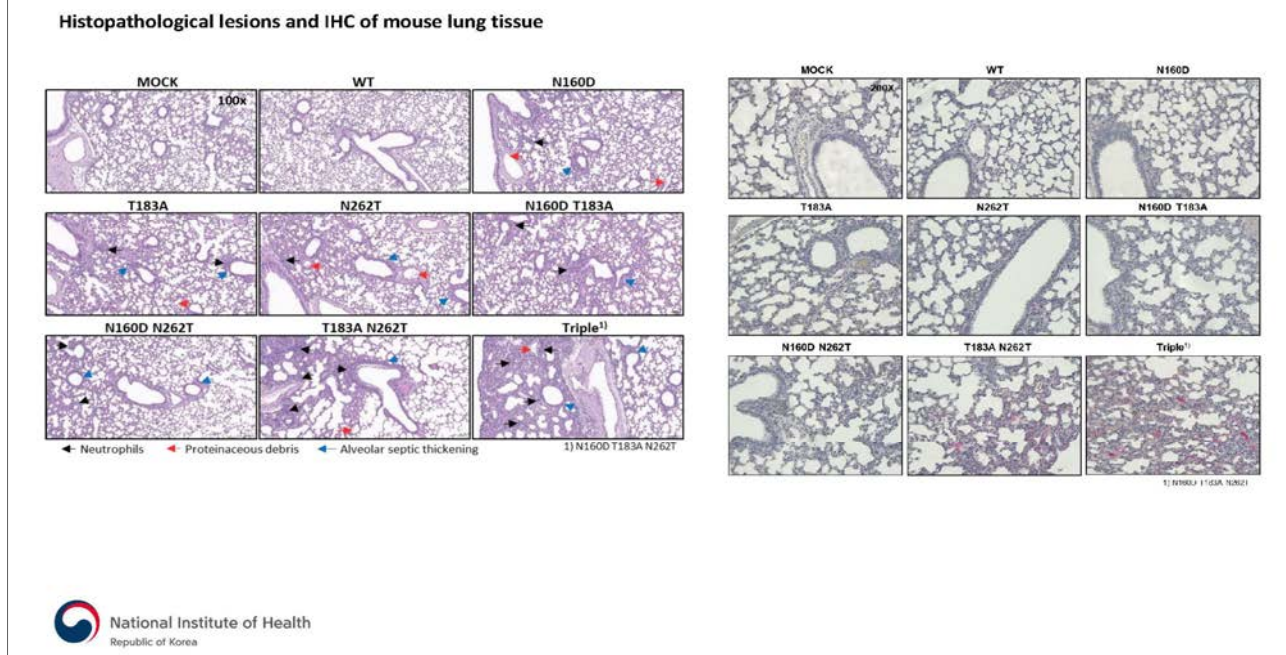
Virus titers in mice tissues infected with 10^5 TCID₅₀ per mouse



Pathogenesis of mutant H3N2 viruses in Balb/c mice

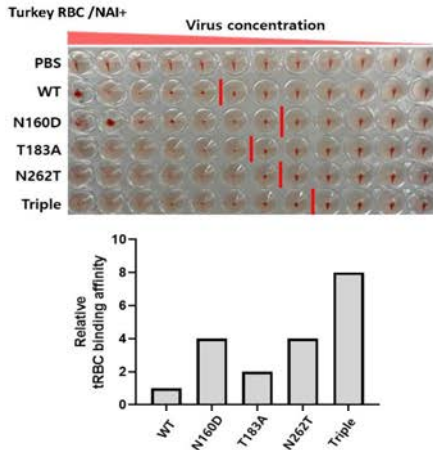


Pathogenesis of mutant H3N2 viruses in Balb/c mice

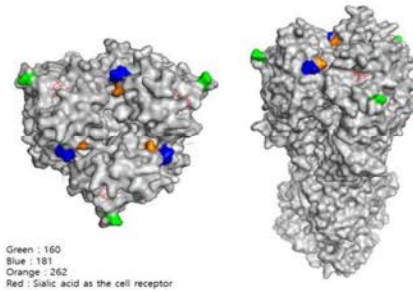
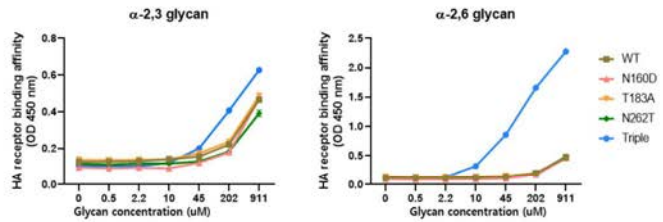


Receptor binding affinity

Hemagglutination assay (HA)

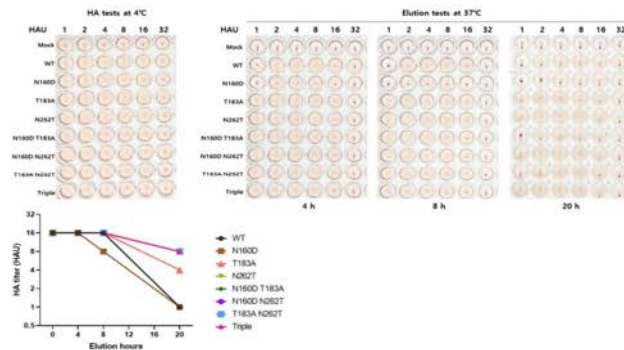


Solid-phase direct virus binding assay

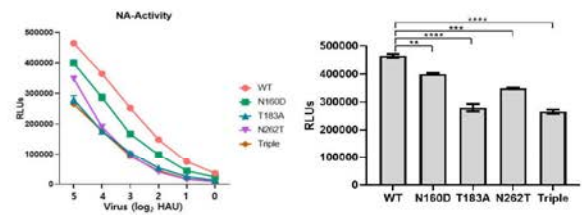


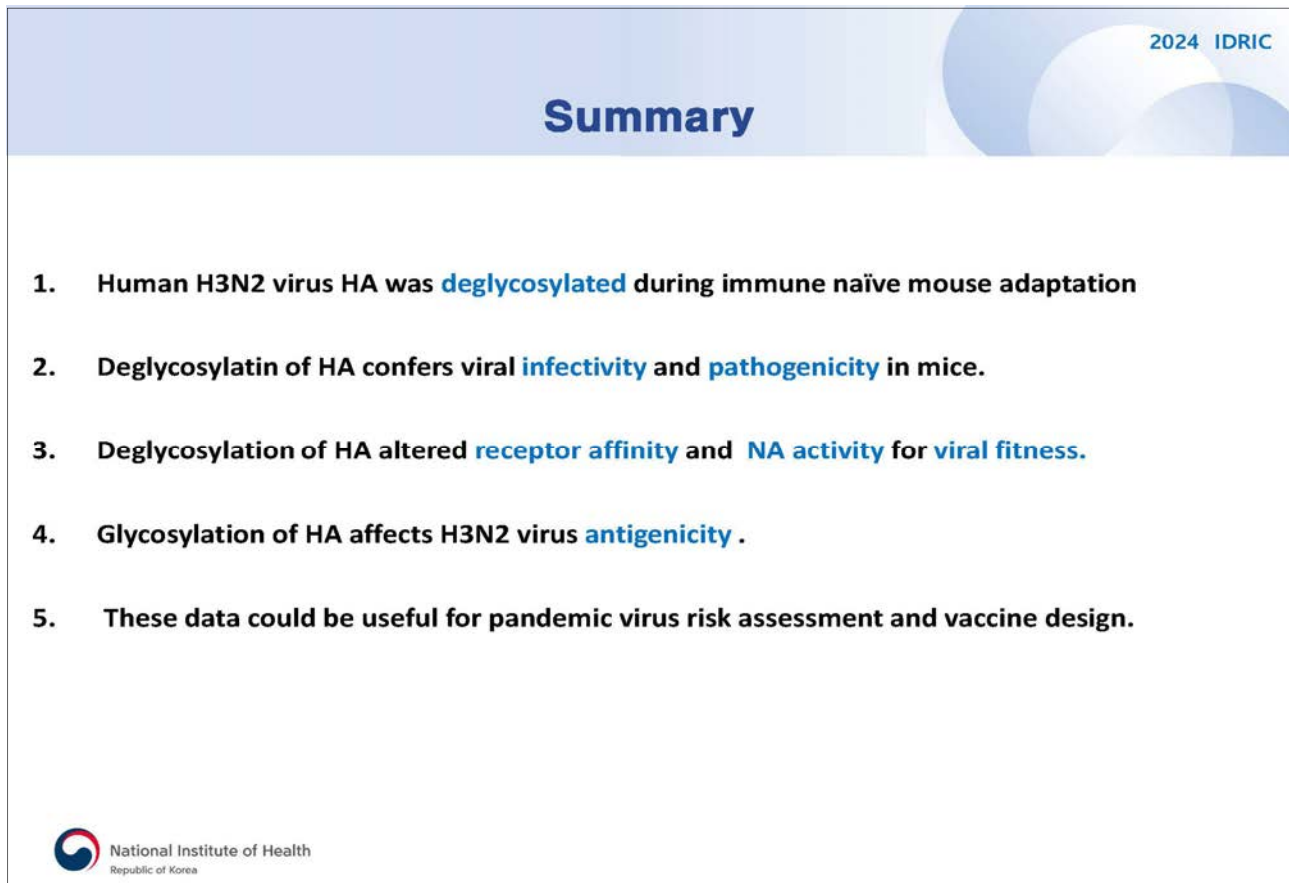
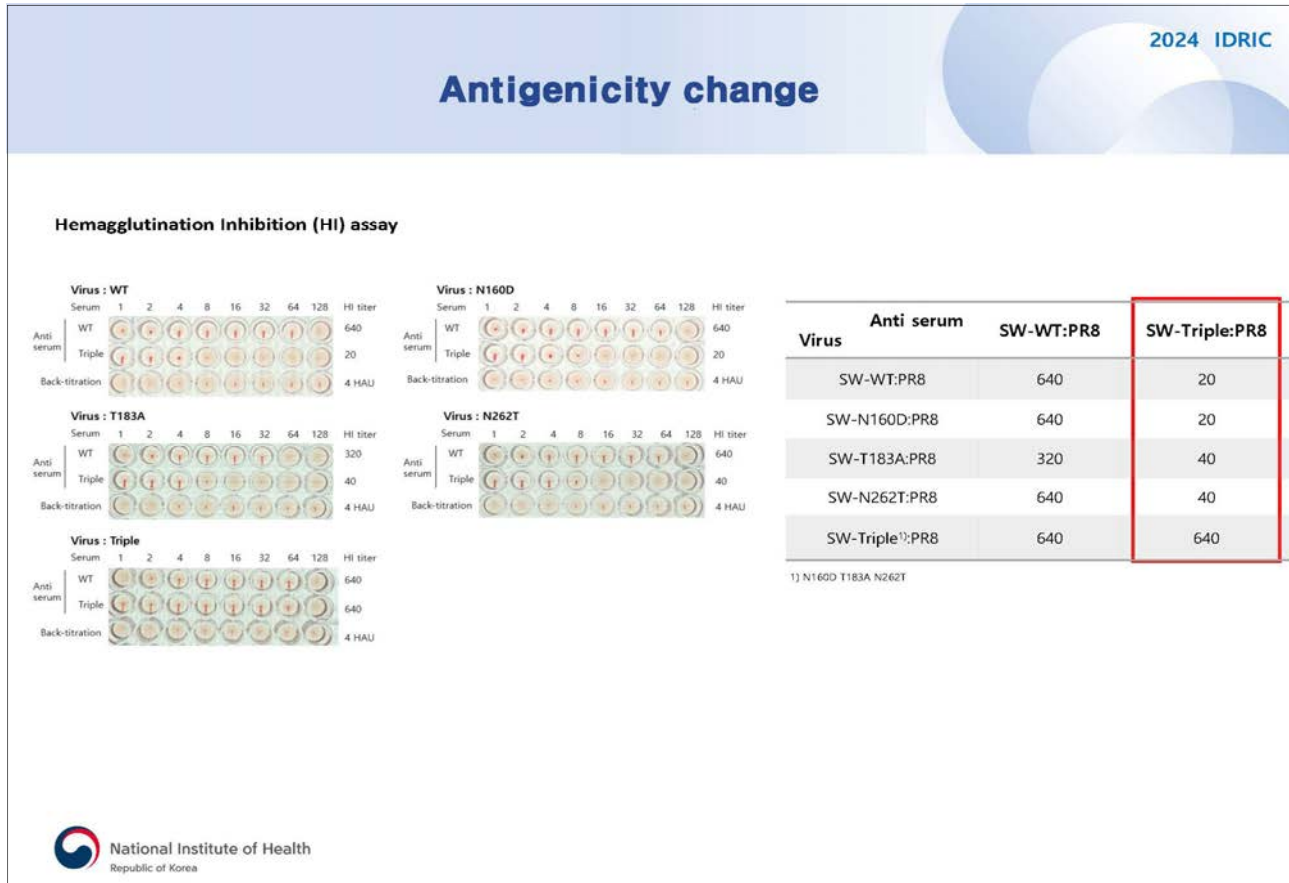
Neuraminidase activity

HA elution assay with tRBCs



Neuraminidase activity assay





03

국내 Mpox 환자의 임상 증상과 바이러스 배출

김민경 교수
국립중앙의료원



Speaker



Kim, Min-Kyung

- ✓ National Medical center
- ✓ Professor

🔍 EDUCATION:

- 2022 PhD candidate in Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea
- 2015 M.P.H., Graduate School of Public Health, Seoul National University, Seoul, Republic of Korea
- 2009 M.D., Seoul National University College of Medicine, Seoul, Republic of Korea

🔍 PROFESSIONAL EXPERIENCE:

- 2020 ~ 현재 Infectious disease physician, National Medical center
- 2019 ~ 2020 Deputy Director, Korea Centers for Disease Control & Prevention (KCDC) Cheongju, Korea
- 2016 ~ 2019 Epidemic Intelligence Officer, Korea Centers for Disease Control & Prevention (KCDC) Cheongju, Korea
- 2015 ~ 2016 Chief Researcher, Seoul Center for Infectious Disease Control, Seoul, Korea
- 2014 ~ 2015 Fellow, Division of Infectious Disease, Department of Internal Medicine, SNUH, Seoul, Korea
- 2010 ~ 2014 Resident, Department of Internal Medicine, SNUH, Seoul, Korea
- 2009 ~ 2010 Intern, Seoul National University Hospital(SNUH), Seoul, Korea

🔍 Topic

Clinical presentation and viral shedding in patients with Mpox in South Korea

🔍 Abstract

국내 엠폭스 유행 초기(2022년 9월부터 2023년 6월) 국립중앙의료원에 입원한 엠폭스 환자들을 대상으로 임상적 특성 분석과 함께 구인두, 항문생식기 병변 및 피부 병변에서 monkeypox virus의 PCR 양성 기간과 배양 양성 기간을 분석하였다.

2024 International Symposium for Infectious
Diseases Research Institutes Cooperation

Clinical Presentation and Viral Shedding in Patients with Mpox in South Korea

Min-Kyung Kim
National Medical Center



Outline

- Background - Global mpox outbreak
- Study methods
- Results (1) - Clinical presentation
- Results (2) - Viral shedding
- Discussion
- Conclusion



Mpox

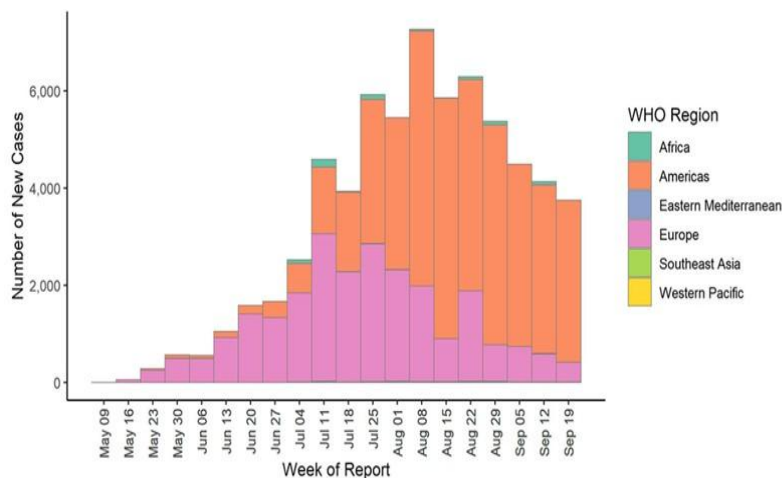
- Mpox(formerly Monkeypox), a zoonotic illness caused by the monkeypox virus, an orthopoxvirus and close relative of variola virus (smallpox).
- The clinical syndrome is characterized by fever, rash, and lymphadenopathy.
 - Complications can include pneumonitis, encephalitis, and secondary bacterial infections.
- Mpox has affected rural communities in west and central Africa since the first human case was reported in the DR Congo in 1970.



Clinical presentation of monkeypox
source: Lancet 2022; 400: 661–69

Mpox Outbreak-global situation

- However, since detection of monkeypox virus transmission outside endemic areas (UK) in May 2022, a large multi-country mpox outbreak has occurred.



<https://www.cdc.gov/poxvirus/mpox/cases-data/technical-report/report-3.html>

Mpox Outbreak-global situation



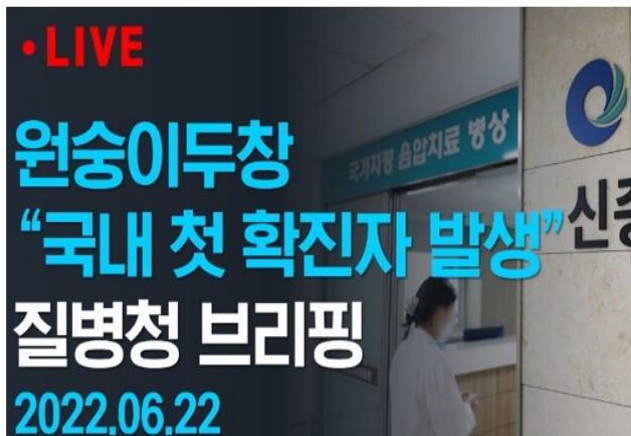
WHO Director-General declares the ongoing monkeypox outbreak a Public Health Emergency of International Concern

23 July 2022 | News release | Reading time: Less than a minute (51 words)

On July 23, the WHO Director-General declared the escalating global monkeypox outbreak a Public Health Emergency of International Concern (PHEIC). Currently, the vast majority of reported cases are in the WHO European Region. WHO/Europe remains committed to partnering with countries and communities to address the outbreak with the required urgency.

World Health Organization director general Tedros Adhanom Ghebreyesus, shown in Geneva last year, declared monkeypox a global emergency on Saturday, despite a lack of consensus among members of WHO's emergency committee. (Salvatore Di Nolfi/Keystone/The Associated Press)

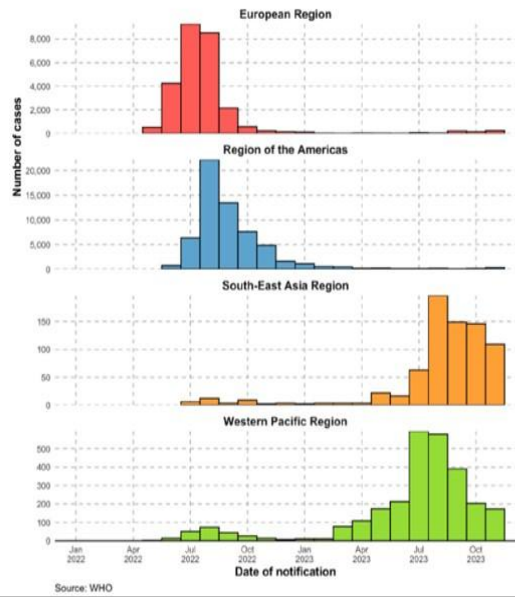
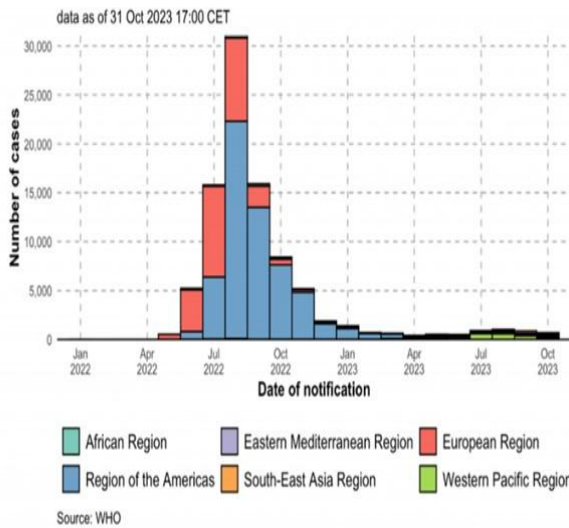
Mpox Outbreak- in South Korea



- In Korea, the first mpox case was confirmed in June, 2022. The patient had a travel history to Europe (Germany).
- Subsequently, two more imported cases and one needle stick injury case were confirmed in 2022.

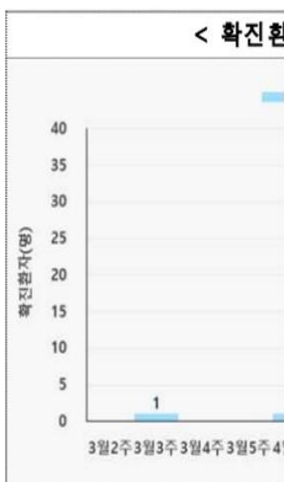
Mpox Outbreak

- Although the number of mpox cases worldwide decreased from September 2022, **Western Pacific region experienced late outbreak in 2023.**



Mpox Outbreak in South Korea

- In South Korea, **domestic outbreak occurred** after the first locally acquired case (the 6th case) was confirmed in **April 2023.**



Purpose of study

- Still, understanding of in-vivo viral kinetics and infectivity is poor and the clinical significance of prolonged viraemia and skin shedding remains uncertain.
- This study **aimed** to describe the **clinical characteristics and viral dynamics of mpox cases** who have been isolated in a referral hospital.

Methods

- Study design: a prospective observational cohort study
- Participants: **hospitalized patients** with confirmed mpox in the National Medical Center in South Korea between September 1, 2022, and June 15, 2023
 - Patients who consented to participate were included
- Epidemiological and clinical characteristics were reviewed.
- Swabs were collected from the **oropharynx (OP), anogenital lesions (AL) and skin lesions (SL)** on hospital days 1, 2, 4, 7, 10, 13, and 21.
- **Blood samples** were collected on hospital days 1, 7, and 14, and during follow-up visits after discharge
 - Sampling schedules were modified according to each patient's condition and date of discharge.

Results

Demographic and clinical characteristics of participants (n=18)

Baseline characteristics	n (%) (N=18)
Men, n(%)	17 (94.4)
Age (years), median (IQR)	32.5 (30-34.8)
Imported cases from overseas travel, n(%)	2 (11.1)
Sexual contact before symptom-onset, n(%)	
Homosexual contact	13 (72.2)
Heterosexual contact	4 (22.2)
Denied to report	1 (5.6)
Smallpox or mpox vaccination before diagnosis, n(%)	0 (0)
People living with HIV, n(%)	9 (50)
CD4 count, cells/ μ L, median (IQR)	547 (494, 692)
History of previous syphilis infection, n(%)	8 (44.4)
Time from symptom onset to mpox diagnostic test (days), median (IQR)	6 (5-7.75)
Length of hospital stay (days)	10 (6.25-11)

Baseline characteristics	n (%) (N=18)
Clinical presentation of mpox, n(%)	n (%) (N=18)
Fever	14 (77.8)
Myalgia	11 (61.1)
Inguinal lymphadenopathy	7 (38.9)
Headache	4 (22.2)
Genital lesion (penile, public, and female vulva)	14 (77.8)
Anal or perianal lesion	14 (77.8)
Other skin lesion (except ano-genital lesion)	10 (55.6)
Con-comittant infection	
Sexually-transmitted disease	7 (38.9)
Peri-lesional cellulitis	4 (27.8)
Treatment	
Tecovirimat	13 (72.2)
Antibiotics for syphilis or con-comittant STD	5 (27.8)
Famciclovir ^a	2 (11.1)
Pain killer	15 (83.3)
Antihistamine	10 (55.6)

Table 1. Demographic and baseline characteristics of the patients

Variables	All patients (N = 60)
Age, yr, median (range)	32 (21-58)
Male	58 (97)
Nationality	
Republic of Korea	54 (90)
China	1 (2)
Japan	1 (2)
Philippine	1 (2)
Taiwan	1 (2)
Russia	1 (2)
Vietnam	1 (2)
Race	
Asian	59 (98)
White	1 (2)
Sexual orientation	
Homosexual/bisexual	51 (85)
Unknown	9 (15)
HIV infection	
Negative	35 (58)
Previously diagnosed	18 (30)
Newly diagnosed	7 (12)
Concomitant STI, No. of cases/No. of tested (%)	15 (25)
Neisseria gonorrhoeae	2/51 (4)
Mycoplasma genitalium	1/51 (2)
Mycoplasma hominis	1/51 (2)
Ureaplasma species	10/51 (20)
Ureaplasma urealyticum	5/51 (10)
Ureaplasma parvum	4/51 (8)
Unknown species	1/51 (2)
Gardnerella vaginalis	4/51 (8)
Primary or secondary syphilis	4/59 (7)
Jynneos vaccination	4 (7)
PrEP	1 (2)
PEP	2 (3)
Vaccination after recovery from Mpox	1 (2)

Table 2. Clinical manifestation, diagnosis, and treatment of the patients

Variables	All patients (N = 60)
Initial presenting symptoms	
Constitutional symptoms	53 (88)
Pain or mucocutaneous lesions in anogenital area	28 (47)
Extragenital mucocutaneous lesions	29 (48)
Clinical symptoms	
Fever (> 38°C)	13 (22)
Sweat	8 (13)
Sore throat	16 (27)
Chills	27 (45)
Cough	1 (9)
Lymphadenopathy (all inguinal)	9 (15)
Headache	11 (18)
Myalgia	23 (38)
Back pain	1 (2)
General weakness	6 (10)
Fatigue	7 (12)
Pruritis	1 (2)
Conjunctivitis	1 (2)
Nausea/vomiting	1 (2)
Anal pain or discharge	7 (12)
Proctitis	3 (5)
Skin lesions	60 (100)
Initial skin manifestation	
Maculopapular	36 (60)
Vesiculopustular	49 (82)
Eschar	13 (22)
Site of skin lesions	
Face	28 (47)
Trunk or limbs	48 (80)
Palms or soles	21 (35)
Anogenital area	51 (85)

PCR/culture positive rate by specimen

Detection of MPXV DNA and infectious virus shedding

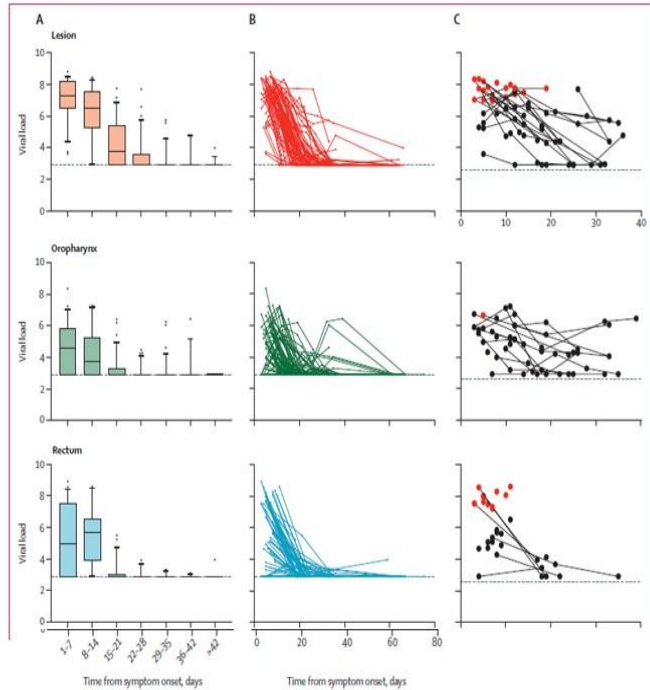
Viral shedding by specimen

Discussion

Viral dynamics in patients with monkeypox infection: a prospective cohort study in Spain



- An prospective, multicentre study of mpox outpatients in Spain, June 28 - Sept 22, 2022.
- **Participants were asked to collect** samples from their **skin lesions, oropharynx, and blood** (dried blood spot) on days **1, 8, 15, 22, 29, and 57** after the screening visit, and samples from their **rectum (swab), semen (collection container), and vagina (swab)** on days **1, 15, 29, and 57**.



Lancet Infect Dis 2023; 23: 445–53

Systematic Reviews

Viral load dynamics and shedding kinetics of mpox infection: a systematic review and meta-analysis

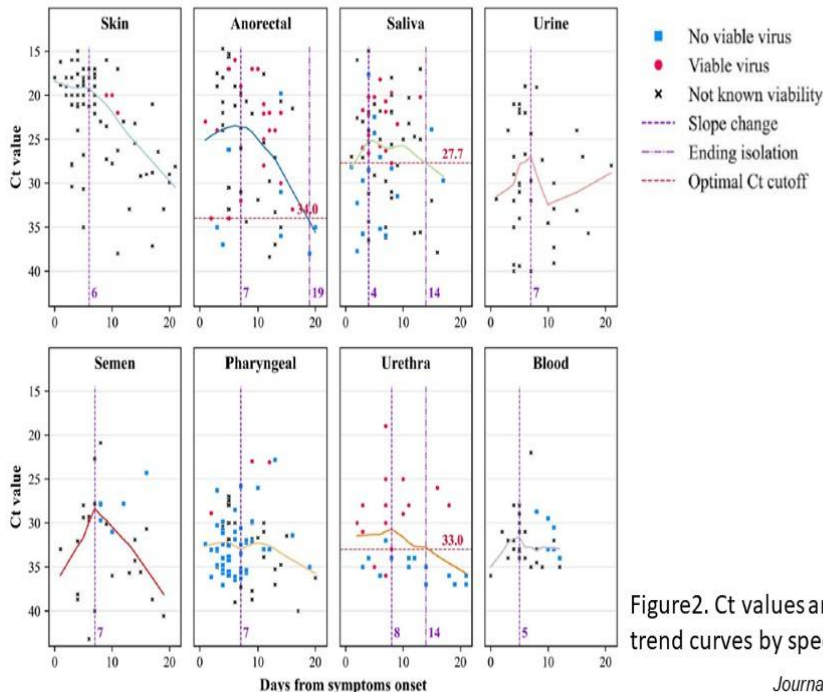


Figure 2. Ct values and its temporal trend curves by specimen types

Journal of Travel Medicine, 2023, 1–10



Limitations

- First, most participants did not have samples collected after discharge, we could not determine the maximum duration of viral shedding.
- Second, the interval of sample collection and duration of follow up differed among participants.
- Third, the number of participants and number of samples was relatively small. However, we cultured all samples with positive PCR results, to maximize the amount of data on viable virus from the available samples.

Conclusion

- Viral DNA was detected for up to 23, 19, and 15 days from symptom onset in AL, SL, and OP samples, respectively and infectious virus was isolated for up to 15 days from symptom onset in all three sample types.

Thank You
For Your Attention!

Any Questions



04

한국의 코로나19 후유증 조사연구 사업

이재갑 교수
한림대학교



Speaker



Jacob Lee

- ✓ Hallym University college of Medicine
- ✓ Associate Professor

Q EDUCATION:

- 2016 Korea University Graduate School, Ph.D.
- 2003 Korea University Graduate School, Master of Medicine
- 1999 Korea University, MD

Q PROFESSIONAL EXPERIENCE:

- Present Associate Professor, Hallym University college of Medicine
- 2022 ~ Present Long COVID-19 Syndrome Research Leader
- 2020 ~ Present Korea Disease Control and Prevention Agency Infectious Disease Crisis Management Committee Member
- 2018 ~ Present Small and Medium Hospital Infection Control Consulting System Manager
- 2021 ~ 2022 Daily Life Restoration Support Committee Medical Quarantine Division Member
- 2020 ~ 2021 Central Disaster and Safety Countermeasures Committee Member
- 2015 Ebola Emergency Relief Team (2nd Leader)
- 2004 ~ 2007 International Cooperation Volunteer (Kazakhstan) KOICA

Topic

Long-COVID Research Project in Korea

Abstract

Overview:

- The NIID initiated a research project on the long-term sequelae of COVID-19 (long-COVID) in 2021.
- A consortium of Hallym University, Gachon University, and Seoul Asan Hospital is conducting the research.
- The project period is from 2021 to the end of 2025.

Research Objectives:

- To investigate the epidemiology and characteristics of long-COVID.
- To analyze the risk factors and prognosis of long-COVID.
- To develop treatment and management strategies for long-COVID.

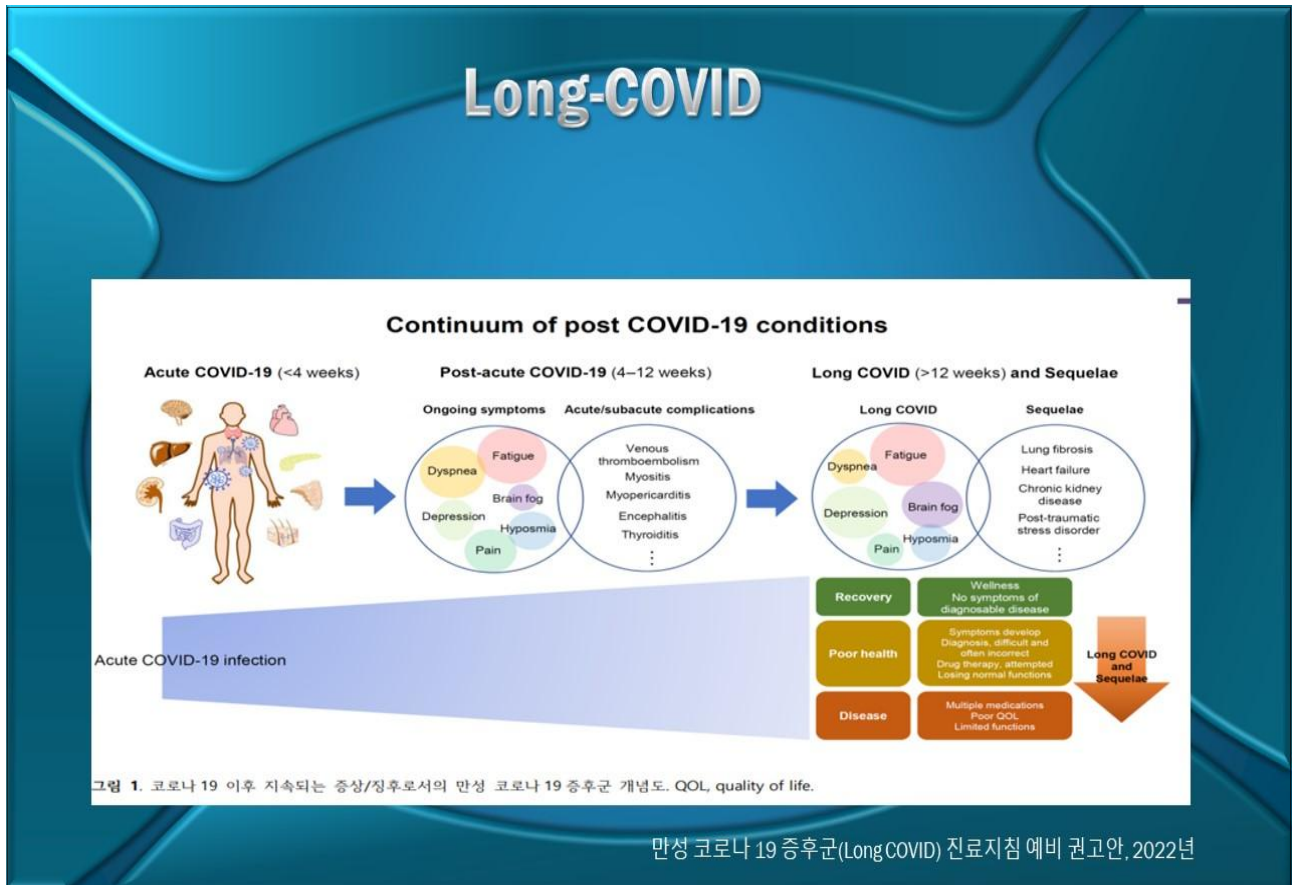
Research Methods:

- A cohort of 10,000 individuals will be assembled to investigate the epidemiology and characteristics of the disease.
- Clinical records of the cohort will be computerized and linked to Korean National Health Insurance data to analyze the characteristics of long-COVID patients.
- Big data information from the Korea Disease Control and Prevention Agency (KDCA) and health insurance information will be linked to analyze the nationwide epidemiology of long-COVID.
- Clinical specimens from the established cohort will be utilized to study the mechanisms of long-COVID, including cognitive impairment, chronic fatigue syndrome, and respiratory complications.

**. Long COVID, post COVID condition -
research in Korea**
한국의 코로나19 후유증 조사연구 사업

Hallym University College of Medicine
Dept of IM, Div. of Infectious Diseases
Jacob Lee

PASC
Long COVID



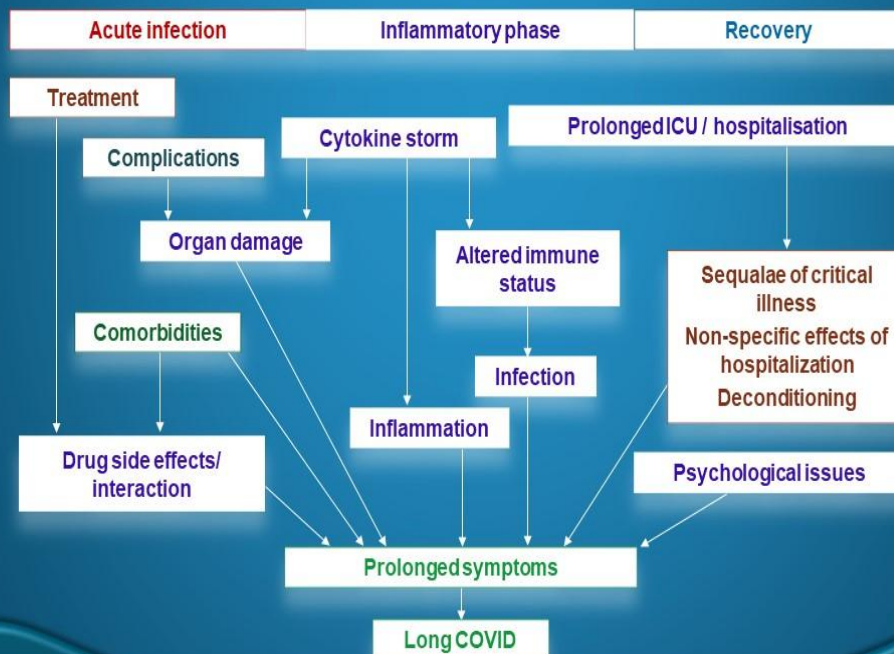
WHO definition : Post-COVID19 Condition

- Post-COVID Conditions, also known as long COVID, are defined as symptoms that persist for at least 2 months after the onset of COVID-19 symptoms, and cannot be explained by other alternative diagnoses.

Definition


- Different definitions of long COVID from different organizations:
- UK NICE
 - Ongoing symptomatic COVID-19: Symptoms or signs that persist for at least 4-12 weeks after diagnosis and improve within 12 weeks.
 - Post-COVID-19 syndrome: Symptoms or signs that persist for more than 12 weeks.
- US NIH
 - Post-acute sequelae of SARS-CoV-2 infection: Symptoms or signs that persist for more than 2 weeks after acute COVID-19.
- Korean Society of Infectious Diseases (Preliminary Recommendations for the Treatment Guidelines for Long COVID, 2022)
 - Post-acute COVID-19: Symptoms or signs that persist for at least 4 weeks after diagnosis and cannot be explained by other diseases.
 - Long COVID: Symptoms or signs that persist for more than 12 weeks.

Pathogenesis of long COVID




Long COVID is known to have about 200 different symptoms


Chronic COVID-19 syndrome is known to have about 200 different symptoms and presents with a wide range of symptoms. The most common symptoms that can persist for up to six months include fatigue, post-exertional malaise, and cognitive dysfunction.




Pain in various parts of the body




Shortness of breath
Cough




Loss of taste/smell




Joint/muscle pain




Chronic fatigue
Fever



Diarrhea
Abdominal pain



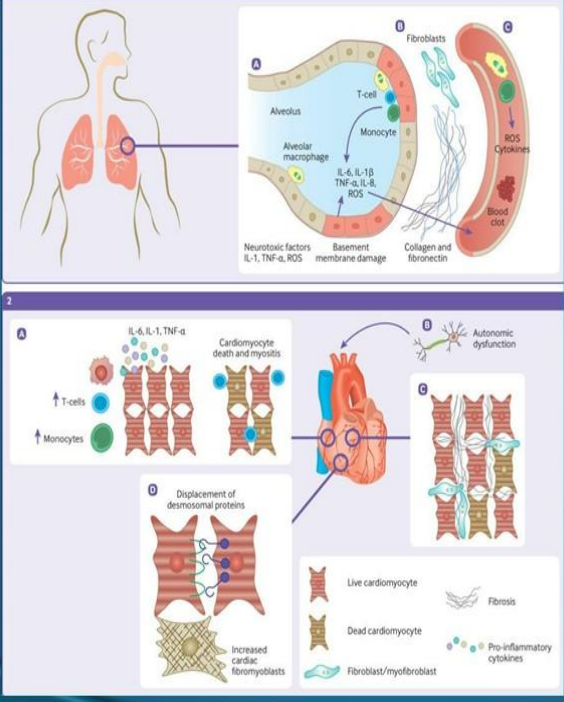
Sleep disturbances
Depression

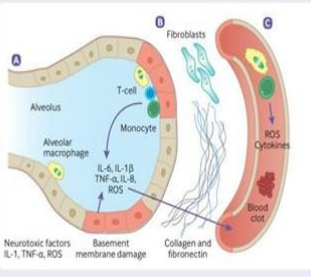


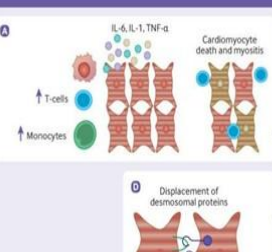
Hair loss, rash

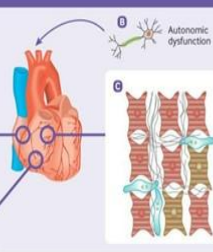
Davis H, et al. *Nat Rev Microbiol*.2023;21(3):133-146. 2. Davis H, et al. *EClinicalMedicine*.2021;38:101019


Long COVID-19 : cardiopulmonary involvement










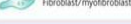





 Live cardiomyocyte

 Dead cardiomyocyte

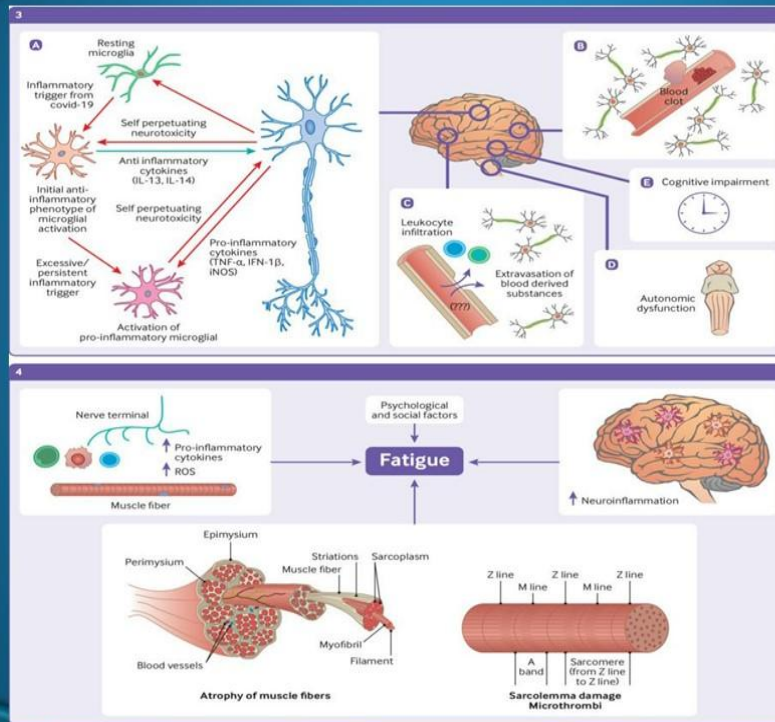
 Fibrosis

 Fibroblast/myofibroblast

 Pro-inflammatory cytokines

BMJ 2021;374:n1648

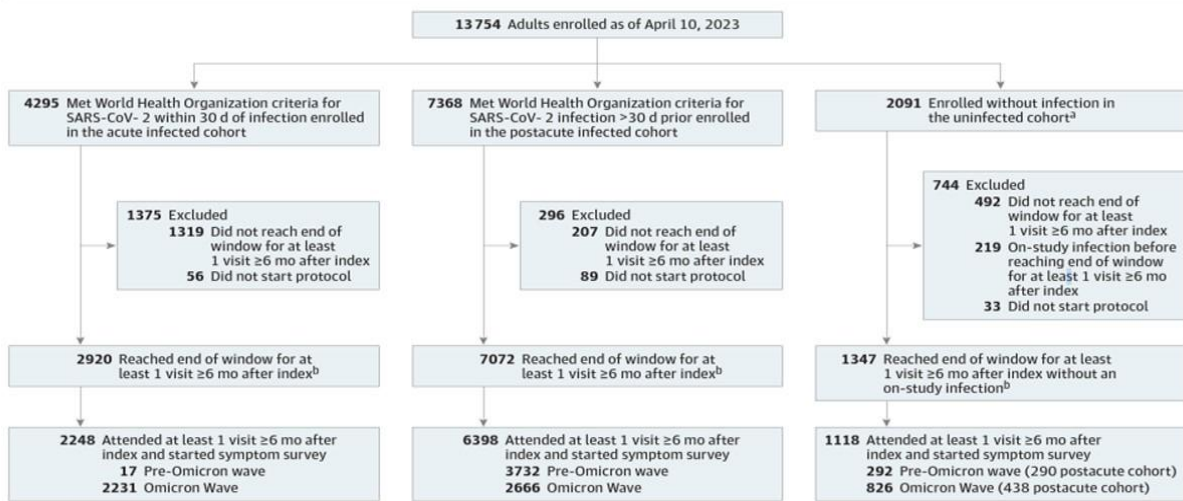
Long COVID-19 : neurologic symptom



BMJ 2021;374:n1648

Development of a Definition of Post acute Sequelae of SARS-CoV-2 Infection

Figure 1. RECOVER Adult Analysis Cohort



JAMA.2023;329(22):1934-1946. doi:10.1001/jama.2023.8823

Development of a Definition of Post acute Sequelae of SARS-CoV-2 Infection

Table 2. Model-Selected Symptoms That Define PASC and Their Corresponding Scores^a

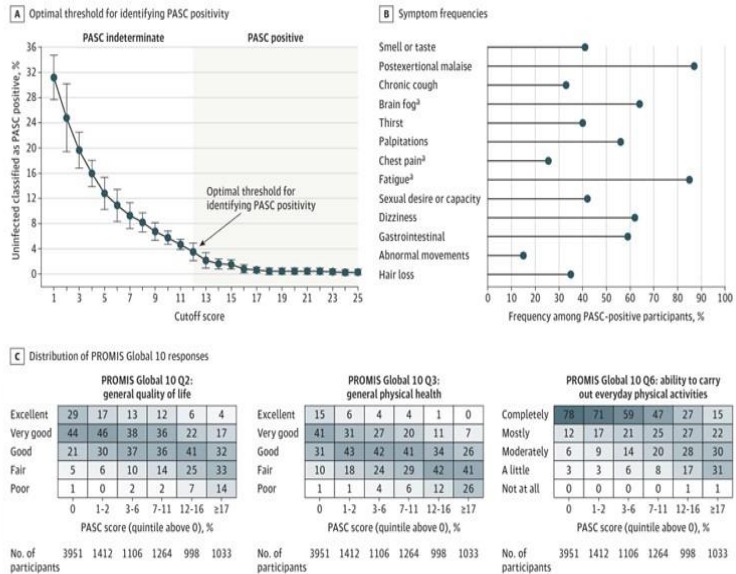
Symptom	Log odds ratio	Score
Smell/taste	0.776	8
Postexertional malaise	0.674	7
Chronic cough	0.438	4
Brain fog ^b	0.325	3
Thirst	0.255	3
Palpitations	0.238	2
Chest pain ^b	0.233	2
Fatigue ^b	0.148	1
Sexual desire or capacity	0.126	1
Dizziness	0.121	1
Gastrointestinal	0.085	1
Abnormal movements	0.072	1
Hair loss	0.049	0

Abbreviation: PASC, postacute sequelae of SARS-CoV-2 infection.

^a Least absolute shrinkage and selection operator was used to identify which symptoms defined PASC. A symptom score was assigned by dividing the estimated log odds ratio by 0.10 and rounding to the nearest integer. For each person, the total score was defined as the sum of the scores for each symptom a person reported.

^b Additional severity criteria required (eTables 1 and 2 in Supplement 3).

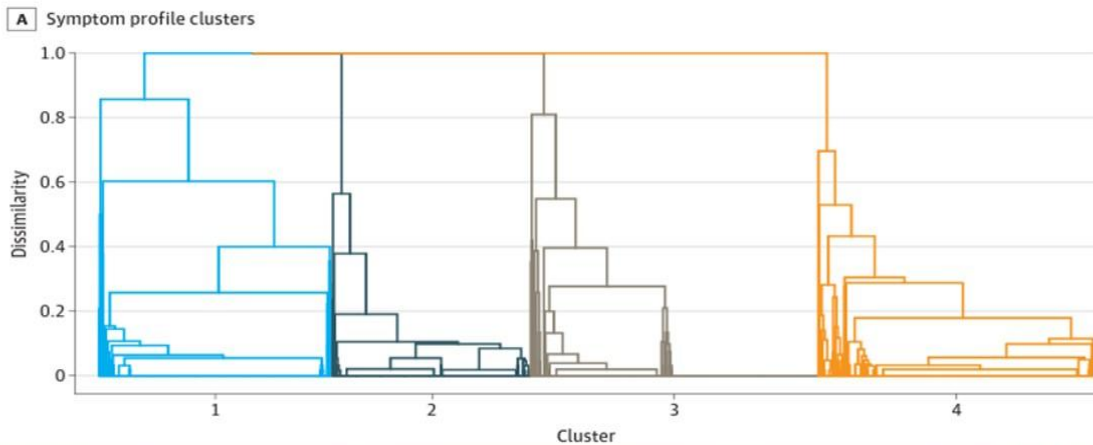
Figure 2. Defining the Postacute Sequelae of SARS-CoV-2 Infection (PASC) Score and a Decision Rule



JAMA.2023;329(22):19341946.doi:10.1001/jama.2023.8823

Development of a Definition of Post acute Sequelae of SARS-CoV-2 Infection

Figure 3. Identification of Postacute Sequelae of SARS-CoV-2 Infection (PASC) Subgroups and Their Characteristics



JAMA.2023;329(22):19341946.doi:10.1001/jama.2023.8823

코로나19 후유증
조사연구사업(R&D)

빅데이터 기반
코로나19 후유증 연구

가천대학교 길병원
예방의학교실

정재훈

Correlation between COVID-19 vaccination and risk of myocardial infarction and ischemic stroke

New Online

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Research Letter

July 22, 2022

Association Between Vaccination and Acute Myocardial Infarction and Ischemic Stroke After COVID-19 Infection

Young-Eun Kim, PhD¹; Kyungmin Huh, MD²; Young-Joon Park, MD, MPH³; Kyong Ran Peck, MD, PhD³; Jaehun Jung, MD, PhD⁴

[Author Affiliations](#) | [Article Information](#)
 JAMA. Published online July 22, 2022. doi:10.1001/jama.2022.12992

COVID-19 Resource Center

코로나19 후유증
조사연구사업(R&D)

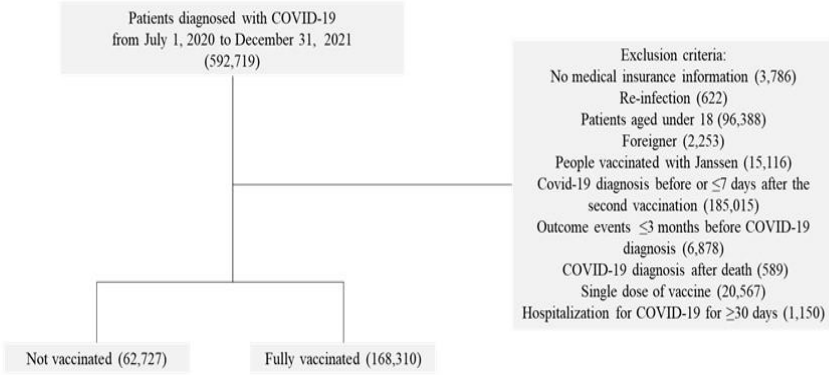
빅데이터 기반
코로나19 후유증 연구

가천대학교 길병원
예방의학교실

정재훈

Correlation between COVID-19 vaccination and risk of myocardial infarction and ischemic stroke

Association between vaccination and acute myocardial infarction and ischemic stroke after COVID-19: Study design



1. Around 590,000 patients aged ≥18 years who were diagnosed with COVID-19, between July 2020 and December 31, 2021 were targeted.
2. A total of 231,037 patients with COVID-19 were included, of whom 62,727 were never vaccinated and 168,310 were fully vaccinated
3. Compared the risk of AMI and ischemic stroke that occurred 31-120 days after COVID-19

코로나19 후유증
조사연구사업(R&D)

빅데이터 기반
코로나19 후유증 연구

가천대학교 길병원
예방의학교실

정재훈

Correlation between COVID-19 vaccination and risk of myocardial infarction and ischemic stroke



Association between vaccination and acute myocardial infarction and ischemic stroke after COVID-19: Baseline characteristics

	Unweighted population			Weighted population		
	Not vaccinated	Fully vaccinated	Standardized difference	Not vaccinated	Fully vaccinated	Standardized difference
Sex	62,727	168,310				
Male	30,407 (48.48)	79,176 (47.04)	0.029	45.11	47.21	0.042
Female	32,320 (51.52)	89,134 (52.96)		54.89	52.79	
Age, median [IQR], y	45.4 (18.1)	54.3 (17.1)	0.504	53.4 (20.3)	51.9 (17.6)	0.087
18-39	28,467 (45.38)	36,444 (21.65)		30.39	26.80	
40-64	24,183 (38.55)	80,647 (47.92)		39.71	46.66	
>65	10,077 (16.06)	51,219 (30.43)		29.90	26.51	
Insurance plan for low income	3,308 (5.27)	6,310 (3.75)	0.074	4.47	4.24	0.011
Comorbidities						
Charlson comorbidity index, median [IQR]	0 [0, 2]	1 [0, 2]				
Charlson comorbidity index ≥5	4,001 (6.38)	11,792 (7.01)	0.025	7.26	6.87	0.015
Diabetes	4,479 (7.14)	19,929 (11.84)	0.161	9.17	11.06	0.063
Hypertension	6,782 (10.81)	37,166 (22.08)	0.308	20.07	19.03	0.029
Dyslipidemia	2,254 (3.59)	13,618 (8.09)	0.193	4.25	7.57	0.141
Previous history of outcome events	909 (1.45)	2,704 (1.61)	0.013	2.29	1.46	0.062
Severity of COVID-19						
Severe	6,136 (9.78)	5,298 (3.15)	0.289	12.45	2.84	0.399
Critical	3,514 (5.60)	1,772 (1.05)	0.276	8.52	0.95	0.397

1. Patients who were never vaccinated were younger and less comorbidities. However, there was differences in COVID-19 severity rates
2. After weighting, there was no significant differences in sex, age, insurance plan and comorbidities

코로나19 후유증
조사연구사업(R&D)

빅데이터 기반
코로나19 후유증 연구

가천대학교 길병원
예방의학교실

정재훈

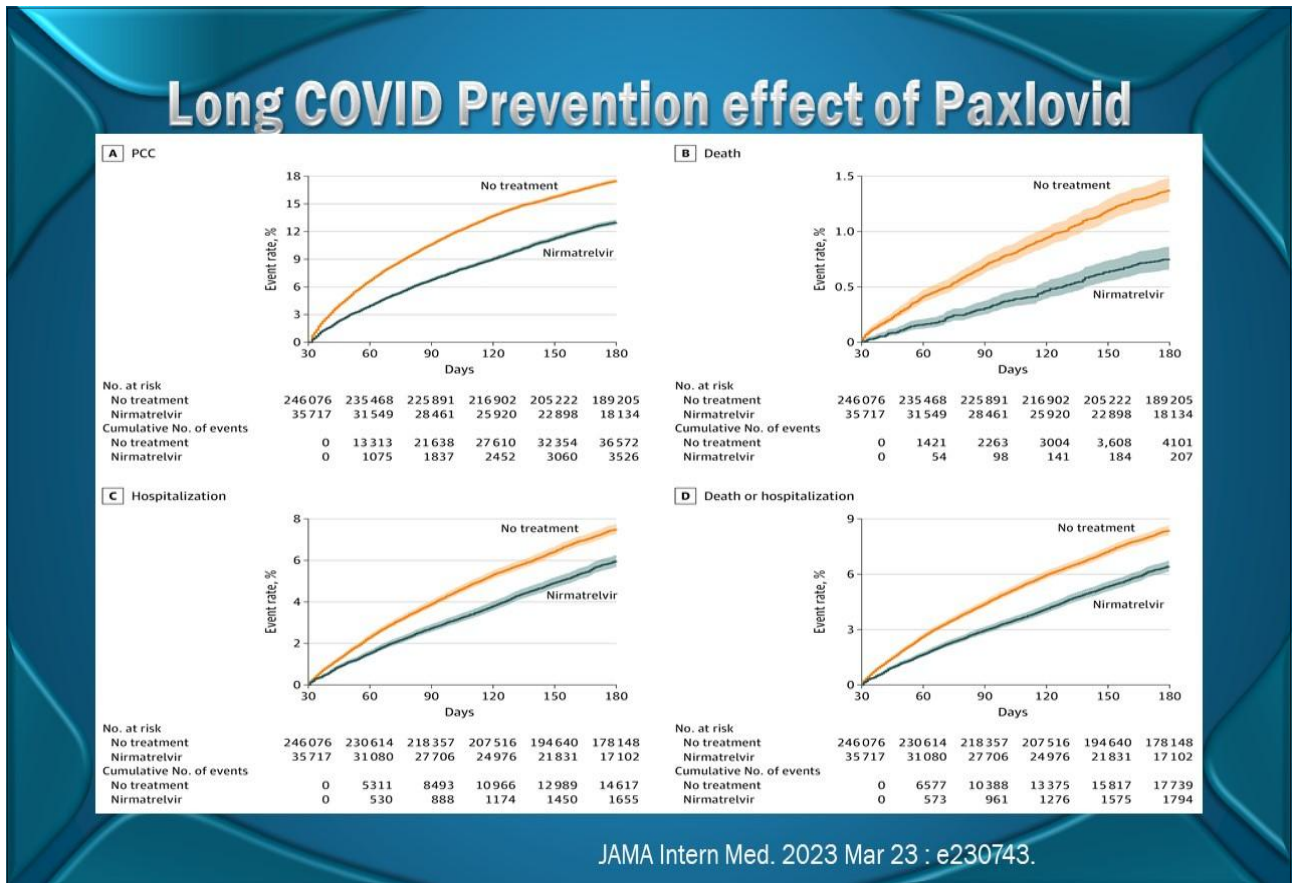
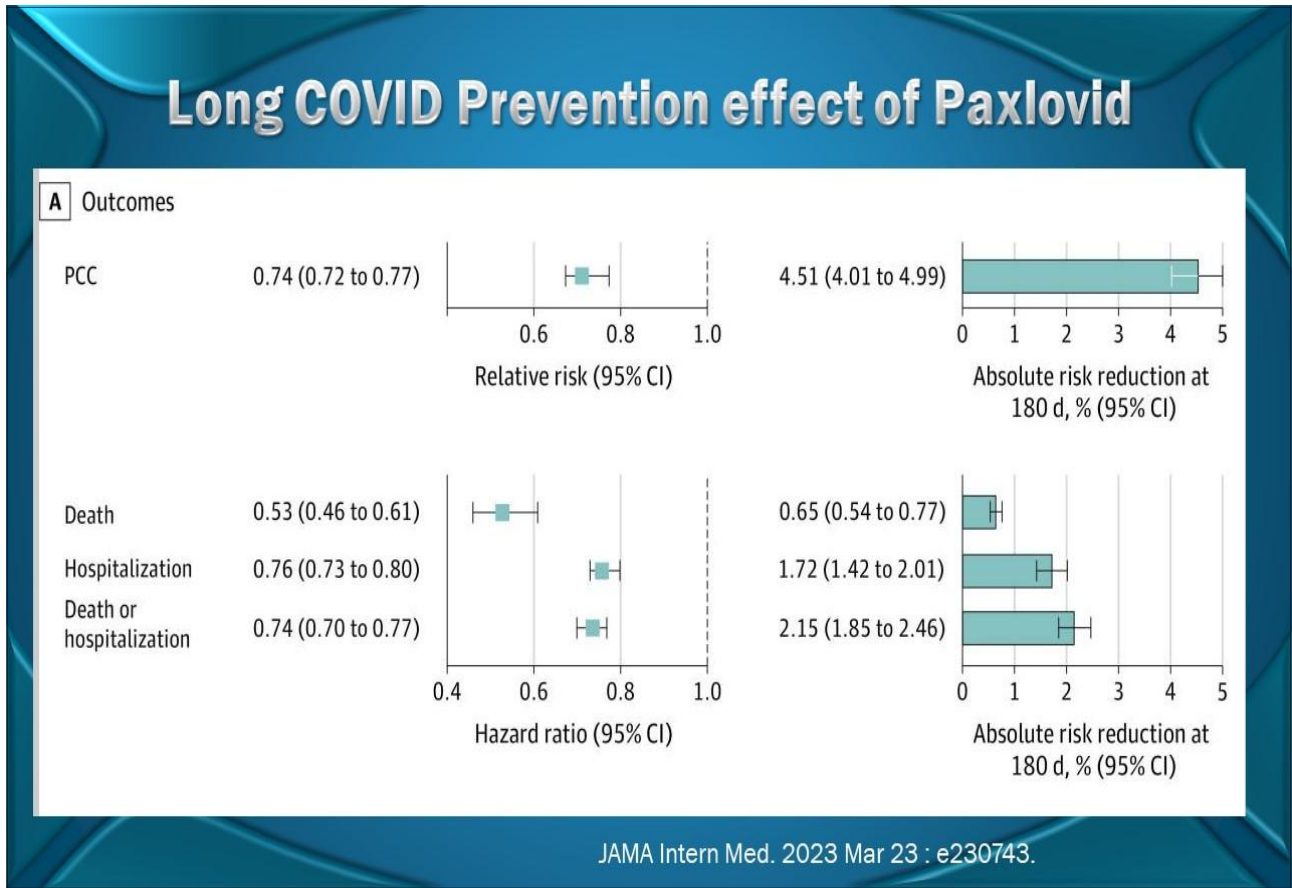
Correlation between COVID-19 vaccination and risk of myocardial infarction and ischemic stroke

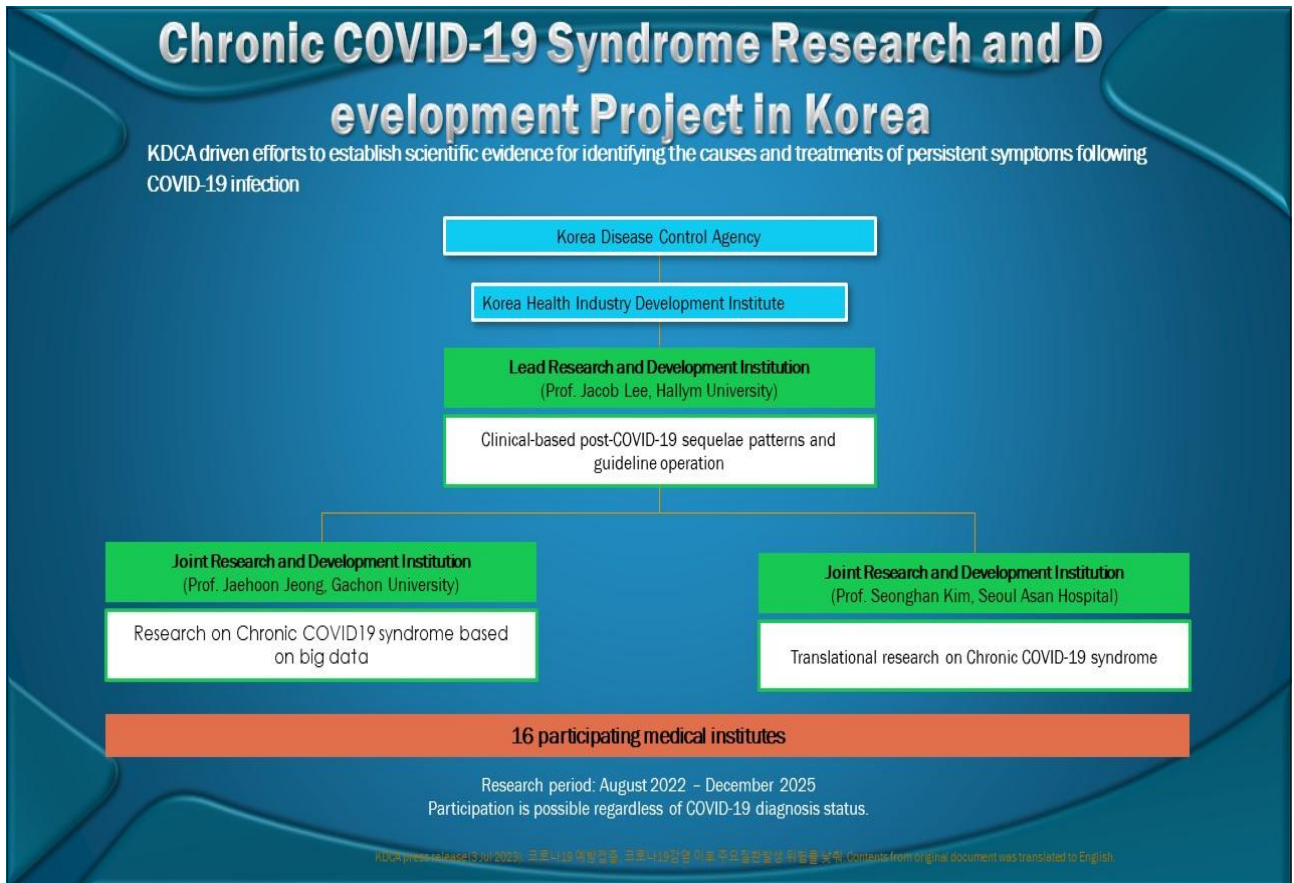


Association between vaccination and acute myocardial infarction and ischemic stroke after COVID-19: Risk assessment

	Number of events		Incidence per 1,000,000 person day		Adjusted HR (95% CI)	P Value
	Not vaccinated	Fully vaccinated	Not vaccinated	Fully vaccinated		
	(62,727)	(n=168,310)				
Composite outcome	31	74	6.18	5.49	0.42 (0.29-0.62)	<0.001
Acute myocardial infarction	8	24	1.60	1.78	0.48 (0.25-0.94)	0.03
Ischemic stroke	23	50	4.59	3.71	0.40 (0.26-0.63)	<0.001
Subgroup						
Male	17	48	6.98	7.59	0.41 (0.26-0.66)	<0.001
Female	14	26	5.44	3.63	0.42 (0.23-0.76)	0.004
Age, y						
40-64	11	22	5.48	3.39	0.38 (0.20-0.74)	0.004
>65	20	51	33.99	12.42	0.41 (0.26-0.66)	<0.001
Charlson comorbidity index						
≤5	25	56	5.22	4.45	0.40 (0.26-0.60)	<0.001
≥5	6	18	25.04	19.79	0.54 (0.24-1.22)	0.14
Diabetes						
No	23	46	4.89	3.87	0.38 (0.24-0.61)	<0.001
Yes	8	28	26.29	17.58	0.47 (0.25-0.91)	0.03
Hypertension						
No	20	46	4.41	4.39	0.50 (0.31-0.80)	0.004
Yes	11	28	23.11	10.90	0.34 (0.18-0.62)	<0.001
Dyslipidemia						
No	26	67	5.24	5.05	0.44 (0.29-0.65)	<0.001
Yes	5	7	97.55	33.26	0.33 (0.10-1.07)	0.06
Severe or Critical COVID-19						
No	22	65	5.02	5.00	0.37 (0.25-0.55)	<0.001
Yes	9	9	14.38	18.51	0.66 (0.20-2.23)	0.51

1. A lower risk for outcome events in fully vaccinated patients was observed in most subgroups
2. Reduced risk of AMI and ischemic stroke by 0.37 in vaccinated group, even in mild and severe COVID-19





Future Strategies to expand Long COVID-19 management

Clinical-based Chronic COVID-19 syndrome patterns and guideline operation

- Establish and operate a cohort of COVID-19 cases, including children and adolescents, to investigate patterns of post COVID-19 syndrome and to provide treatment guidelines

Research on Chronic COVID19 syndrome based on big data


- Establish a database of consent-based materials such as clinical research and translational research, and developing a platform for their utilization

Translational research on Chronic COVID-19 syndrome

- Translational research to understand causes of chronic COVID-19 syndrome, identify biomarkers, and more

*treatment guideline soon to be announced in Feb.

Active promotion of the research projects to enroll participants partnering with Government and medical institutes



<http://koloc.or.kr/kr/index.do>

코로나19 후유증
조사연구사업(R&D)

주관 연구과제

임상기반
코로나19 후유증
양상 및 가이드라인 연구

한림대학교 강남성심병원
감염내과

이재 갑

Long COVID Cohort Study in Korea

Retrospective and prospective

• 10,000

Prospective cohort


• 1,000

COVID-19-negative cohort

• 1,000

Inpatient/severe patient cohort

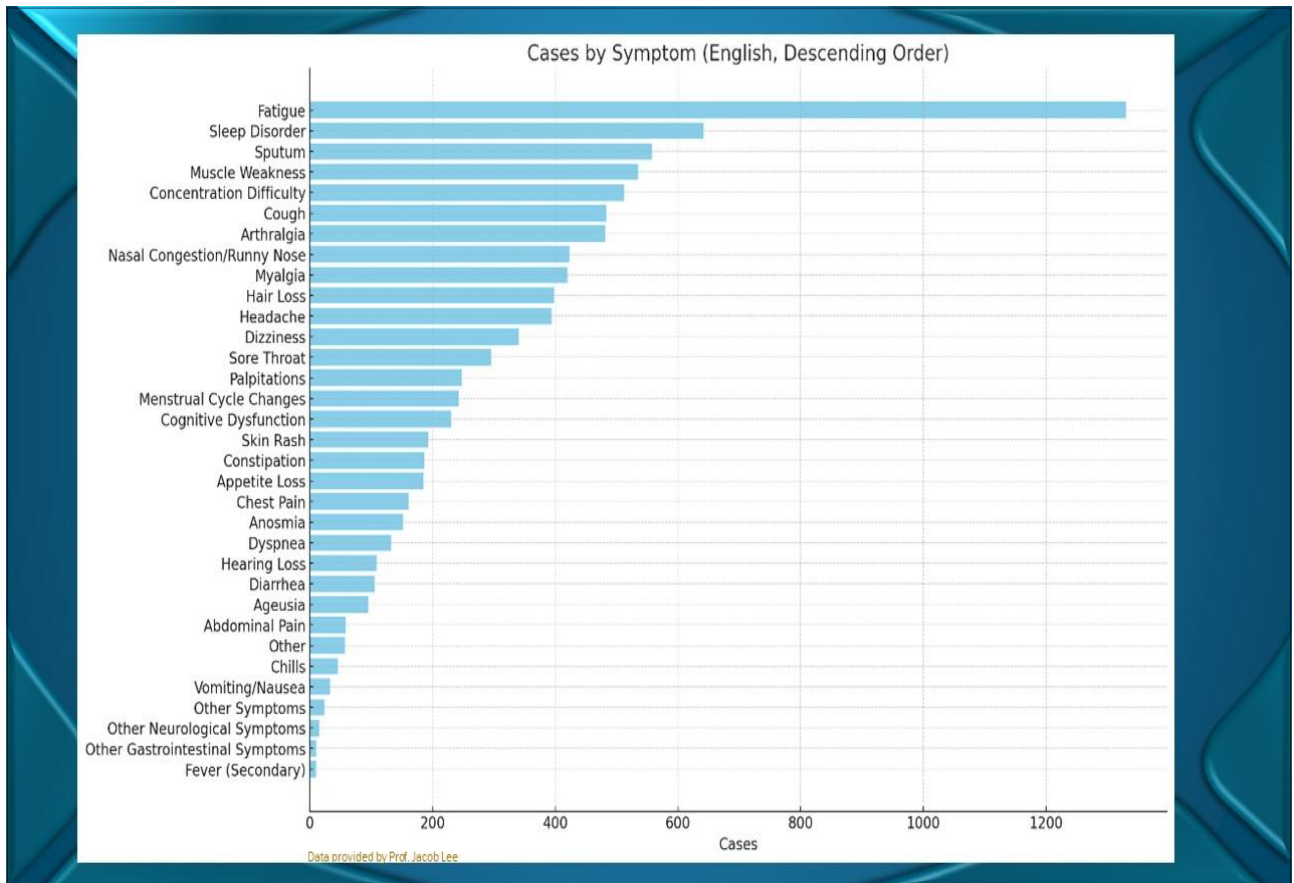
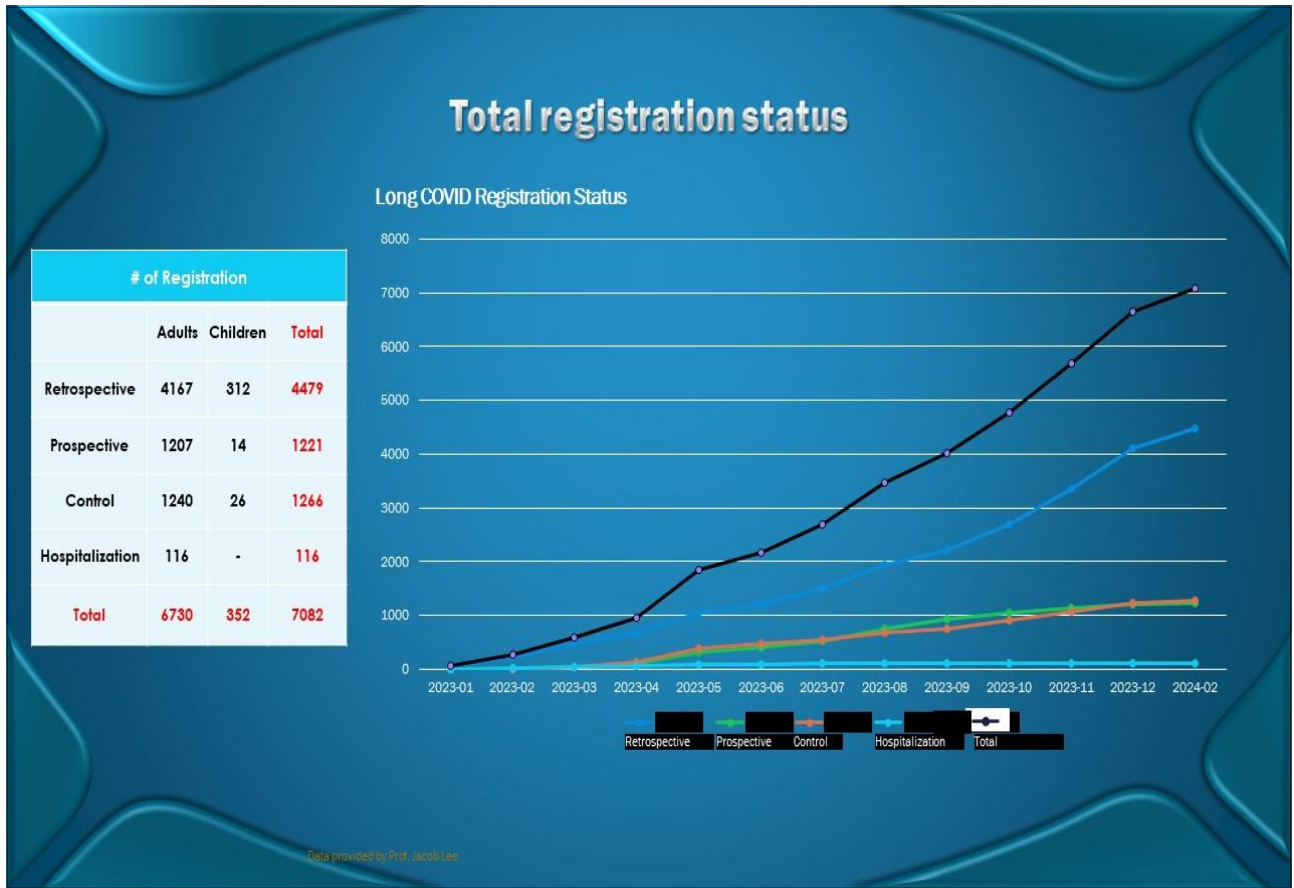
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한림대학교의료원
HANYANG UNIVERSITY MEDICAL CENTER

가천대 경주병원
GACHON UNIVERSITY GYEONGJU HOSPITAL

서울아산병원
Seoul National University Asan Medical Center



코로나19 후유증
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한림대학교 강남성심병원
감염내과

이재갑

Long COVID Clinical Guidelines

- ✓ 대한감염학회는 2022년 7월 만성 코로나19 증후군에 대한 예비 권고안을 발표
- ✓ 이 가이드라인은 코로나19 후유증에 대한 진단과 치료와 관련하여 의료행위의 왜곡을 방지하고 과학적 근거를 통한 진료를 위하여 개발 되었음
- ✓ 주관연구기관은 코로나19 후유증 자침 위원회를 구성하여 2023년 진료지침을 제정할 예정임
- ✓ 자침은 2년을 주기로 개정할 예정임

만성 코로나 19 증후군(Long COVID)
진료지침 예비 권고안

Preliminary guidelines for clinical evaluation and management of long COVID

대한감염학회
Long COVID 진료지침 개발위원회*

코로나19 후유증
조사연구사업(R&D)

Long COVID Long-term Research Tracking Research Database Concept

Hospitals
(Currently 15 hospitals involved)

National Health Insurance System
h-well NHIS

Public Big Data
국립암센터
KDCA Korea Disease Control and Prevention Agency

↓ Data collection ↓

Vaccination

Demographic

Symptoms

Diagnostic

Pathology

Screening

Surgey

Genetic

Medicine

1

Data integration

2

Long-term Follow-up

3

Establishment of a national integrated database

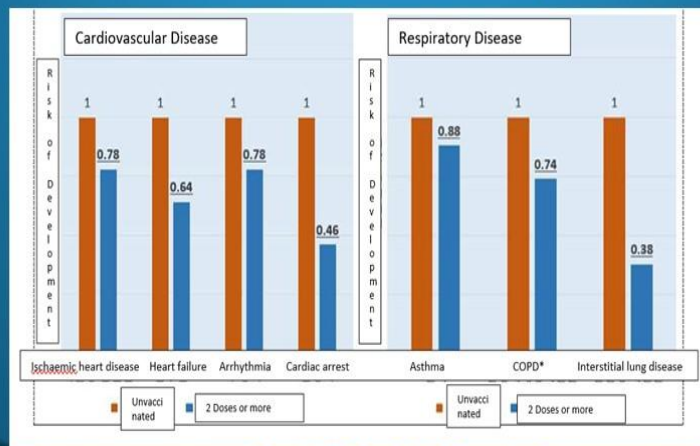
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Epidemic management

Interim analysis result of Post - COVID-19 syndrome using big data

- Design of study: 15 Jan 2022 to 15 Apr 2022. During the Omicron wave, 12,309,934 confirmed cases were observed for 4 months after the infection to compare the risk of 27 major diseases by vaccination status and number of doses.
- Outcomes. 1
 - Compared to the unvaccinated, those who have received two or more doses of vaccine have a reduced risk of cardiovascular disease, blood clots, kidney disease, respiratory disease, cirrhosis, diabetes, and other diseases after COVID-19 infection.

Risk Assessment: Association between COVID-19 vaccination and development of illness



MOCA press release (3 Jul 2022). 코로나19 예방접종, 코로나19감염 이후 주요 질환 발생 위험을 낮춰. Contents from original document was translated to English.

Interim analysis result of Post - COVID-19 syndrome using big data

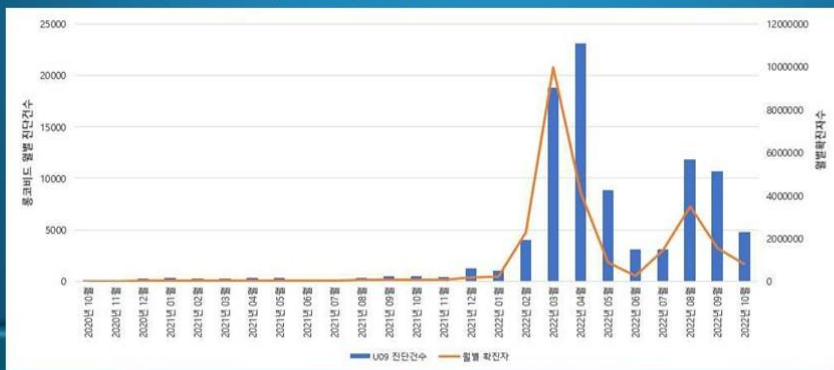
- Outcomes. 2
 - Those who received three doses were at a reduced risk of developing cardiovascular disease, kidney disease, e tc. despite being more than 10 years older on average than those who received two doses.

Disease	Two doses	Three doses	Adjusted risk rate	P-value
Cardiovascular disease				
Heart Failure	1.28	2.51	0.85(0.77-0.93)	<.001
Arrhythmia	1.15	2.29	0.84 (0.76-0.93)	<.001
Cardiac arrest	0.31	0.62	0.73 (0.60-0.89)	0.002
Blood clot-related conditions				
Pulmonary embolism	0.55	0.86	0.79 (0.68-0.93)	0.004
Kidney Disease				
Dialysis	0.23	0.47	0.73 (0.57-0.92)	0.007
Liver Disease				
Acute Pancreatitis	0.82	1.03	0.87 (0.76-0.99)	0.04

MOCA press release (2 Jul 2022). 코로나19 예방접종, 코로나19감염 이후 주요 질환 발생 위험을 낮춰. Contents from original document was translated to English.

Analysis using chronic COVID-19 syndrome diagnosis codes

- Design of study: Oct 2020 – Oct 2022. Notable aspects of cases diagnosed with U09 [post-COVID-19 syndrome] in Korea
- Outcomes:
 - (Overall and gender breakdown) Total patients 94,393, outpatient 91,593, inpatient 3,059
 - Incidence rates are higher in women [0.47%] than men [0.34%]
 - (Age) Higher incidence rates in older age groups (60+)
 - Incidence rate is almost 8 times higher for those aged 60+ at 0.87% compared to 0.11% for those under 10 years old
 - (Monthly) Highest long-covid cases detected immediately following the Omicron wave (23,112). One-month gap between the Omicron BA.1/2 and the highest long-Covid cases.



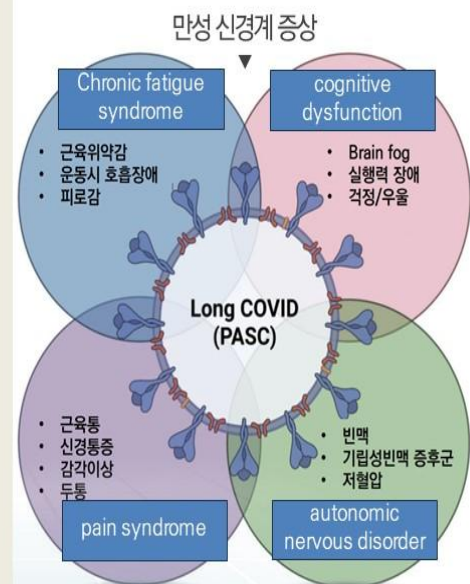
KDCA press release(3 Jul 2023). 코로나19 예방접종, 코로나19감염 이후 주요질환 발생 위험률 낮춰. Contents from original document was translated to English.

코로나19 후유증

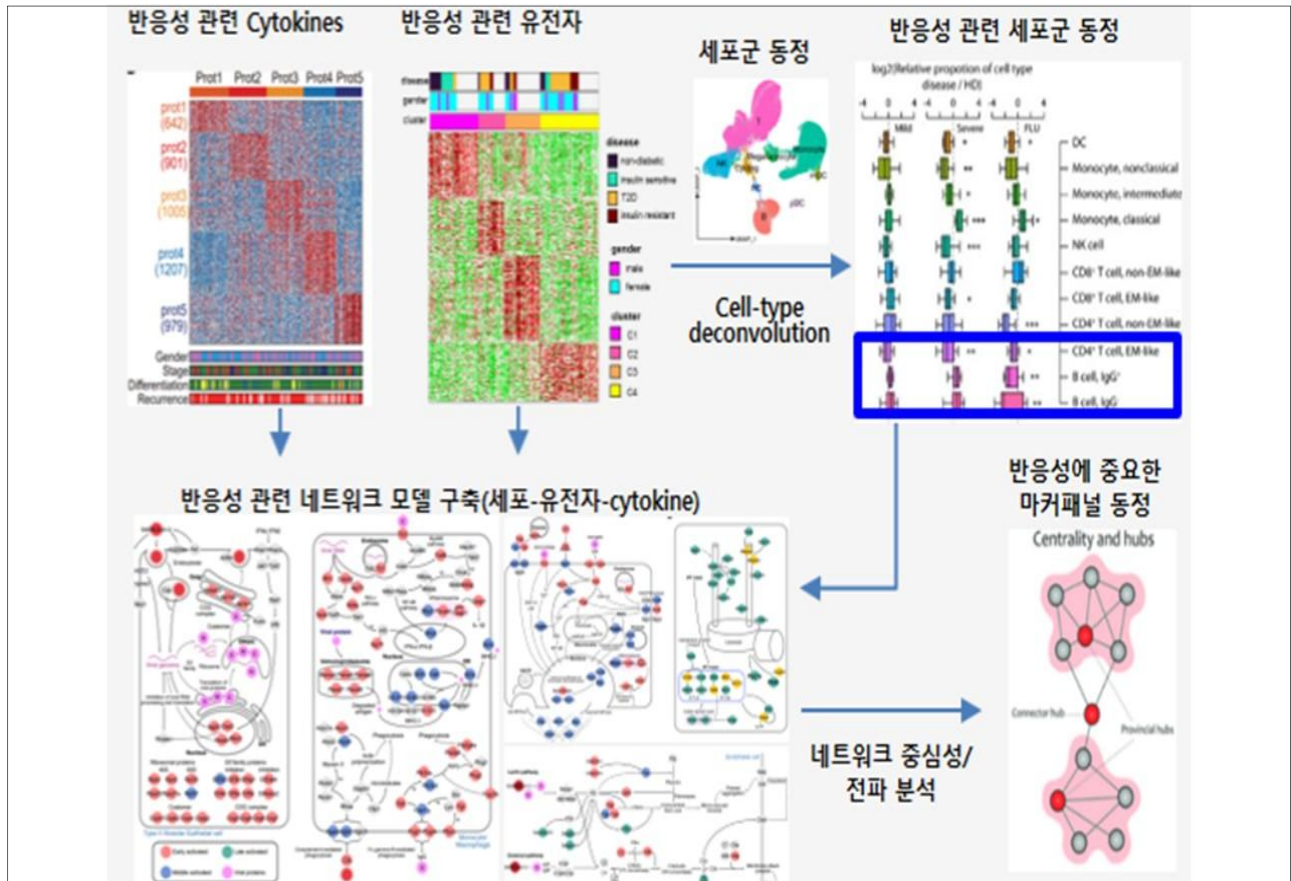
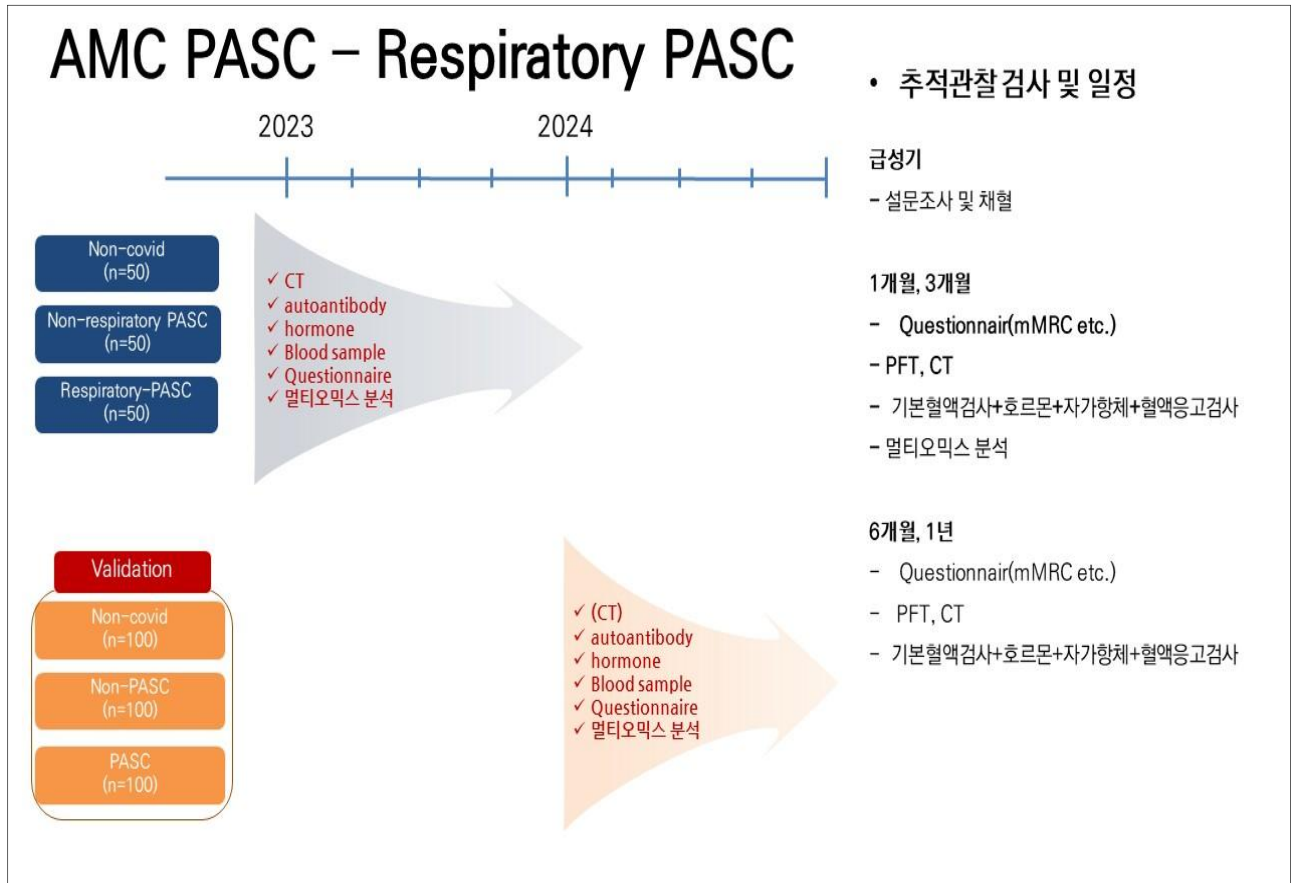
COVID19 and chronic neurological symptoms



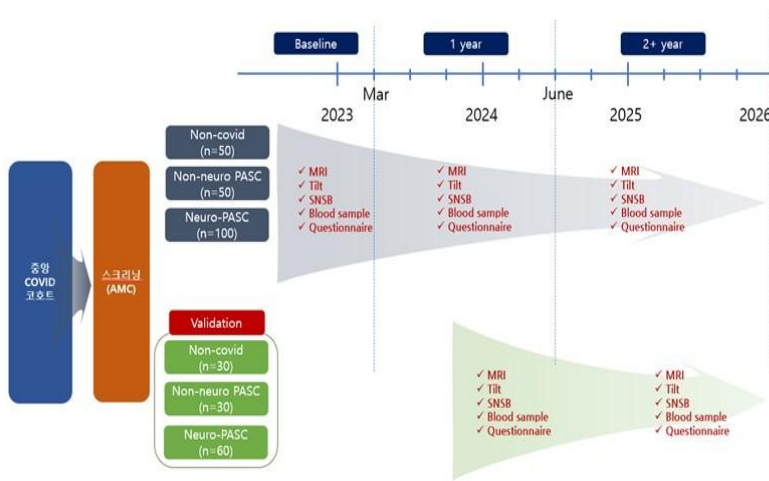
- Chronic neurological symptoms are commonly reported as a sequelae of COVID19 (~20%)
- Chronic fatigue and cognitive decline are the main symptoms, and they have a significant impact on quality of life. → Management such as prevention and treatment is urgently needed in COVID19 patients.
- The pathophysiology is not yet known, and it can occur even in patients who had no acute symptoms, especially in the acute phase. → Disease monitoring biomarkers are needed to identify the mechanism of occurrence and identify risk groups.



Brain, 2021



AMC – Neurologic PASC



• 추적관찰 검사 및 일정

스크리닝(Neuro-PASC)

- 인지기능과 피로도 조사(간단한 설문)

3개월 주기

- 증상변수(피로도): FAS 및 DSQ-SF

- Neuro-PASC 관련 여러 신경학적 증상(설문)

: 어지럼, 걱정(anxiety), 우울, 수면, 삶의 질 등

6개월 주기

- 혈액 검사(혈액 바이오마커 분석 용도)

1년 주기

- 증상변수(인지기능): 신경심리검사(SNSB)

- 중추신경계 뇌 영상(Brain MRI)

- 자율신경계검사(Tilt table)

Conclusion

- The COVID-19 pandemic is the worst pandemic of the 21st century
- COVID-19 is not simply an infection that ends with recovery, but is causing long-term sequelae.
- Korea is conducting research on a long COVID cohort by providing large-scale research funds led by the government.
- Currently, 4,500 cohort members have been registered and the epidemiological data of patients will be analyzed
- Joint research institutions are conducting research through big data-based analysis and translational research

세션 2.

신종감염병 치료제개발 현황 및 전략

Chair



Ki-Soon Kim

- ✔ Institute of Viral Disease Department of Microbiology, College of Medicine, Korea University
- ✔ Professor

🔍 EDUCATION:

- 2000 Ph.D. / Department of Life Science, College of Natural Science, Chung-Ang University
- 1990 M.S. / Department of Biology, College of Natural Science, Korea University Graduate School
- 1988 B.S. / Department of Biology, College of Natural Science, Korea University

🔍 PROFESSIONAL EXPERIENCE:

- 2022 ~ Present Advisory member of Infectious Disease Policy Beauru, Seoul Metropolitan city, Korea
- 2022 ~ Present Committee member of Government-wide R&D Fund for Infectious Disease Research (GFID), Korea
- 2021 ~ Present Advisory member of Korea Pest Control Association, Korea
- 2020 ~ Present Committee member of Bureau of Infectious Disease Policy, KCDA, Korea
- 2006 ~ Present Lifetime member, The American Society of Virology
- 1990 ~ Present Committee member, The Korean Society of Virology
- 1990 ~ 2019 Director, Researcher, Divisions of Influenza and respiratory viruses, Department of Virus Research, National Institute of Health, Korea
- 2004 ~ 2006 University of Nebraska Medical Center, NE, USA, Visiting Scientist
- 1996 ~ 1997 Department of Virology II, National Institute of Infectious Diseases, Tokyo, Japan, Visiting Scientist
- 1994 ~ 1994 NIID, Tokyo, Japan, "Polio Eradication Program", WHO fellow

01

신속 팬데믹 대응을 위한 플랫폼과 기술들

Dimitri LAVILLETTE

한국파스퇴르연구소



Speaker



Dimitri LAVILLETTE

- ✔ Institut Pasteur Korea
- ✔ Chief Scientific Officer

🔍 EDUCATION:

- 2009 Dr Habil, Habilitation à diriger les recherches (HDR), ENS Lyon, France
- 2000 PhD in Virology, University Claude Bernard Lyon1/ Ecole Normale Supérieure, Lyon, France
- 1997 D.E.A of Differentiation, Genetic and Immunology, University Claude Bernard, Lyon, France

🔍 PROFESSIONAL EXPERIENCE:

- 2022 ~ Present Institut Pasteur Korea, Chief Scientific Officer, Korea
- 2014 ~ 2022 Institut Pasteur of Shanghai – Chinese Academy of Sciences, Principal Investigator and Professor, China
- 2012 ~ 2014 Claude Bernard Lyon 1 University, Associate Professor (2012–2014) UMR 5557 CNRS INRA VetAgroSup, Microbial Ecology
- 2011 Glycobiology Institute, Visiting scientist; Oxford, U.K.
- 2003 ~ 2012 ENS Lyon, INSERM U758, Human virology, Associate Professor, France
- 2003 ~ Present National Center of Scientific Research (CNRS), Tenure staff scientist position CR1; France
- 2001 ~ 2003 Oregon Health Sciences University, Post Doc. Oregon, U.S.A
- 2000 ~ 2001 Mayo Clinic, Visiting scientist Rochester, MN, U.S.A.

Q Topic

Platforms & Tools to Enable Rapid Pandemic Response

Q Abstract

The recent COVID-19 pandemic has caused economic and social damage worldwide and gives us considerable concerns about a new pandemic in the future. Unlike other diseases, infectious diseases are very difficult to prepare for, and they quickly begin to spread around the world before humanity prepares in advance. Due to this, it is very difficult to fight a new strain of virus that appears quickly and spreads rapidly by the method of developing a general treatment applied to other diseases. A strategy for the development of potential treatments by families of pathogens, using prototypes, can be implemented following different priorities of different agencies. Infectious diseases progress through the process of infection, spread and pathogenicity. Strategic approaches of treatment are applied for each stage of progression. Therapeutic agents such as monoclonal antibodies or variable domains of heavy-chain antibodies (VHH) being used for inhibiting infection, and small compound inhibitory agents of viral replication are being used as therapeutic agents that prevent the spread or amplification of pathogens after infection. In addition, agents to control immune response against the pathogenesis are being applied as therapeutics for infectious diseases to reduce the severity and fatality rate. The prevention strategies with the elaboration of vaccines are dramatically increasing as well. This presentation will discuss the development strategies against infectious diseases that are investigated in the Institut Pasteur Korea such as VHH derived from camelids and antiviral drugs in a preparedness program.

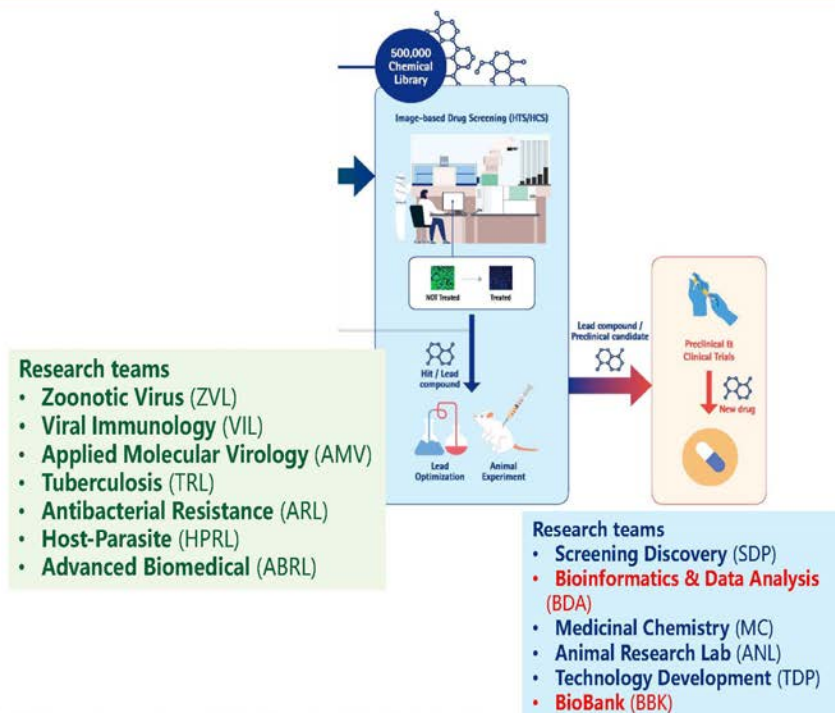
Platforms & Tools to Enable Rapid Pandemic Response

Dimitri LAVILLETTE, PhD, Dr. Habil
Chief Scientific Officer Institut Pasteur Korea

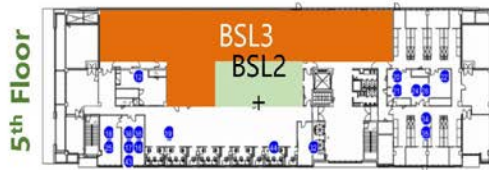
Dimitri.Lavillette@ip-korea.org



IPK's Drug Discovery Approach



IPK Drug Screening Platform



Biological Safety Level 3

- HCS: Confocal mode >10,000 pts/day
- Multi-label Reader: >20,000 pts/day

Biological Safety Level 2+

- HCS: Confocal mode >20,000 pts/day
- Multilabel Reader: >25,000 pts/day

Biochemical

- Multi-label Reader: >20,000 pts/day



Chemical Library

[IPK Diversity sets]
IPK Legacy: ~ 230K
IPK 2015: ~ 100K
IPK MedChem: ~ 9.5K

[IPK Pilot] Drugs & Bioactives: ~ 12K

[IPK Natural Products] NCI Collections: ~ 150K

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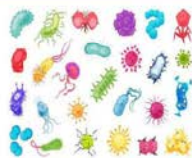
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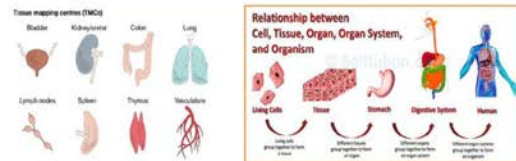
RESPONSIVENESS : Task Force rapidly mobilizable, available people/reagents/models

What do we need to prepare for the next outbreak to do drug screening rapidly?

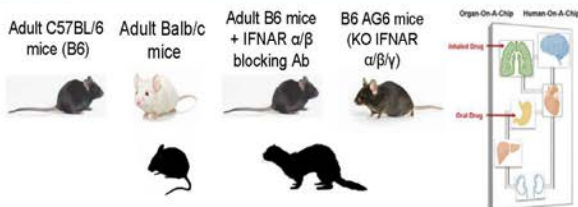
1. Pathogen Access



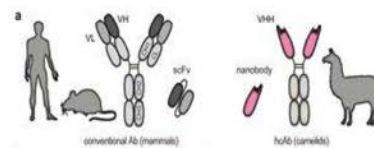
2. Cell lines



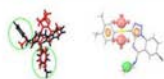
3. Animal Models



4. Detection



5. Drug Library



6. Trained team, infrastructures and funds

Threat: During outbreak, regular channels, collaborators, close doors "lockdown" prevent delivery of reagents...
Need to secure relative independence

RESPONSIVENESS : Task Force rapidly mobilizable, available people/reagents/models

What do we need to prepare for the next outbreak to do drug screening rapidly?

1. Pathogen Access

Secure collaborative channels (Pasteur Network)
Secure regulations (Nagoya protocol, Korea - Biosafety team)

Development of molecular clones (virus)

Biobank Import "prototypes" for different family of pathogens



GISB mail? Website?



Pathogens Biobank IPK
Liquid Nitrogen freezer room

Prioritizing the world's greatest pathogen threats

There are over 1,400 species of human pathogens in the world. These include viruses, bacteria and fungi.

To guide future research efforts, the World Health Organization (WHO) R&D Blueprint for Epidemics launched on 21 November 2022, a global initiative to scientifically review all pathogens that could cause a future global pandemic (i.e. COVID-19) or an epidemic of international concern.

How are the most dangerous pathogens shortlisted?

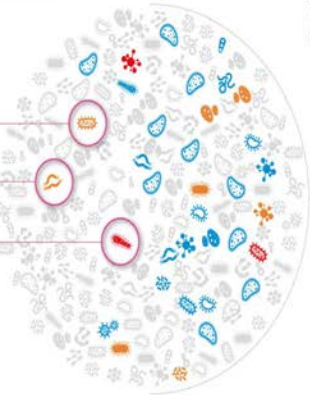
- 200 plus** Global experts are independently reviewing and shortlisting pathogens of pandemic threat.
- 30** Virus families are being studied to ensure all viruses that can infect humans are reviewed for any pathogens.
- 1** Bacteria group is being studied to scientifically screen for any bacteria pathogens.

Pathogen X
A yet unknown pathogen not currently infecting humans but could be pathogenic due to their zoonotic risk, mode of transmission, global warming, tropical deforestation, or other factors.

Key scientific criteria to shortlist

How transmissible are they?
How virulent are they?
Are there sufficient vaccines or treatments in the event of an epidemic or pandemic?

Pathogen reviewed and not shortlisted. These are viruses or bacteria unlikely to cause an epidemic or pandemic or there is equitable access to safe and effective vaccines / treatments.
Pathogen reviewed and not shortlisted. These are viruses or bacteria that have epidemic or pandemic potential but where there is equitable access to safe and effective vaccines / treatments.
Pathogen reviewed and shortlisted. These are viruses or bacteria where there are no or insufficient vaccines / treatments.
Pathogen reviewed and shortlisted. These are viruses or bacteria where the epidemic or pandemic potential is currently unknown but shortlisted as potential Pathogen X.

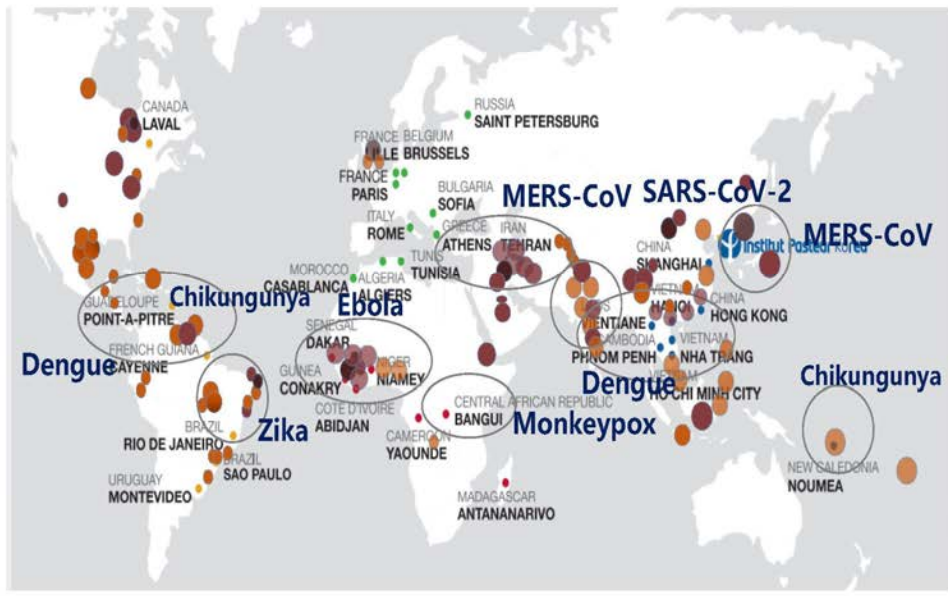


The final shortlist of priority pathogens

The list is expected in early 2024 and will shortlist priority viral families, the highest threat pathogens, the prototype pathogens for research and any Pathogen X.
The list will be used to guide investments into researching safe and effective vaccines and treatments.

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

Pasteur Network Ideally positioned at the frontline of outbreaks



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Collaboration with Institut Pasteur de Dakar



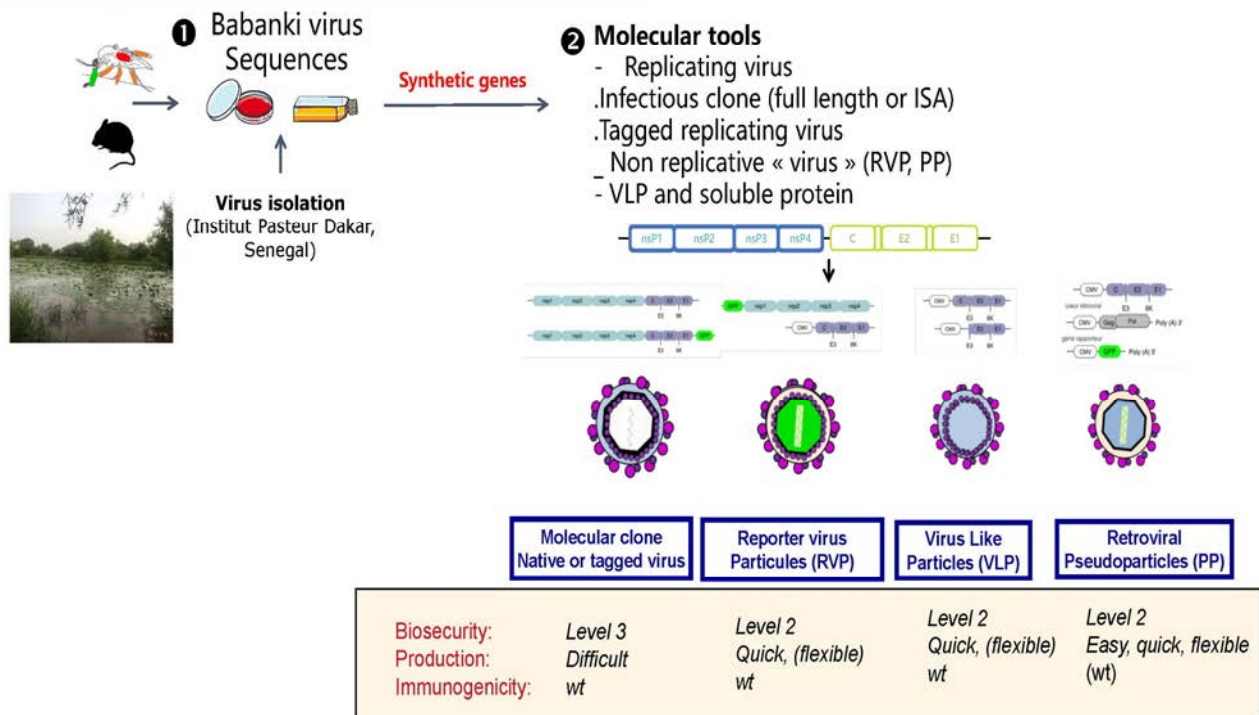
Try to go beyond the WHO' s R&D Blueprint virus disease priority list



RESPONSIVENESS : Task Force rapidly mobilizable, available people/reagents/models

What do we need to prepare for the next outbreak to do drug screening rapidly?

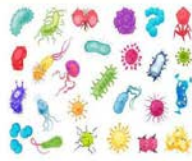
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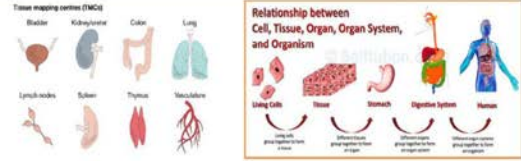
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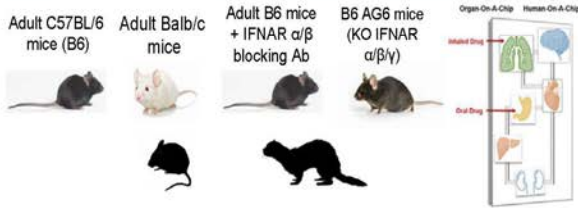
1. Pathogen Access



2. Cell lines



3. Animal Models



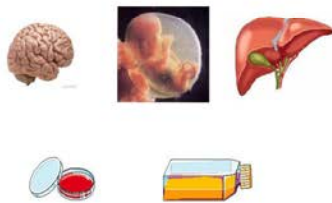
RESPONSIVENESS : Task Force rapidly mobilizable, available people/reagents/models

What do we need to prepare for the next outbreak to do drug screening rapidly?

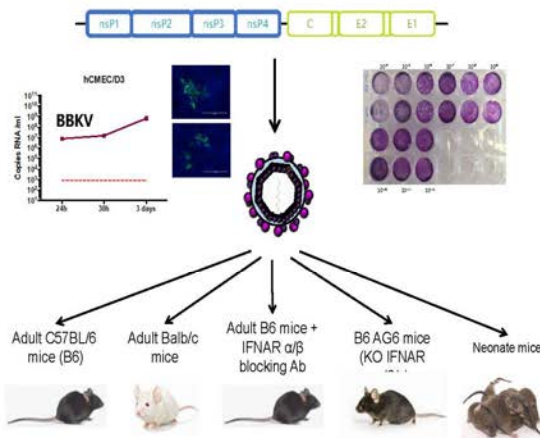
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Risk Assessment Studies:

Tropism and Pathogenesis
Vector Competence



3. Animal Models

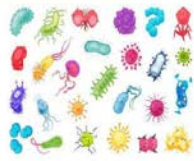


Risk Assessment Studies:

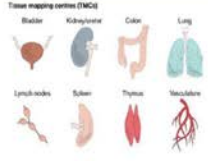
Tropism and Pathogenesis
Vector Competence

RESPONSIVENESS : Task Force rapidly mobilizable, available people/reagents/models
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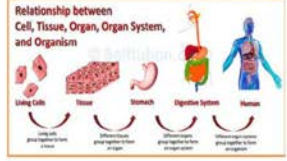
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3. Animal Models



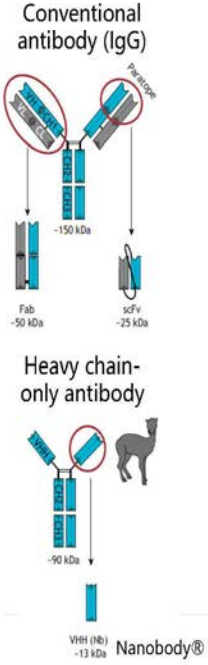
4. Detection



Objective

Antibody development platforms

Antibody development considerations: Time, cost; diversity, affinity...



💡 In vitro platform

- 1. Library screening**
Synthetic nanobody; naïve human Ab library
- 2. Engineer related antibody**
Potential coronavirus nAb.
Mutation, bispecific, multivalence, appendant...
- 3. Optimization platform**
Phage display, affinity maturation...

Fast, low cost, easy manipulation.

💡 In vivo immunization

- 1. Convalescent human**
(Or vaccinated).
Specific B cell cDNA; single B cell sorting.
- 2. Rodent immunization**
Hybridoma; humanized mouse
- 3. Immunization of others**
Llama/Alpaca - nanobody

Somatic hypermutation, V(D)J recombination.

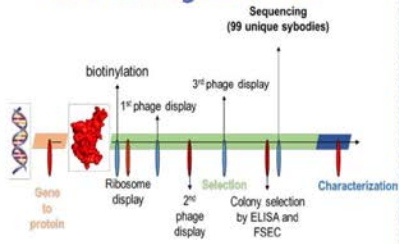
12

Conclusion

Development of neutralizing nanobodies and human monoclonal antibodies.

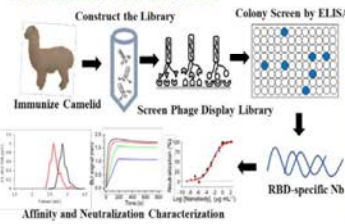
We reported different antibodies (MR3-Fc, DL4, DL28, FD20 and Ab08) against SARS-CoV-2 isolated using RBD, and they show good neutralizing potential.

Synthetic nanobody selection against RBD



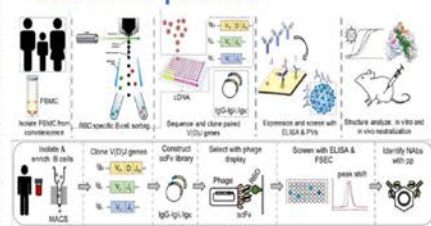
100 sybodies in 12 days

Usual route for nanobody discovery by immunizing camelid with RBD



28 nanobodies in 3 months

Human monoclonal antibody isolated from convalescent of COVID-19 patients



1 mAb in 2 months,
1 mAb in 1.5 months

Li T, Zhou B, Luo Z, Lai Y, Huang S, Zhou Y, Li Y, Gautam A, Bourgeau S, Wang S, Bao J, Tan J, Lavillette D*, Li D*. *Front Microbiol.* 2022 Jun 2;13:875840. doi: 10.3389/fmicb.2022.875840

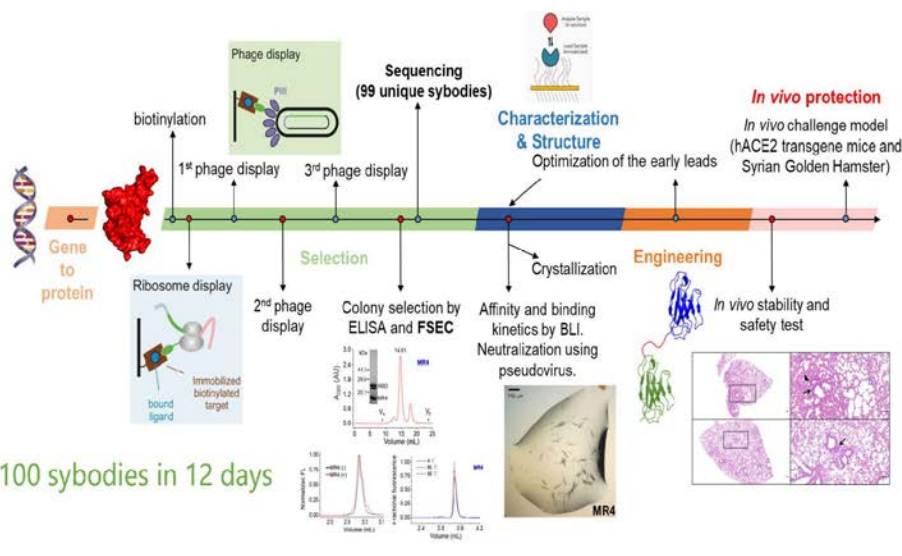
A Spike-destroying human antibody effectively neutralizes Omicron-included SARS-CoV-2 variants with therapeutic efficacy. Meng L, Zha J, Zhou B, Cao L, Jiang C, Zhu Y, Li T, Lu L, Zhang J, Yang H, Feng J, Gu Z, Tang H, Jiang L, Li D, Lavillette D*, Zhang X*. *PLoS Pathog.* 2023 Jan 27;19(1):e1011085. doi: 10.1371/journal.ppat.1011085

13

Results

Nanobody : FAST, low cost, stable

Synthetic nanobody (Sybody) selection against RBD



100 sybodies in 12 days



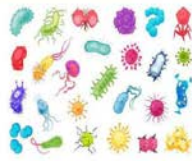
Markus Seeger, Institute of Medical Microbiology, University of Zurich, Zurich, Switzerland. *Nature Protocols* volume 15, pages1707–1741 (2020)

14

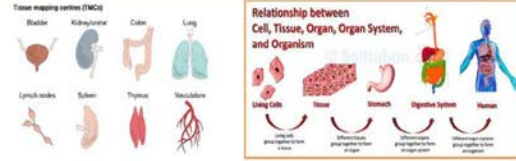
RESPONSIVENESS : Task Force rapidly mobilizable, available people/reagents/models

What do we need to prepare for the next outbreak to do drug screening rapidly?

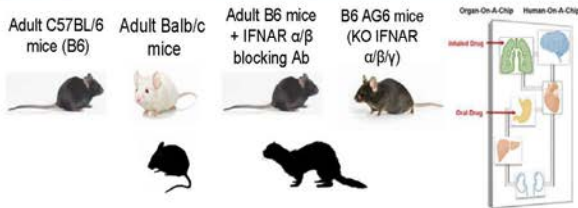
1. Pathogen Access



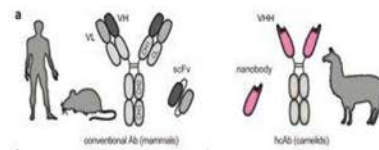
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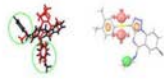
3. Animal Models



4. Detection



5. Drug Library

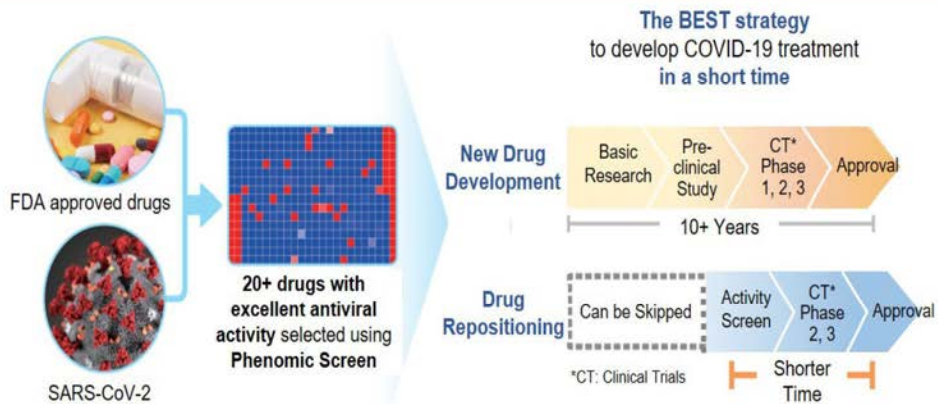


6. Trained team, infrastructures and funds

Threat: During outbreak, regular channels, collaborators, close doors "lockdown" prevent delivery of reagents...
Need to secure relative independence

Drug Repositioning Strategy @ IPK

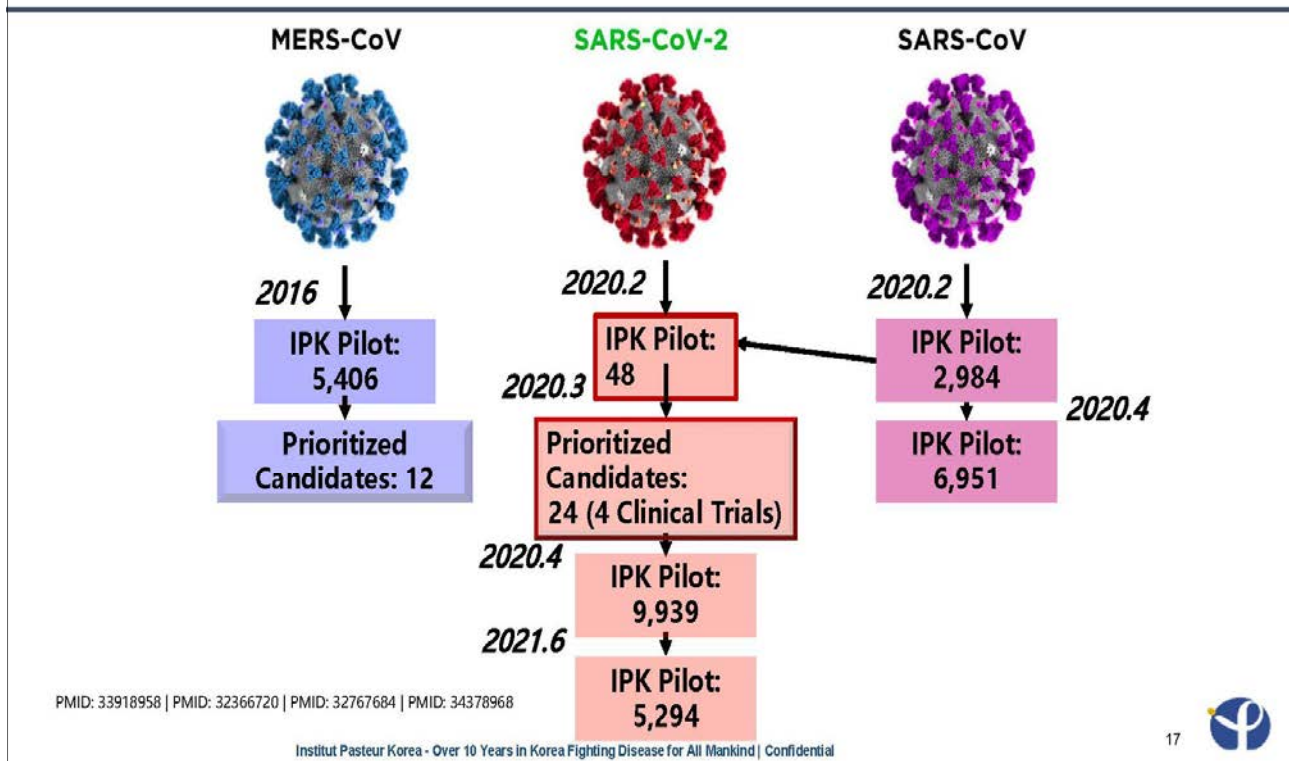
IPK PILOT LIBRARY (Small Molecule): Approved, Investigational, Bioactives, Natural Products



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Drug Repositioning HTS against Coronaviruses



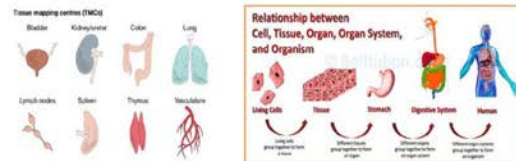
RESPONSIVENESS : Task Force rapidly mobilizable, available people/reagents/models

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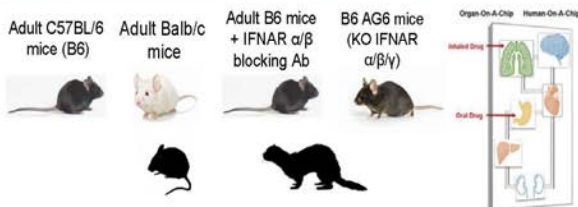
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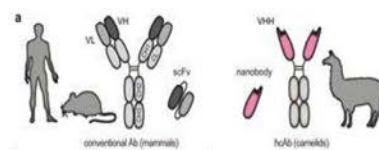
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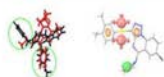
3. Animal Models



4. Detection



5. Drug Library



6. Trained team, infrastructures and funds

Expanding and Operating (A)BSL-3 Open Labs > Research Resource Center (RRC)

Purpose	Establish core research infrastructure facilitating basic research on infectious disease Operate as metropolitan open labs & support scientific community
Major facility	1 Biosafety Level 3 facility (249.27m ² , 4 laboratories, 1 equipment room) 1 Animal Biosafety Level 3 facility (328.39m ² , 2 breeding rooms, 3 laboratories, 2 autopsy rooms) 1 Biobank (148.79m ² , 2 storage rooms, 3 laboratories)
Budget	Approx. 16.9 billion KRW (9.8 billion KRW in 2022) by MSIT
Period	2021~2023 (3 years)



(Total 1,688m²(511py))

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Expanding and Operating (A)BSL-3 Open Labs > Research Resource Center (RRC)



- Plan**
- Establish operation of IACUC.
 - Kick-off meeting hold in October 2023.

<https://rrc.ip-korea.org>

Mail: RRCS_Team@ip-korea.org

20



Thank you

감사합니다

Dimitri LAVILLETTE, PhD, Dr. Habil
CSO
Applied Molecular Virology Team Head
Dimitri.Lavillette@ip-korea.org



02

SARS-CoV-2 S2 타겟 백신 및 치료항제 개발

조은위 센터장
한국생명공학연구원



Speaker



Cho, Eun-Wie

- ✔ Korea Research Institute of Bioscience and Biotechnology (KRIBB)
- ✔ Principal Researcher

🔍 EDUCATION:

- 2001 Ph.D in Biological Science, Korea Advanced Institute of Science & Technology (KAIST), Biological Science

🔍 PROFESSIONAL EXPERIENCE:

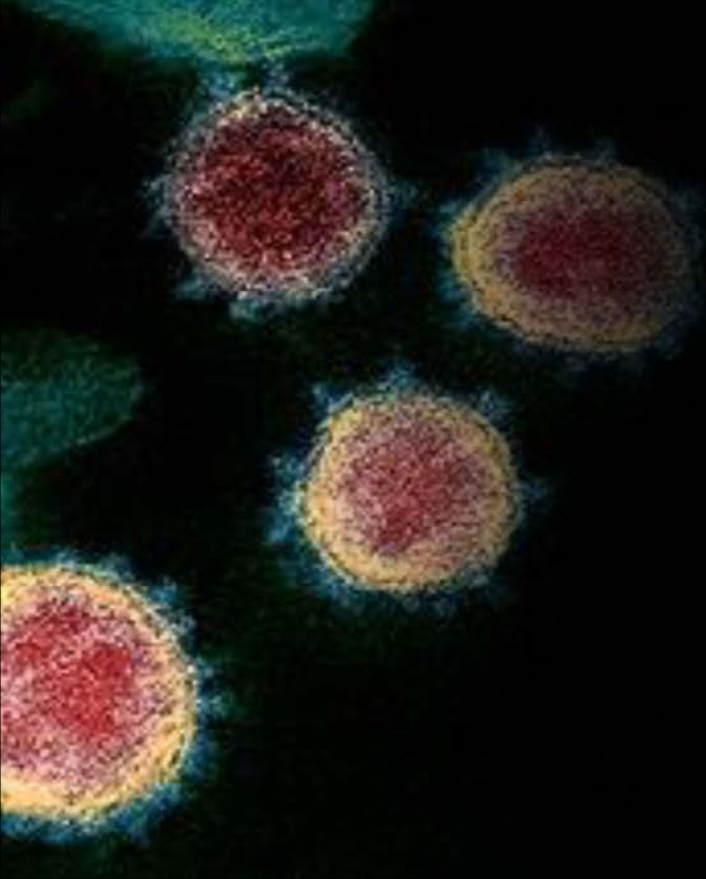
- 2007~Present Principal Researcher, Rare Disease Research Center, Korea Research Institute of Bioscience and Biotechnology (KRIBB)
- 2010~2024 Adjunct professor, University of Science and Technology (UST)

🔍 Topic


Development of SARS-CoV-2 S2 Targeted Vaccines and Therapeutic Antibodies

🔍 Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), had a major impact on both the global health and economy. Numerous virus-neutralizing antibodies were developed against the S1 subunit of SARS-CoV-2 spike (S) protein to block viral binding to host cells and were authorized for control of the COVID-19 pandemic. However, frequent mutations in the S1 subunit of SARS-CoV-2 enabled the emergence of immune evasive variants. To address these challenges, broadly neutralizing antibodies targeting the relatively conserved S2 subunit and its epitopes have been investigated as antibody therapeutics and universal vaccines. In this talk, we will present our findings, focusing on the properties of S2 antibodies and progress in the development of S2 peptide vaccines. We expect that these findings will lead to the design of S2 vaccines with improved efficacy and the discovery of therapeutic antibodies with high potency.




Development of SARS-CoV-2 S2 Targeted Vaccines and Therapeutic antibodies

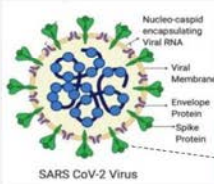


KOREA RESEARCH INSTITUTE OF BIOSCIENCE AND BIOTECHNOLOGY (KRIBB)
Eun-Wie Cho


SARS-COV-2 and COVID-19 PANDEMIC



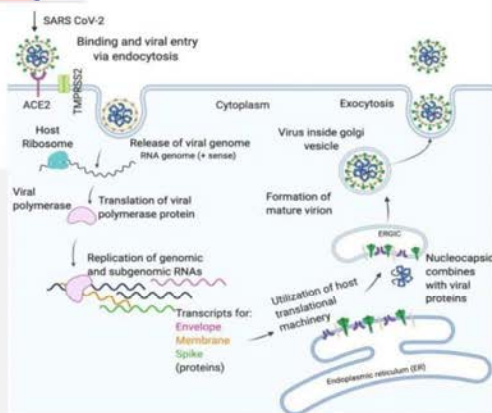
SARS-CoV-2 isolated from a patient in the U.S. (TEM image; NIAID-RML)



SARS CoV-2 Virus




Alveoli: Cells in the lung




(Commun Biol. 2020 PMID: 32641750)

774,593,066
Number of COVID-19 cases reported to WHO (cumulative total)



7,028,881
Number of COVID-19 deaths reported to WHO (cumulative total)



WHO Regions: Africa, Americas, Eastern Mediterranean, Europe, South-East Asia, Western Pacific

(Source: World Health Organization. 4 February 2024)

- 2019. 12. SARS-CoV-2 was first reported in Wuhan.
- 2023. 5. WHO declares end to COVID global health emergency.

Responding to SARS-CoV-2: Diagnostics, Vaccines and Therapeutic Antibodies

Time from discovery of virus to first approved/authorized treatment (years)

Disease	Discovery Period	Treatment Period
SARS-CoV-2	2019-2020	2020
Hepatitis C	1987-1989	1996
HIV	1981-1987	1987
Hepatitis B	1966-1968	1981
Influenza	1933-1936	1968

(by LabCorp)

Early mAb intervention against COVID-19

(Adv Drug Deliv Rev. 2021. PMID: 33309815)

Diagnostics

(ACS Infect Dis. 2022. PMID: 35940589)

Traditional development

15 years or longer

SARS-CoV-2 vaccine development

10 months to 1.5 years total

(Nature. 2020. PMID: 32967006)

SARS-CoV-2 Vaccines

	Live Attenuated Vaccines	Inactivated Vaccines	DNA Vaccine	RNA Vaccines	Subunit Vaccines	Replicating Viral Vector Vaccine	Non-Replicating Viral Vector Vaccines
	<p>Live, weakened (attenuated) vaccines which do not cause disease. Elicits strong immune response. Potential contraindications in immunocompromised patients.</p> <p>Examples: Mumps Vaccine, Yellow Fever</p>	<p>Whole virus or pathogen grown in culture and killed. Less potent than live attenuated vaccines. Safer than live vaccines. Requires booster doses due to weaker induction of immunity.</p> <p>Examples: Polio Vaccine, Pertussis Vaccine</p>	<p>DNA plasmids containing DNA sequence encoding for viral pathogenic antigens. No risk for disease. Strong immune response. Easily developed. Possibility of tolerance to antigen.</p> <p>Examples: Currently in use for Ebola. SARS-CoV-2 vaccines in development.</p>	<p>These vaccines use mRNA sequences that encode for viral antigenic proteins. Often carried by lipid nanoparticles. Cheaper, easily produced. Reactogenicity in susceptible patients.</p> <p>Examples: Moderna SARS-CoV-2 Vaccine, Pfizer-BioNTech SARS-CoV-2 Vaccine, mRNA vaccine</p>	<p>Present antigens to the immune system without genetic material from viral particles. Focused immune response toward antigen, safer due to lack of viral genetic material. Require multiple doses to induce long term immunity.</p> <p>Examples: Hepatitis B Vaccine, Pertussis Vaccine, HPV vaccine</p>	<p>Low pathogenic viruses are altered to viral vectors to produce similar protein/antigens as the disease causing virus. Limited efficacy on preexisting immunity. Observe powerful immune response.</p> <p>Examples: SARS-CoV-2 Vaccinations in development</p>	<p>Only produce antigen, unable to replicate inside of the body unless replicating viral vector vaccines. Safer vaccine. Requires higher dosing to induce immunity.</p> <p>Examples: Dimer Adenovirus SARS-CoV-2 Vaccine, Dimer SARS-CoV-2 Vaccinations in development</p>
Mechanism of Action:							

(The Adv Vaccines Immunother. 2021. PMID: 34870090)



SARS-CoV-2 Therapeutic Antibodies:

Neutralizing antibodies directed against the SARS-CoV-2 spike protein

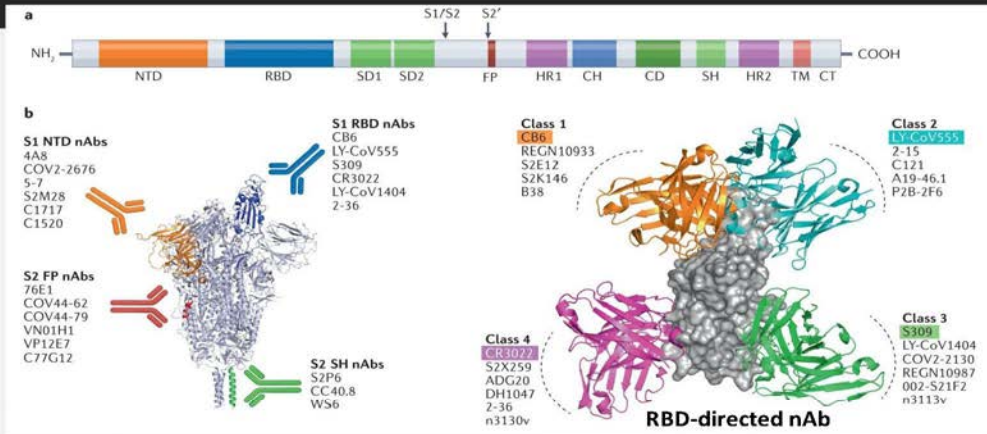


Table 1. FDA and/or EMA/EUA therapeutic antibodies to treat COVID-19.

INN (a)	Other Names	Commercial Name	Company	EUA	
				FDA	EMA
Casirivimab	REGN 10933	REGEN-COV, Ronapevri	Regeneron Pharmaceuticals	21 November 2020 [9,10]	11 November 2021 [11,12]
Imdevimab	REGN 10987	REGEN-COV, Ronapevri	Regeneron Pharmaceuticals	21 November 2020 [9,10]	11 November 2021 [11,12]
Bamlanivimab	BAM, LY381253, LY-CoV555	N/A (b)	Eli Lilly and Company	9 February 2021 [13]	EMA withdrew the application on 29 October 2021 [14]
Etesevimab	CB6, ETE, LY332479, LY-CoV016	N/A (b)	Eli Lilly and Company	9 February 2021 [13]	EMA withdrew the application on 29 October 2021 [14]
Sotrovimab	S309, VR-7331 OSK, 4192136	Xevudy	OcularGen/Novartis (OSK)	26 May 2021 [15]	18 December 2021 [16]
Regdanvimab	CT-P59	Regeneron	Celltrion	N/A	11 November 2021 [12,17]
Cilgavimab	COV2-2130, AZD1961	Evushid	Attra Zeneca	8 December 2021 [18]	24 March 2022 [19]
Tixagevimab	COV2-2198, AZD8895	N/A	Attra Zeneca	8 December 2021 [18]	24 March 2022 [19]
Bebtelovimab	LY-CoV1404	N/A	Eli Lilly and Company	11 February 2022 [20]	N/A

(a)—International proprietary name (b)—N/A, non-applicable



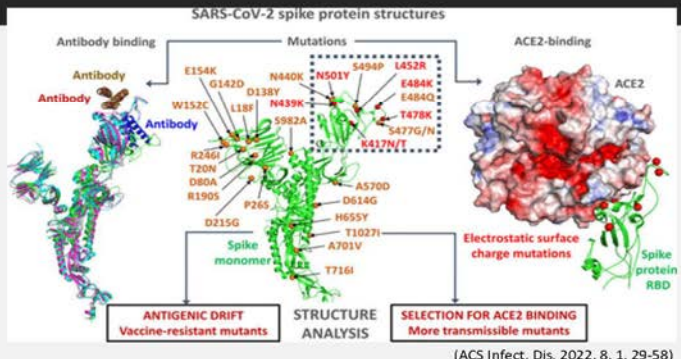
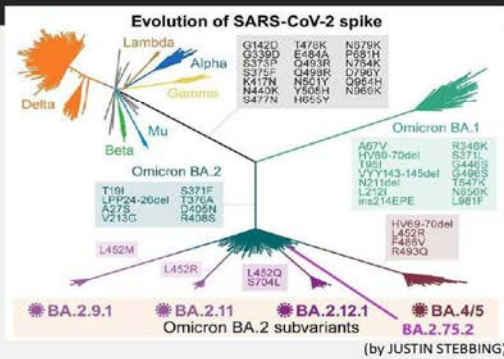
(Nat Rev Immunol. 2023. PMID: 36168054)

(Int J Mol Sci. 2022. PMID: 36077159)



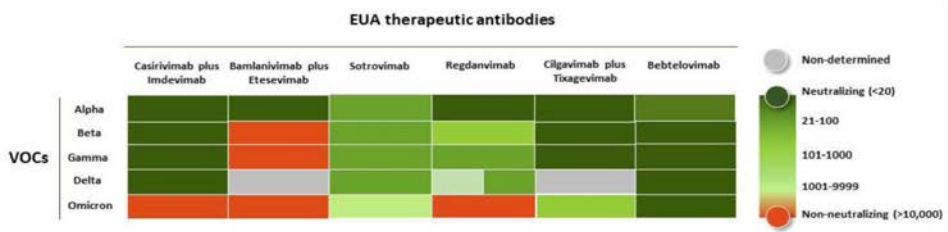
Immune Evasion of SARS-CoV-2:

Evolution and Mutations of the SARS-CoV-2 Spike Protein



(ACS Infect. Dis. 2022, 8, 1, 29-58)

Neutralization potency of the EUA-approved anti-COVID-19 antibodies when challenged with SARS-CoV-2 VOCs. (The heat-map based on the neutralization values of pseudovirus assays against SARS-CoV-2 variants)



(Int J Mol Sci. 2022. PMID: 36077159)

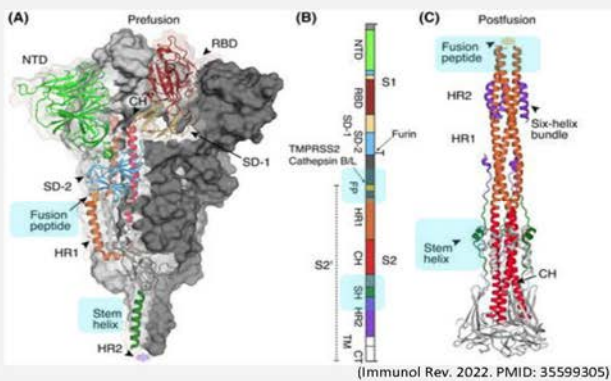
2022



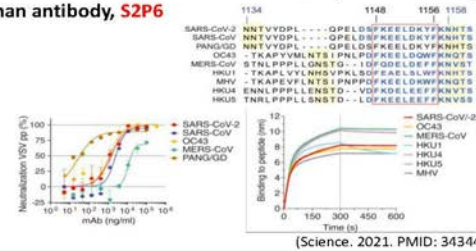
Broadly neutralizing antibodies to SARS-CoV-2 and other human coronaviruses

Broadly neutralizing epitopes in S2 subunit

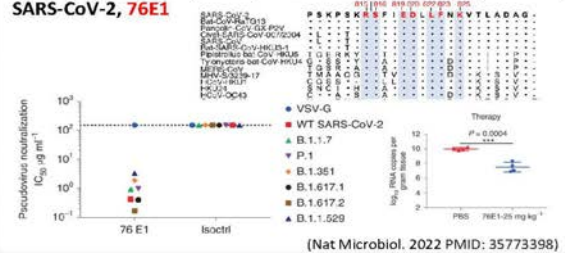
1. S2 stem helix
2. Fusion peptide



1. Broad betacoronavirus neutralization by a stem helix-specific human antibody, **S2P6**



2. A human antibody with pan-coronavirus reactivity including SARS-CoV-2, **76E1**



- ✓ incredibly broad neutralization spectrum against HCoVs (α -CoVs, β -CoVs)
- ✓ less potent than RBD-targeting antibodies.

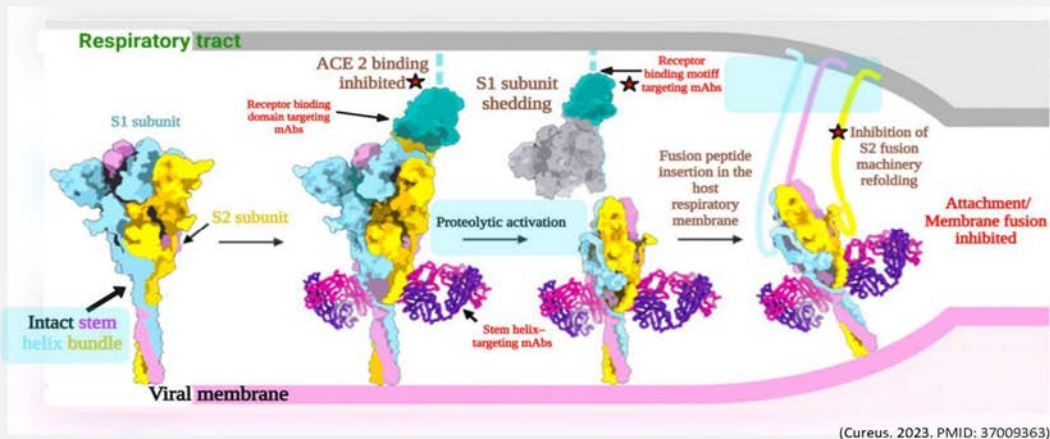
2022



Broadly neutralizing antibodies to SARS-CoV-2 and other human coronaviruses

Broadly neutralizing epitopes in S2 subunit

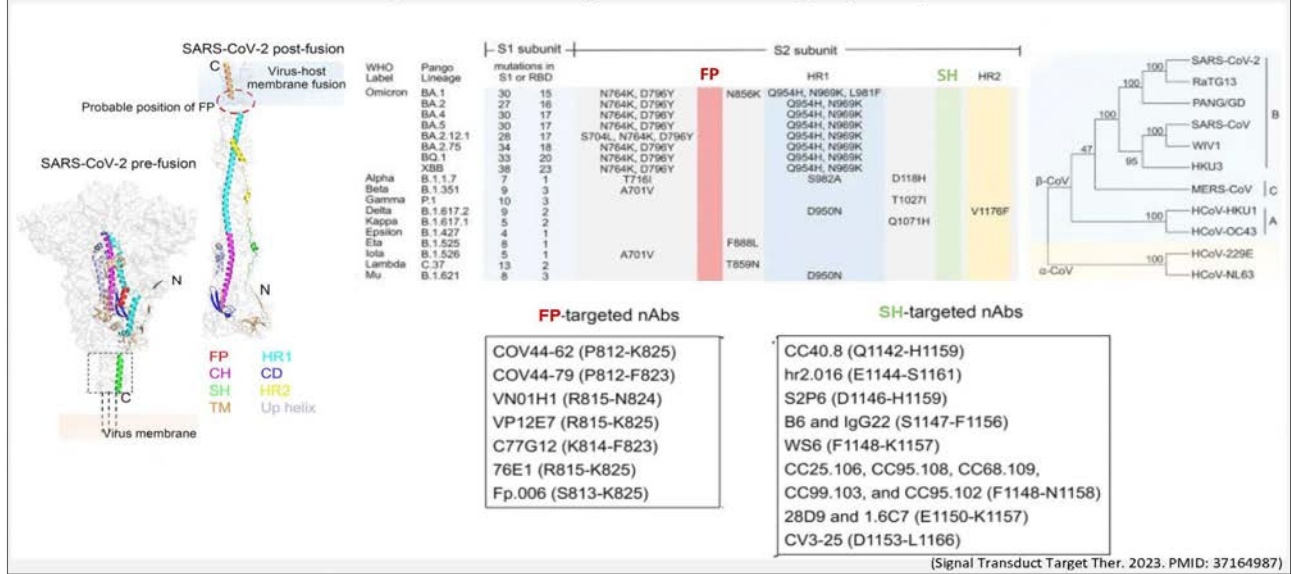
1. S2 stem helix
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- ✓ incredibly broad neutralization spectrum against HCoVs (α -CoVs, β -CoVs)
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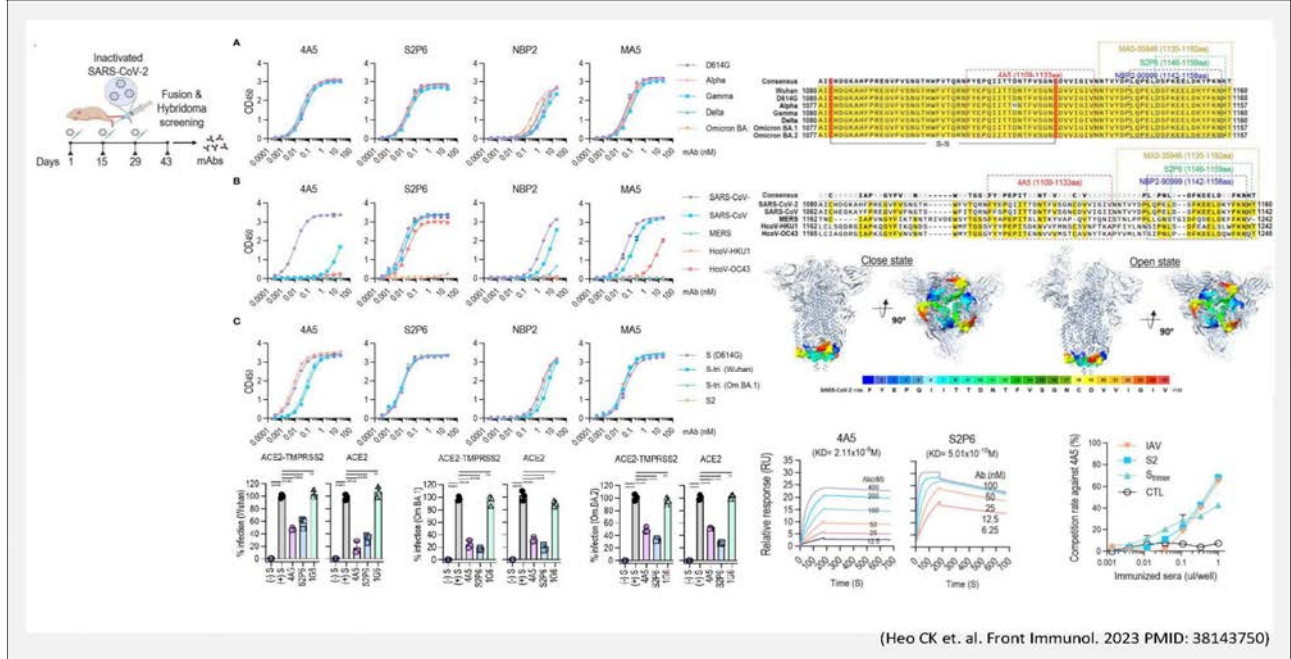
Universal Vaccine Design to SARS-CoV-2 and other human coronaviruses

- S2 targeted universal vaccine
- Immuno-focusing on broadly neutralizing epitopes



(Signal Transduct Target Ther. 2023. PMID: 37164987)

A Novel Broadly Neutralizing SARS-COV-2 S2 antibody, 4A5



(Heo CK et al. Front Immunol. 2023 PMID: 38143750)

SARS-CoV-2 S2-based Universal Vaccine

- Focusing on immunodominant B cell epitopes in S2 subunit
- Viral Nanoparticle displaying B cell epitopes

(Moon KB et al. Sci Rep. 2022. PMID: 35046461)

(Unpublished Data)

SARS-CoV-2 S2-based Universal Vaccine

- Focusing on immunodominant B cell epitopes in S2 subunit
- Viral Nanoparticle displaying B cell epitopes

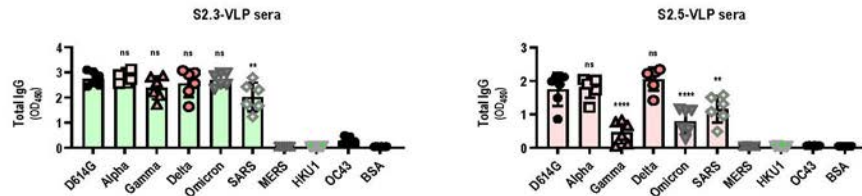
S2.X-VLP	
S2.1	HDGKAHFRFREGVEYS (C)
S2.2	WEVTQRNFYEPQIITTDNTEVSGN (C)
S2.3	NTVYDPLQPELDSFKELDKYFK (C)
S2.4	HTSPDVLGDIISGI (C)
S2.5	ASVWNIQKEIDRIAEVAKNI (C)

(Manuscript in preparation)

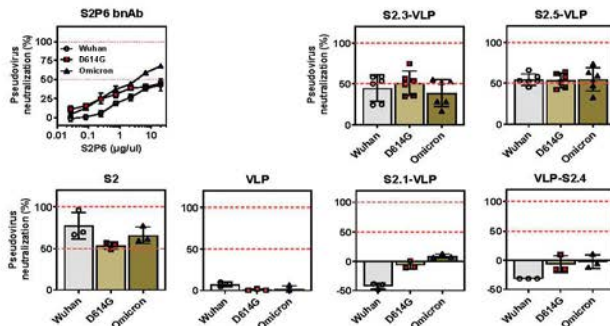


SARS-CoV-2 S2-based Universal Vaccine

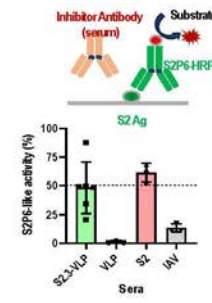
ELISA binding of mouse sera to S proteins of SARS-CoV-2 variants



SARS-CoV-2 pseudovirus neutralization of mouse sera



S2P6 bnAb-like activity



(Manuscript in preparation)

References

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- Challenges and opportunities for antiviral monoclonal antibodies as COVID-19 therapy. Cruz-Teran C, et al. Adv Drug Deliv Rev. 2021. PMID: 33309815
- Two Years into the COVID-19 Pandemic: Lessons Learned. da Silva SJR, et al. ACS Infect Dis. 2022. PMID: 35940589
- SARS-CoV-2 vaccines in development. Krammer F. Nature. 2020. PMID: 32967006
- Comprehensive literature review on COVID-19 vaccines and role of SARS-CoV-2 variants in the pandemic. Yap C et al., Ther Adv Vaccines Immunother. 2021. PMID: 34870090
- Broadly neutralizing antibodies to SARS-CoV-2 and other human coronaviruses. Chen Y, et al., Nat Rev Immunol. 2023. PMID: 36168054
- Evolution of Anti-SARS-CoV-2 Therapeutic Antibodies. Almagro JC et al., Int J Mol Sci. 2022. PMID: 36077159
- Structure and Mutations of SARS-CoV-2 Spike Protein: A Focused Overview. Mehra R et al., ACS Infect Dis. 2022. PMID: 34856799
- Evolution of Anti-SARS-CoV-2 Therapeutic Antibodies. Almagro JC et al., Int J Mol Sci. 2022. PMID: 36077159
- Protective neutralizing epitopes in SARS-CoV-2. Liu H, et al., Immunol Rev. 2022. PMID: 35599305
- Broad betacoronavirus neutralization by a stem helix-specific human antibody. Pinto D et al., Science. 2021. PMID: 34344823
- Neutralization mechanism of a human antibody with pan-coronavirus reactivity including SARS-CoV-2. Sun X et al., Nat Microbiol. 2022. PMID: 35773398
- Exploring the Potential of Broadly Neutralizing Antibodies for Treating SARS-CoV-2 Variants of Global Concern in 2023: A Comprehensive Clinical Review. Gutlapalli SD et al., Cureus. 2023. PMID: 37009363
- Targetable elements in SARS-CoV-2 S2 subunit for the design of pan-coronavirus fusion inhibitors and vaccines. Guo L et al., Signal Transduct Target Ther. 2023. PMID: 37164987
- Novel S2 subunit-specific antibody with broad neutralizing activity against SARS-CoV-2 variants of concern. Heo CK et al., Front Immunol. 2023. PMID: 38143750
- Construction of SARS-CoV-2 virus-like particles in plant. Moon KB et al., Sci Rep. 2022. PMID: 35046461
- S2-peptide conjugated SARS-CoV-2 VLPs elicit broad protection against SARS-CoV-2 variants of concern. Heo CK et al., Manuscript in preparation

Research team members

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Jihyun Yang, Doo-Jin Kim
(Infectious Disease Research Center, KRIBB)
Ki-Beom Moon, Hyun-Soon Kim
(Plant Systems Engineering Research Center, KRIBB)
Sumin Son, Sang Jick Kim
(Synthetic Biology and Bioengineering Research Center, KRIBB)
Haryoung Poo
(Department of Biomedical Science and Engineering, Konkuk University)

Development of SARS-CoV-2 S2 Targeted Vaccines and Therapeutic antibodies



03

코로나19로부터의 항바이러스제 개발 교훈

한수봉 센터장
한국화학연구원



Speaker



Soo Bong Han

- ✓ Korea Research Institute of Chemical Technology (KRICT)
- ✓ Principal Research Scientist/Head of Infectious Diseases Therapeutic Research Centers

🔍 EDUCATION:

- 2010 The University of Texas at Austin, Ph.D. in Chemistry
- 2004 KAIST, Master of Science in Chemistry
- 2002 Sogang University, Bachelor of Science in Chemistry

🔍 PROFESSIONAL EXPERIENCE:

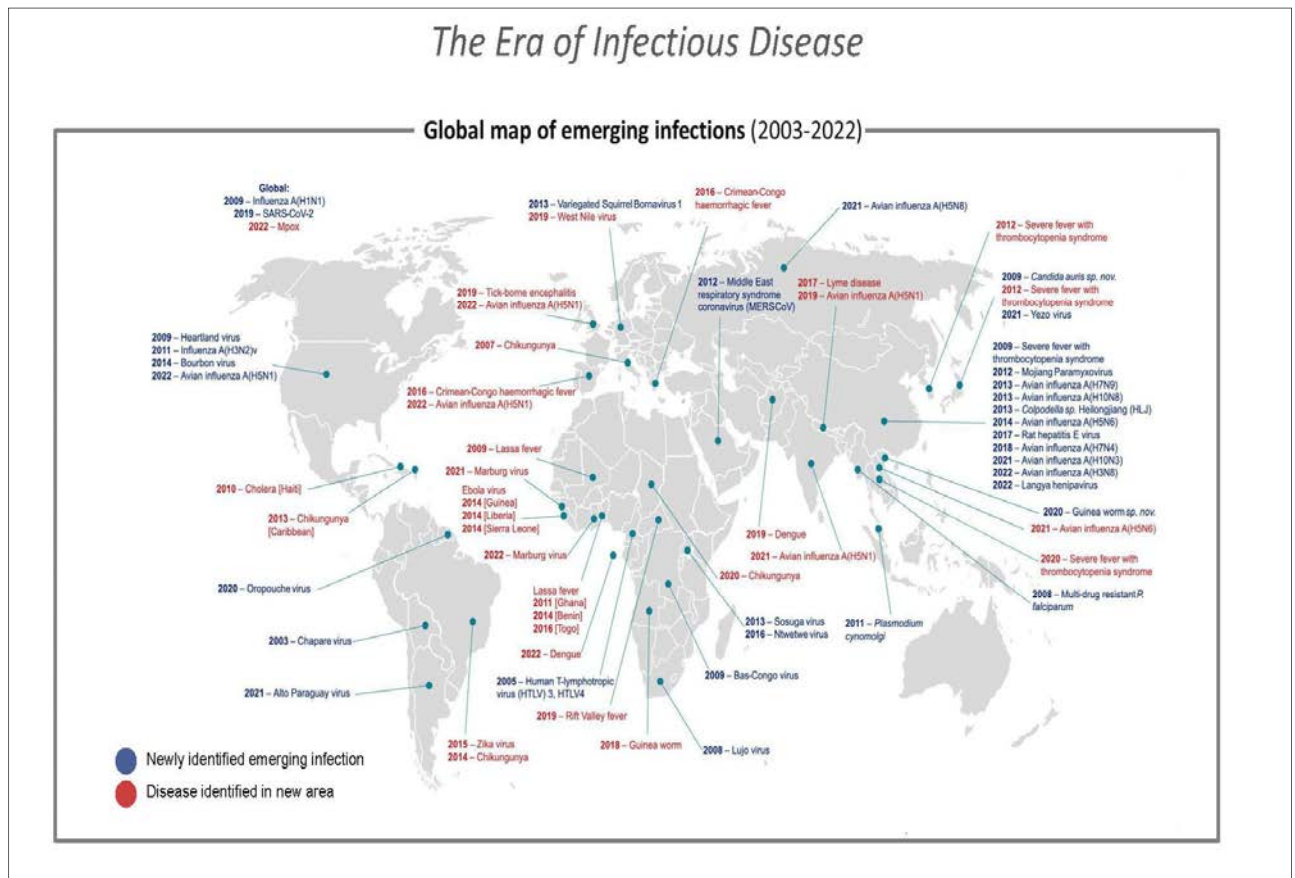
- 2023 ~ Present Head of Infectious Disease Therapeutics Research Center, KRICT
- 2018 ~ 현재 Principal Research Scientist, KRICT
- 2020 ~ 2022 Director of Department of Infectious Disease Research, KRICT
- 2018 ~ 2020 Head of Innovative Therapeutic Research Center
- 2012 ~ 2017 Senior Research Scientist, KRICT
- 2010 ~ 2011 Post-Doctoral Research Scientist, Princeton University

🔍 Topic

Lessons from COVID-19 for the development of antiviral drugs

🔍 Abstract

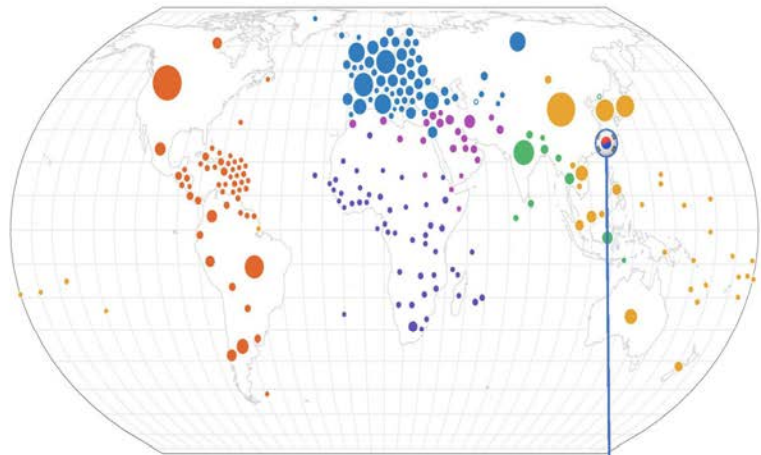
The global response to the COVID-19 pandemic has yielded significant insights that can guide the future development of antiviral drugs. It is important to address the valuable insights gained from the pandemic, which can be utilized to improve the efficiency and effectiveness of strategies for developing antiviral drugs. The urgency of the pandemic underscored the importance of expediting drug development without compromising safety, leveraging innovative technologies and collaborative approaches. Global cooperation and data sharing were paramount, highlighting the need for open communication and resource pooling. The value of broad-spectrum antiviral activity was underscored, offering a versatile approach to combatting multiple viral threats. Repurposing existing drugs for new indications proved successful, demonstrating the potential for accelerated responses. Given the rapid mutation rates of viruses, designing drugs to target critical points in viral replication cycles and considering adaptable drug designs are critical. Combination therapies emerged as a robust strategy, minimizing drug resistance and enhancing efficacy. Clinical trial readiness, sustained research investment, and equitable manufacturing and distribution strategies are essential to streamline drug development and ensure timely global access. In conclusion, the lessons derived from the COVID-19 pandemic offer a roadmap for optimizing antiviral drug development processes, ultimately bolstering global preparedness against future viral outbreaks.



The Era of Infectious Disease



- Climate Change
- Increase in population mobility
- Aging
- Lack of effective treatment



SARS-CoV-2

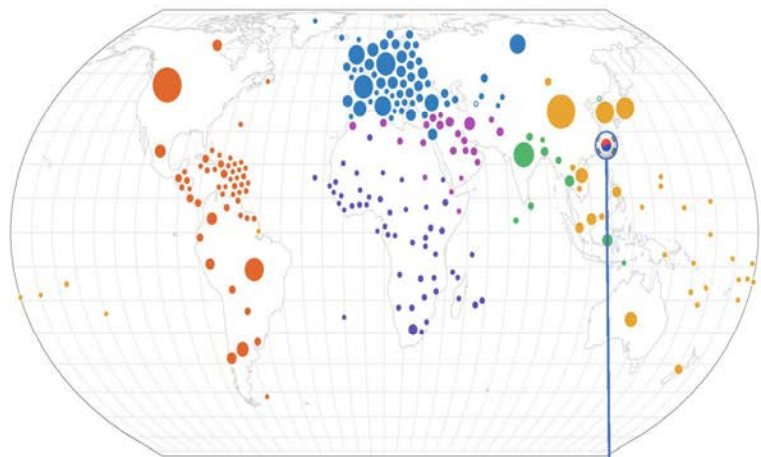
- Confirmed cases: 774,291,287
- Death: 7,019,704
- Vaccine doses: 13,516,282,548

34,571,873 (67%)
35,934
135,927,574 (263%)

COVID-19



Dignosis Vaccine Drug



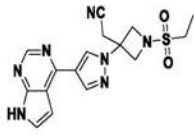
SARS-CoV-2

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34,571,873 (67%)
35,934
135,927,574 (263%)

COVID-19

■ US-FDA approved Drug for COVID-19

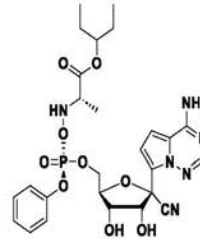


Baricitinib

Rheumatoid Arthritis

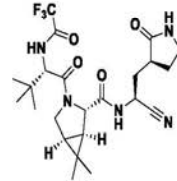


Tocilizumab



Remdesivir

Directing Acting Antiviral

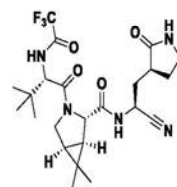


Nirmatrelvir

*emergency use authorization not included

Paxlovid

■ Top drugs by sales in 2022 (USD BD)



Nirmatrelvir




Paxlovid

- Mode of Action : **Direct-Acting Antiviral** (3CL protease inhibitor)


CN1C[C@H](C(F)(F)F)C(=O)N1C(=O)N[C@@H](C#N)C

Nirmatrelvir



Virus life cycle (COVID-19)

Paxlovid



KRIC
한국화학연구원


- Existing Compound Optimization Strategy: **3CL protease inhibitor**

CC(C)C[C@@H](NC(=O)c1ccc(O)cn1)C(=O)N[C@@H](C)C(=O)O


PF-00835231

CN1C[C@H](C(F)(F)F)C(=O)N1C(=O)N[C@@H](C#N)C


Nirmatrelvir




2002



2005

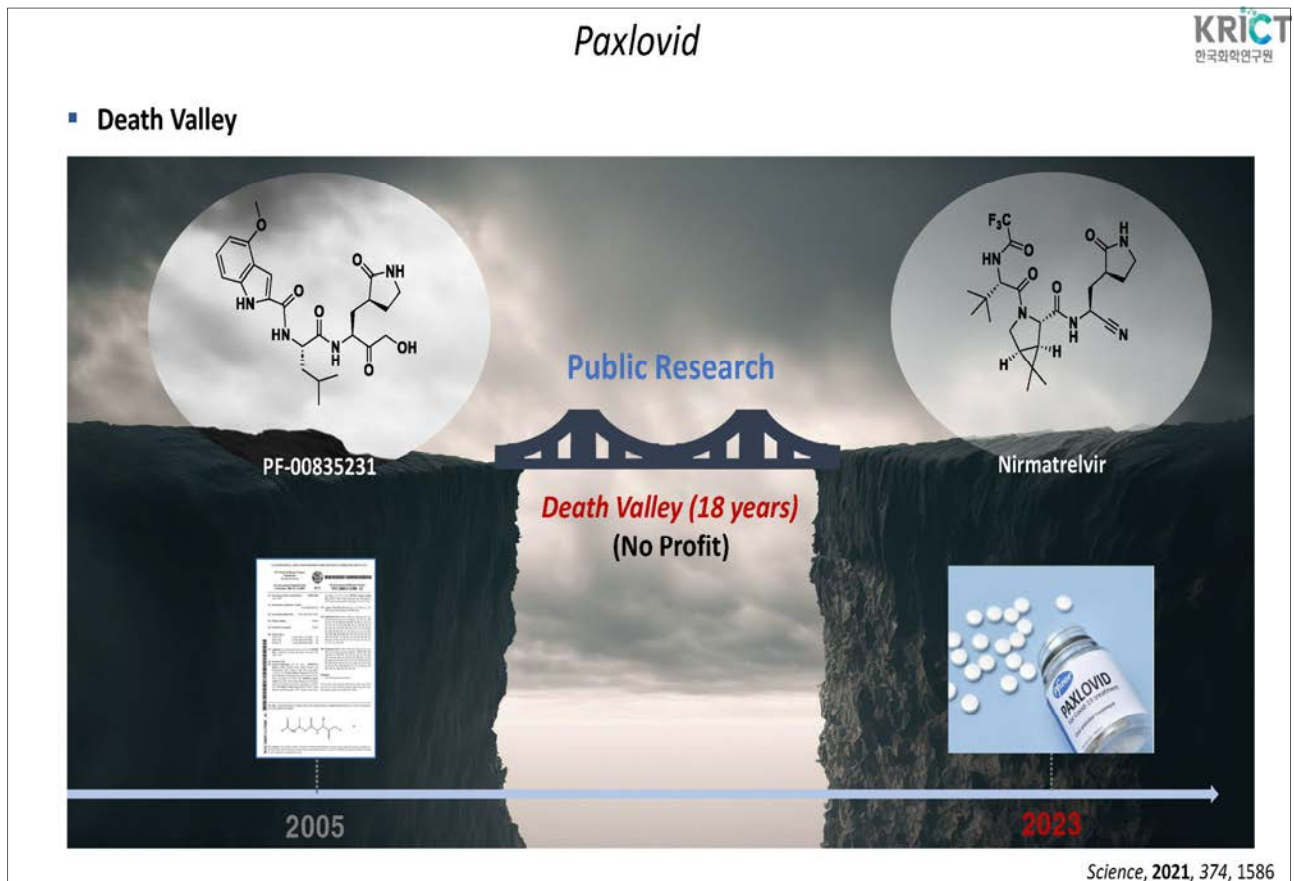
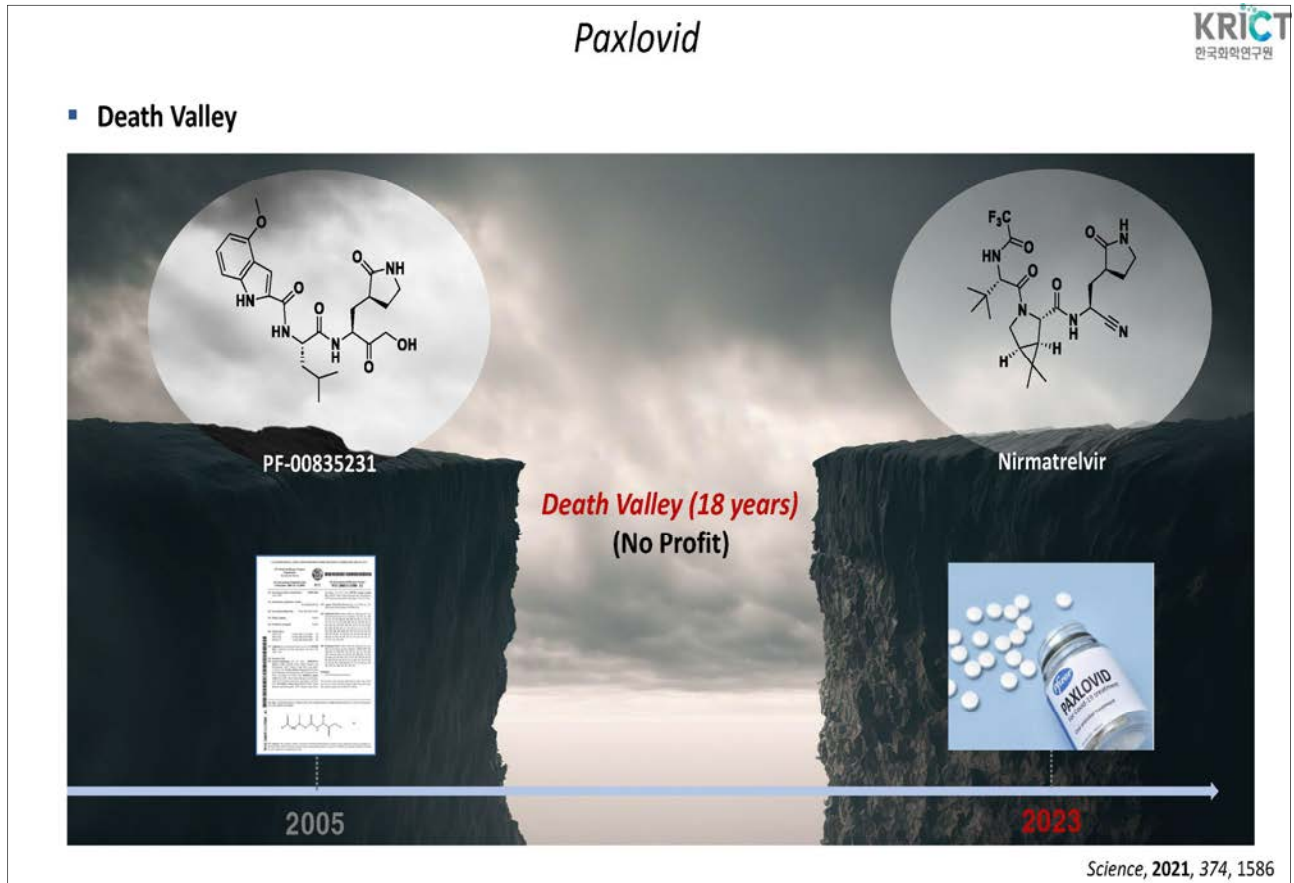


2019



2023

Science, 2021, 374, 1586

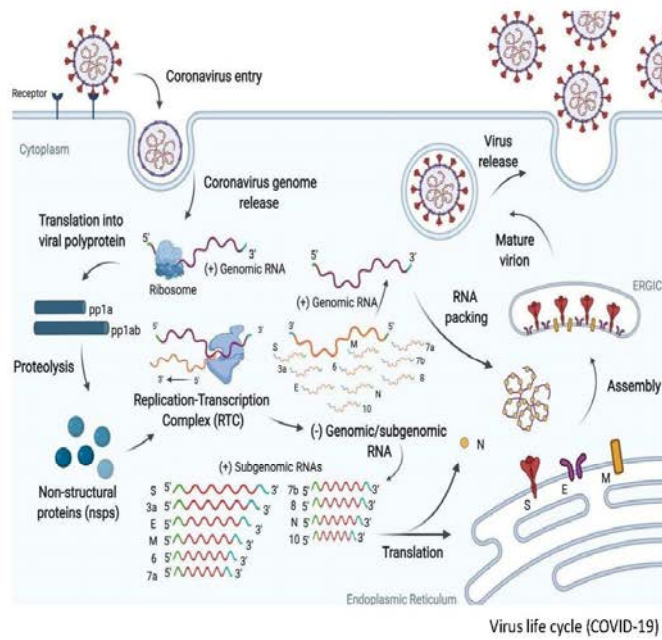


KRICT Direct-Acting Antiviral Chemical Library

Existing Drugs and Compounds

- Protease
- Polymerase
- Integrase
- Reverse transcriptase
- DNA/RNA synthetase
- Entry
- Etc.

Approved – Clinical – Biochemical



KRICT Direct-Acting Antiviral Chemical Library

Existing Drugs and Compounds

- Protease
- Polymerase
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- DNA/RNA synthetase
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- Etc.

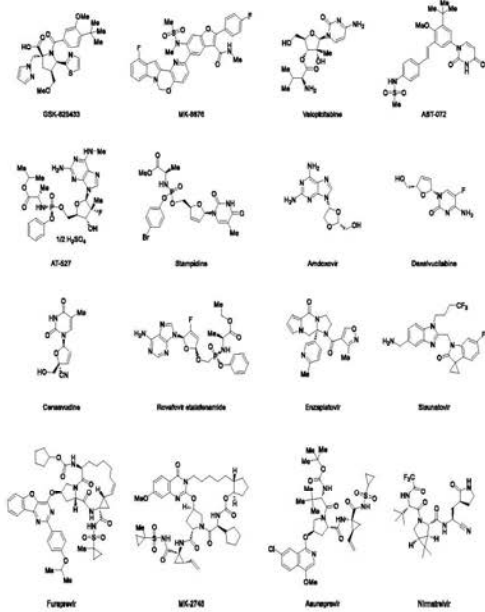
Approved – Clinical – Biochemical

Goal - 1500 compounds (500 compounds collected)



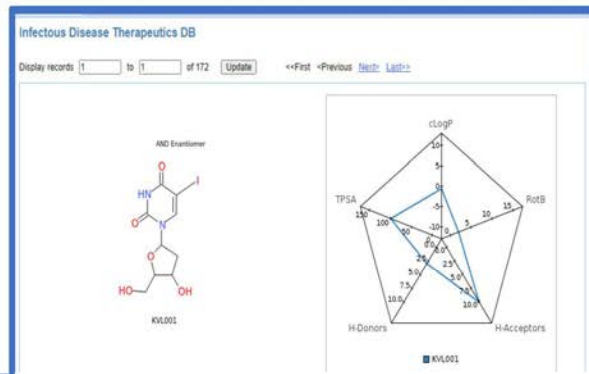
KRICT Direct-Acting Antiviral Chemical Library

- Goal - 1500 compounds (500 compounds collected)



KRICT Direct-Acting Antiviral Chemical Library

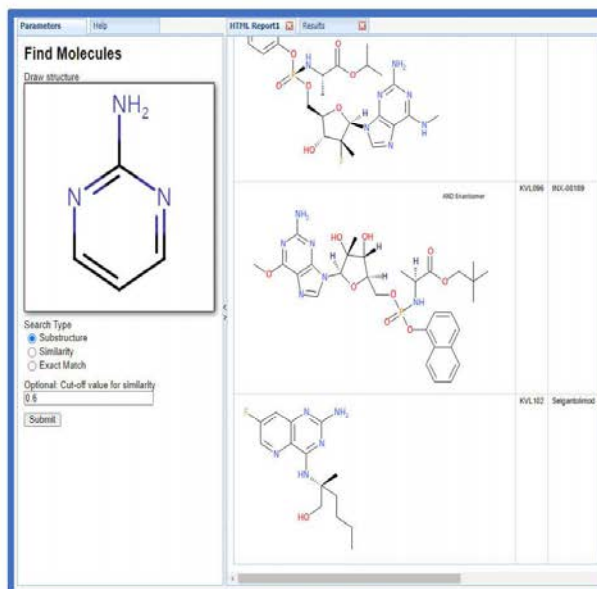
- Web-based DB platform for public use



KRICT Code	Product Name	Synonyms	CAS No	Purity	
KVL001	Idoxuridine	5-Iodo-2'-deoxyuridine	54-42-2	100	
Clinical_Information		Pathway	Research_Area	Target	Class
Launched		Polymerase	Infection; Cancer	HSV	Polymerase1
Physicochemical properties					
MW	HBA	HBD	cLogP	TPSA	
354.09651	10	3	-0.53	99.10	

KRICT Direct-Acting Antiviral Chemical Library

- Web-based DB platform for public use



KRICT Direct-Acting Antiviral Chemical Library

- Advanced Antiviral Drug Library (1000 compound)

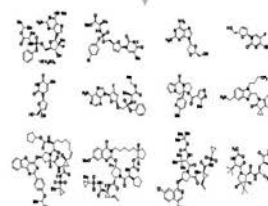
AI based Chemical Library

Antiviral AI

Antiviral Activity Data
ADME & Tox Data
Antiviral Target Structure Data

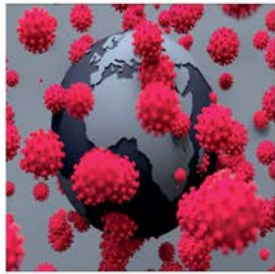


Experiment



New Drug Structure Design

KRICT Direct-Acting Antiviral Chemical Library



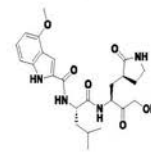
Pandemic outbreak



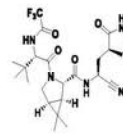
Antiviral AI



DAA Library



Hit



Drug Candidate



Clinical Trial

04

인공지능 기반 신약개발 가속화

김우연 교수
한국과학기술원



Speaker



Woo-Youn Kim

- ✓ KAIST
- ✓ Professor, Department of Chemistry, KAIST

🔍 EDUCATION:

- 2009 Ph.D., Chemistry, POSTECH
- 2004 B.S., Chemistry & Physics, POSTECH

🔍 PROFESSIONAL EXPERIENCE:

- 2024 ~ Present Vice Director, Convergence AI Institute for Drug Discovery, Korea Pharmaceutical and Bio-Pharma Manufacturers Association
- 2022 ~ 2024 Director, Korea AI Center for Drug Discovery and Development, Korea Pharmaceutical and Bio-Pharma Manufacturers Association
- 2020 ~ Present Cofounder & CEO, HITS Inc.
- 2011 ~ Present Assist./Assoc./Full Professor, Chemistry, KAIST
- 2009 ~ 2010 Postdoctoral Fellow, Max-Planck-Institute

🔍 Topic

Acceleration of drug discovery with AI

🔍 Abstract

In recent years, deep learning-based AI has been rapidly developing, bringing significant impact on the field of drug discovery. For instance, AlphaFold has solved the problem of protein structure prediction and generative AI has been actively used for the design of proteins, antibodies, and small molecule drugs. Thus, leading IT companies such as Google DeepMind, MS, and Nvidia as well as big pharma such as AstraZeneca, Merck, and Pfizer are actively investing in the development of AI in this field. In this talk, I will briefly review the latest trends in AI-based drug discovery and introduce generative AI-based drug design research examples.



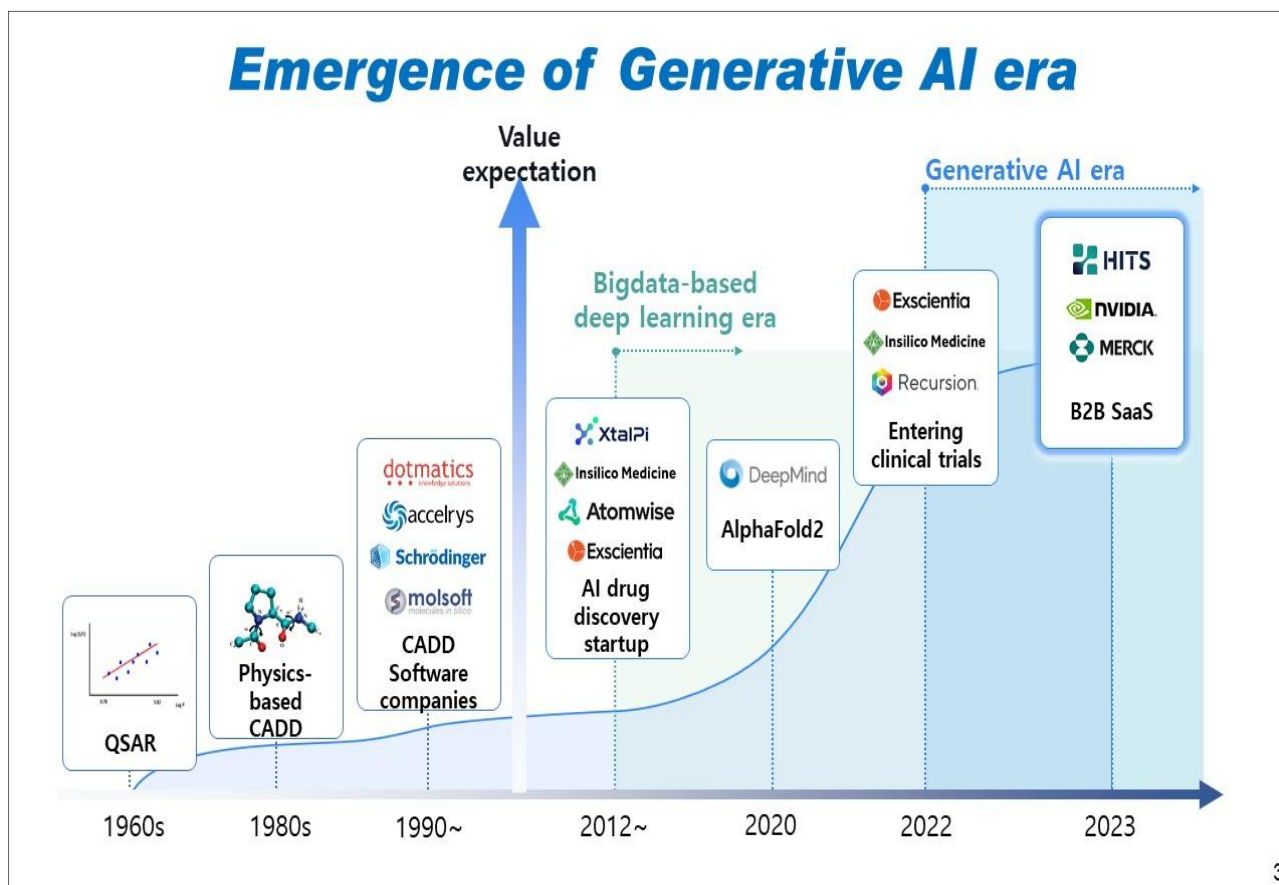
Acceleration of drug discovery with AI

Woo Youn Kim
KAIST & HITS

International Symposium for Infectious Diseases Research Institutes Cooperation
2024. 3. 8 @Grand Hyatt Incheon

Contents

- Introduction
- Generative AI for drug design
- Bioisostere replacement AI for drug resistance
- AI Drug Discovery SaaS Platform – Hyper Lab



Examples of generative AI

- ChatGPT: Chatbot based on NLP

W Please describe how AI can change drug discovery in three sentences.

A AI can accelerate drug discovery by analyzing vast amounts of biological data, identifying potential drug candidates more efficiently, and predicting their safety and effectiveness, reducing the time and cost of development. Machine learning algorithms can uncover hidden patterns in genomic and proteomic data, enabling the discovery of novel drug targets and biomarkers. Additionally, AI-powered simulations can simulate drug interactions with biological systems, aiding in the design of more effective and precise treatments.

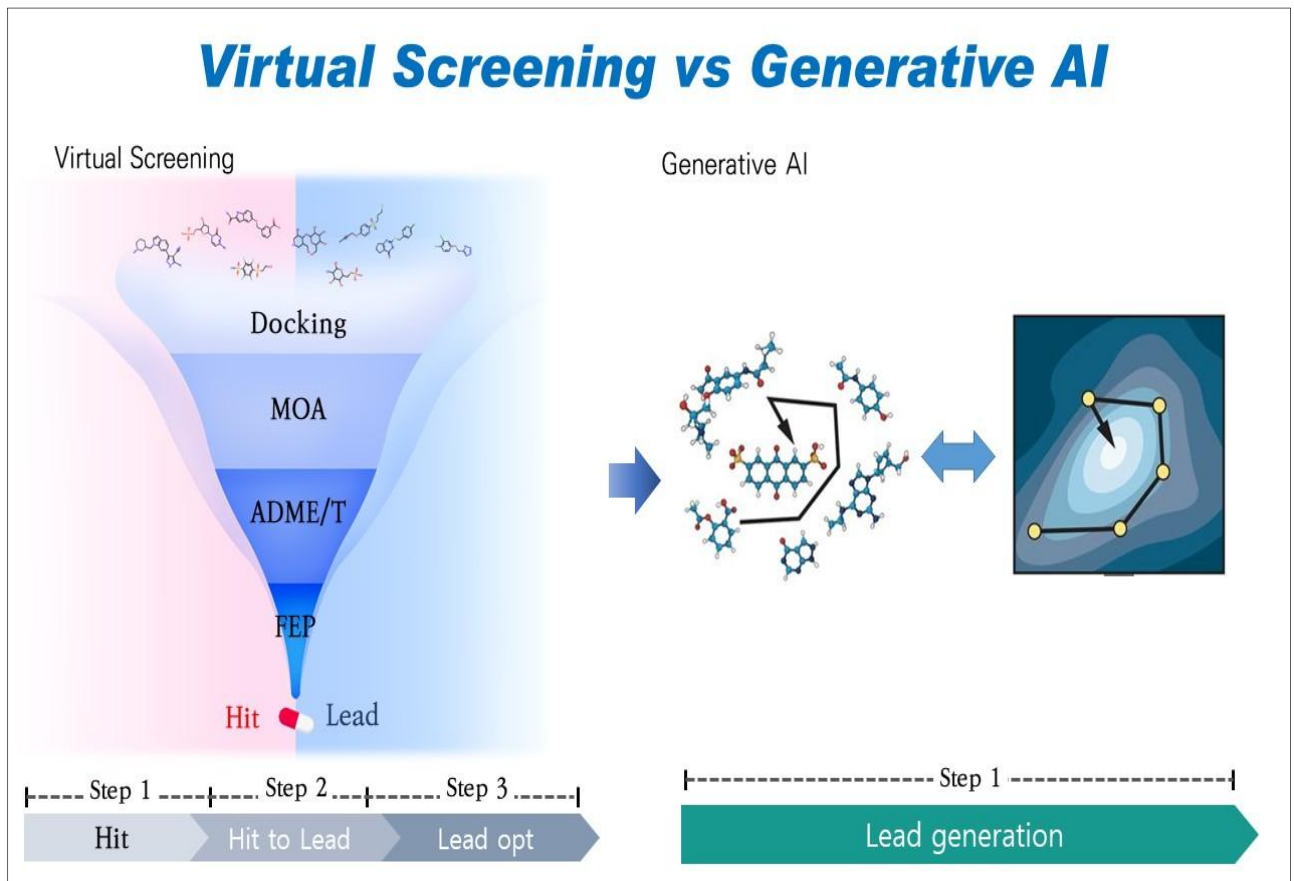
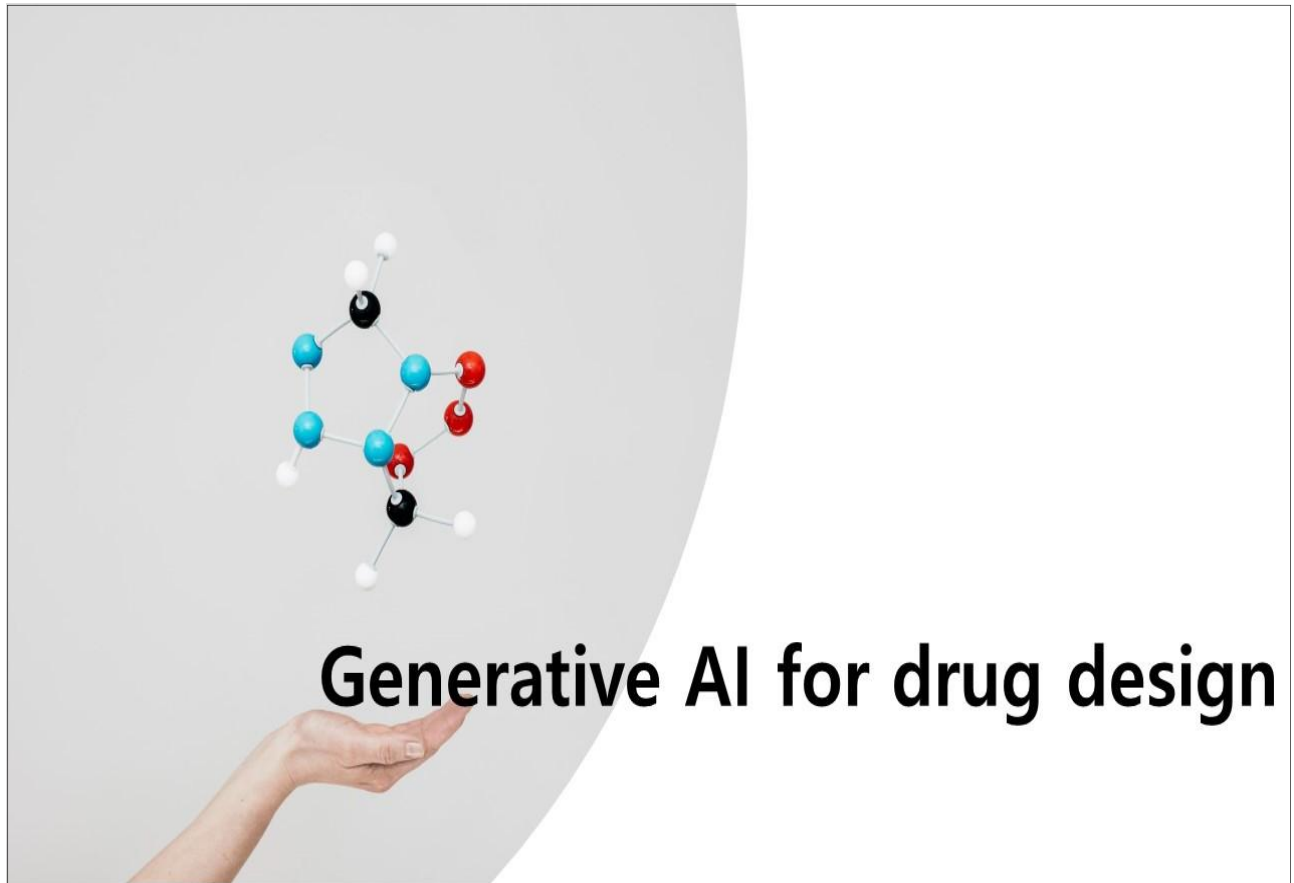
W Some people in the pharmaceutical industry are still saying that AI is premature to revolutionize drug discovery R&D. How do you expect the real impact of AI on the industry in the near future? Please answer me within three sentences.

A While some skepticism remains, AI's real impact on the pharmaceutical industry is already evident in accelerated target identification, drug candidate screening, and predictive analytics. As AI technologies continue to mature and datasets grow, they will likely enhance drug discovery by optimizing lead optimization, toxicity prediction, and clinical trial design. Over the near future, we can expect AI to further reduce costs, expedite drug development timelines, and increase the success rate of bringing innovative therapies to market, solidifying its role as a transformative force in pharmaceutical R&D.

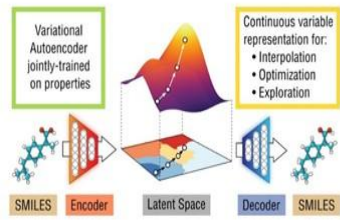
W How about generative AI for drug discovery? Also within three sentences.

A Generative AI in drug discovery can revolutionize the field by designing entirely new molecules with desired properties, streamlining the process of drug development. These AI models can propose novel chemical compounds that have the potential to become promising drugs, significantly expanding the pool of potential candidates. By harnessing generative AI, researchers can explore uncharted chemical space and accelerate the discovery of innovative therapeutics.

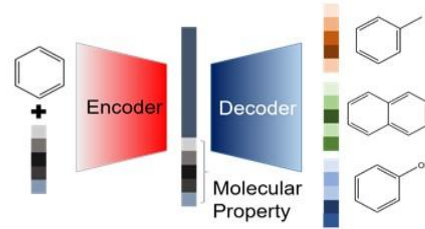
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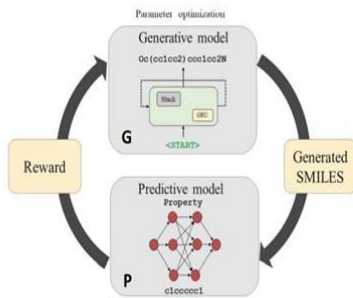
Early works in Generative AI for drug design



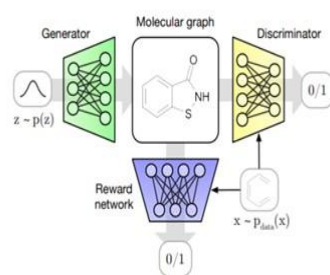
Variational autoencoder (VAE)
(ACS Cent. Sci. 2018, 4, 2, 268-276)



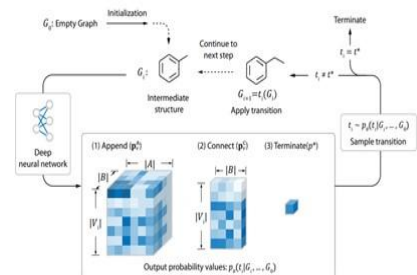
Conditional variational autoencoder (CVAE)
Lim et al., J. Cheminform. 10:31 (2018)



Reinforcement learning
(Science Advances, Vol. 4, no. 7, eaap7885)

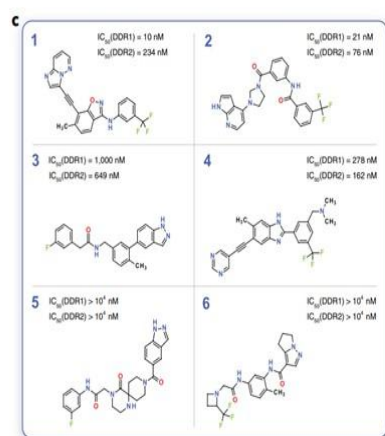
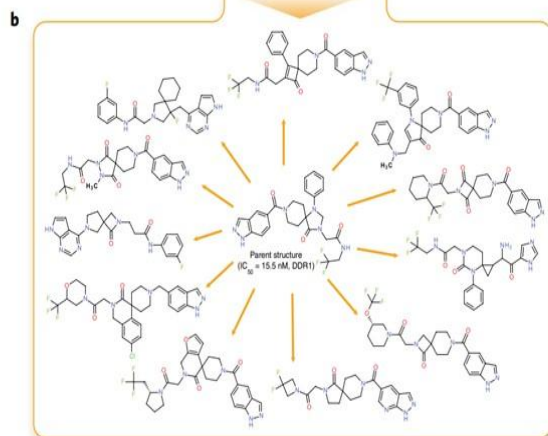
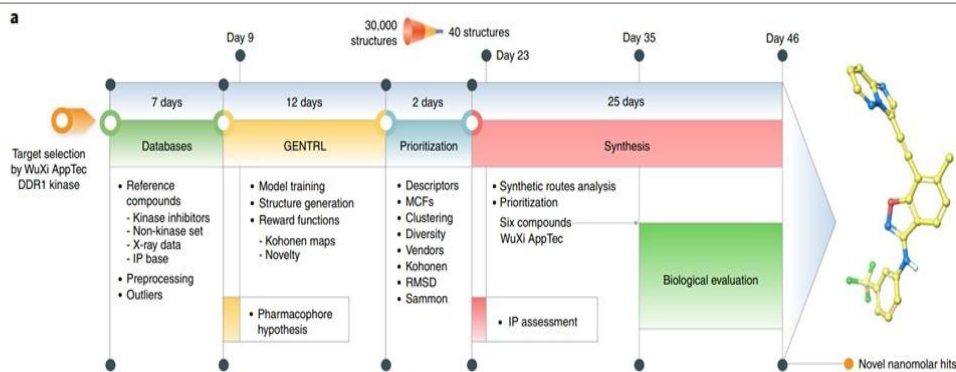


Generative adversarial network (GAN)
(Arxiv:1805.11973)



Graph generative model (GAN)
(Arxiv:1801.07299)

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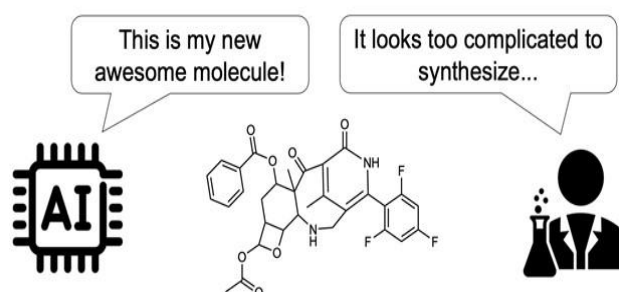
Nat. biotech. 37, 1038 (2019)

8

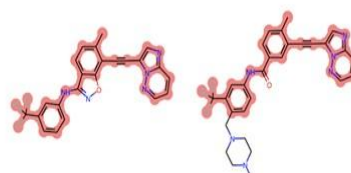
Generative AI for drug discovery

- Generative AI can efficiently explore a vast chemical space
- But conventional Gen AI has two key problems

1. Low synthesizability: atom-based or SMILES generation does not consider synthetic accessibility



2. Low novelty: overfitting to training data

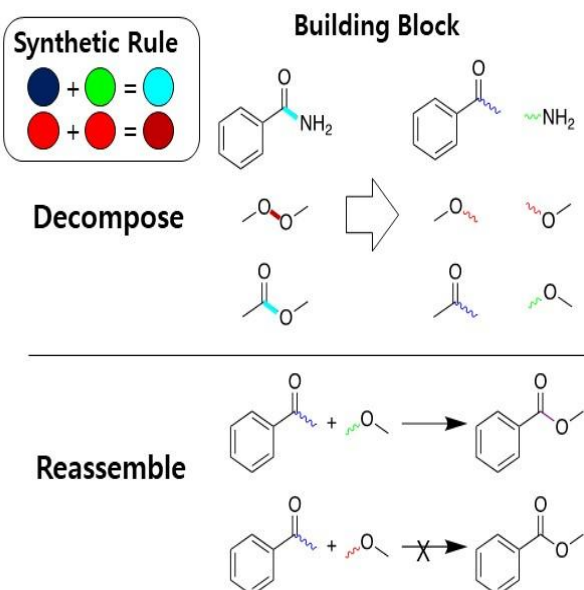


Designed by GENTRL Approved drug
Nat. biotech. 37, 1038 (2019)

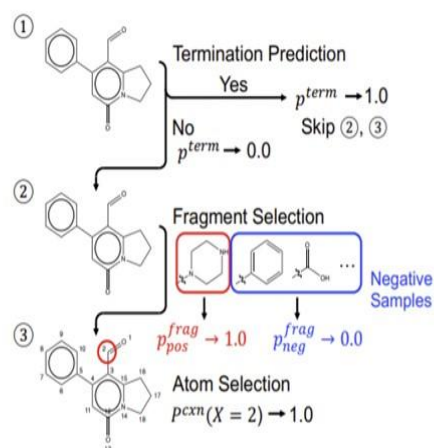
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Improving synthesizability

Breaking Retrosynthetically Interesting Chemical Substructures using BRICS decomposition

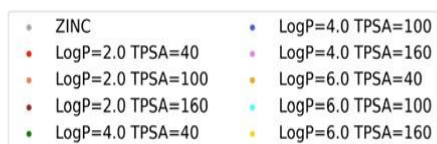
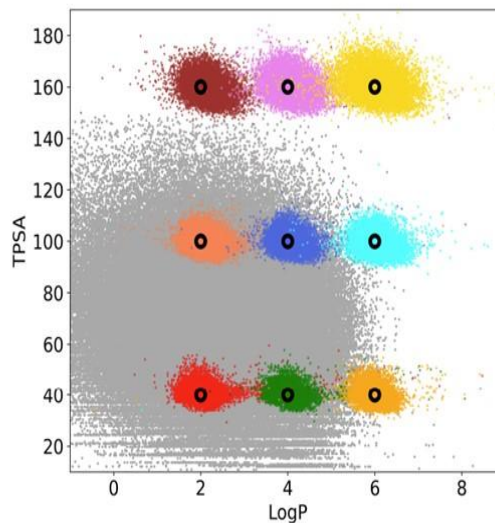
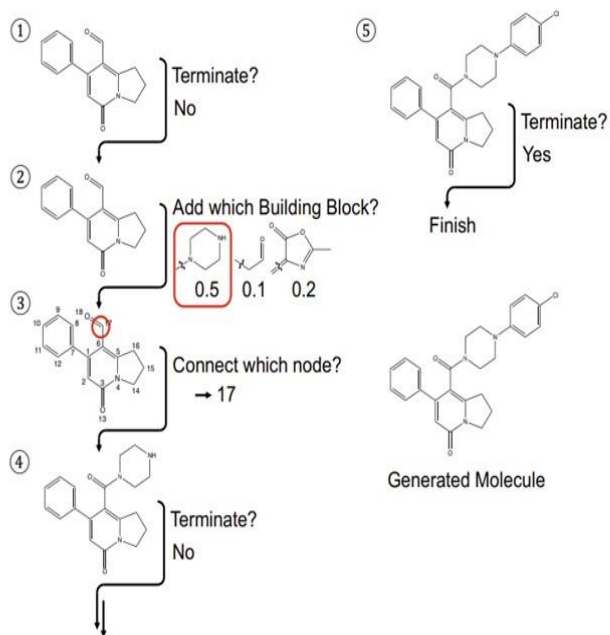


600,000 molecules chosen randomly from a chemical library, resulting in 70,000 unique building blocks.



Seo et al *Adv. Sci.* 2206674 (2023) 10

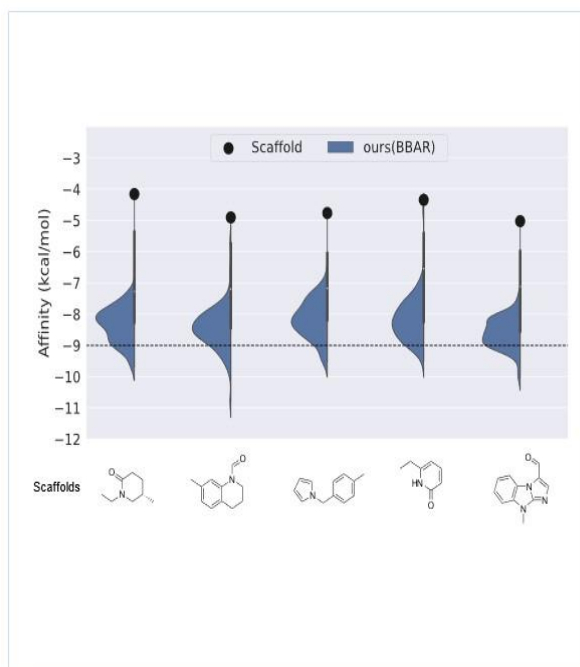
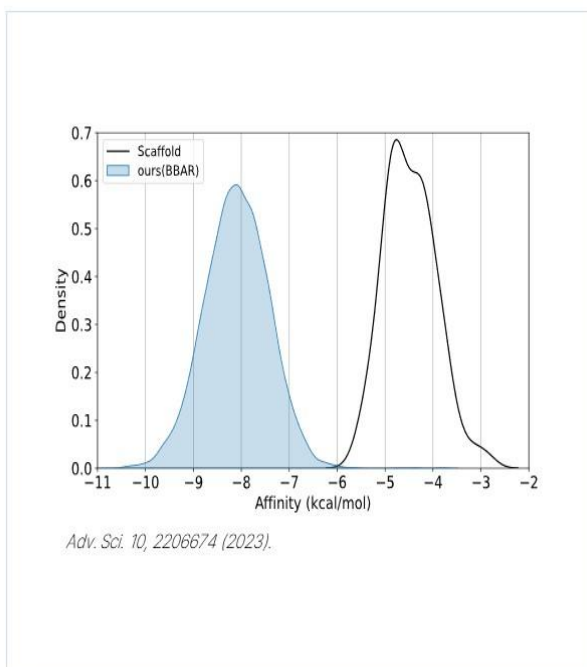
Building block-based generative AI



Seo et al Adv. Sci. 2206674 (2023)

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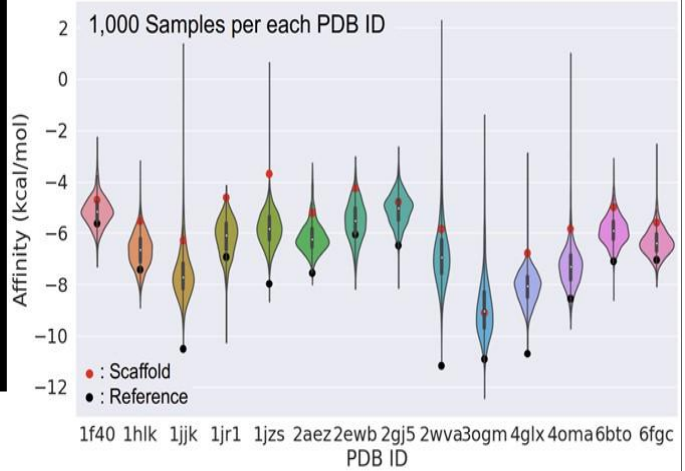
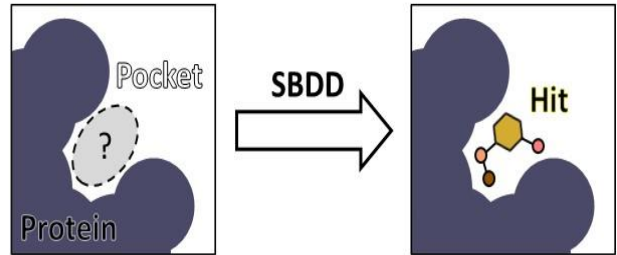
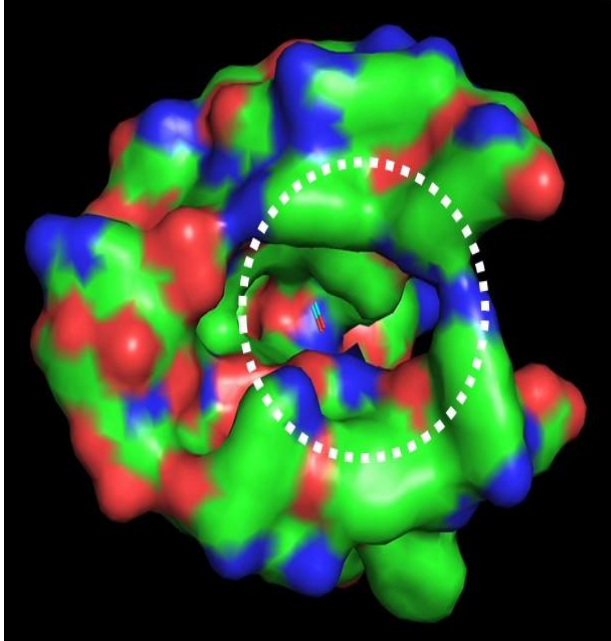
Design of inhibitors against the 3CL Protease of SARS-CoV-2



Docking score distributions of the training set (ZINC), the start core structures (scaffold), and the molecules generated by our model(BBAR)

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Improving novelty



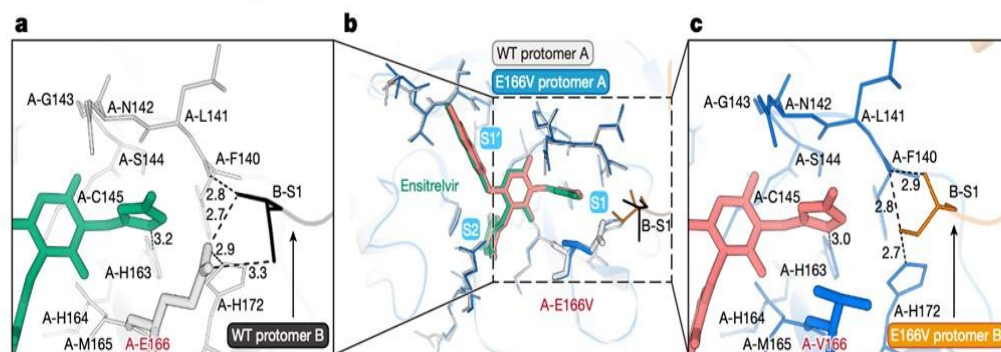
Zhung et al Nat. Comm. (2024)



**Bioisostere
replacement for
drug resistance**

Drug optimization for a mutant with resistance

Ensitrelvir shows drug resistance on the COVID-19 E166V mutant.

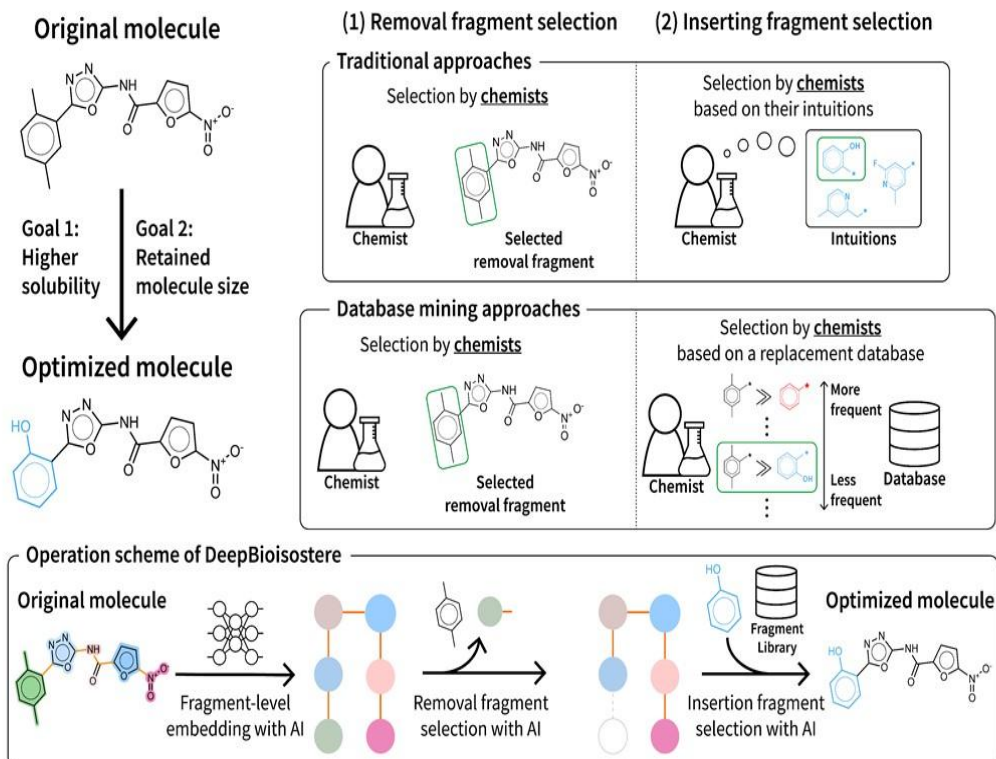


- *Ensitrelvir* is an oral SARS-CoV-2 Main protease inhibitor in a clinical study for treating COVID-19.[1]
- The molecular mechanism of resistance to *Ensitrelvir* of a mutant E166V has been reported.[2]
- Point mutation: E: Glutamic acid(with minus charge) → V: Valine(hydrophobic).
- No significant change in pocket volume

[1] Unoh, Yuto, et al. "Discovery of S-217622, a noncovalent oral SARS-CoV-2 3CL protease inhibitor clinical candidate for treating COVID-19." *Journal of medicinal chemistry* 65.9 (2022): 6499-6512.

[2] Duan, Yinkai, et al. "Molecular mechanisms of SARS-CoV-2 resistance to nirmatrelvir." *Nature* 622.7982 (2023): 376-382. 15

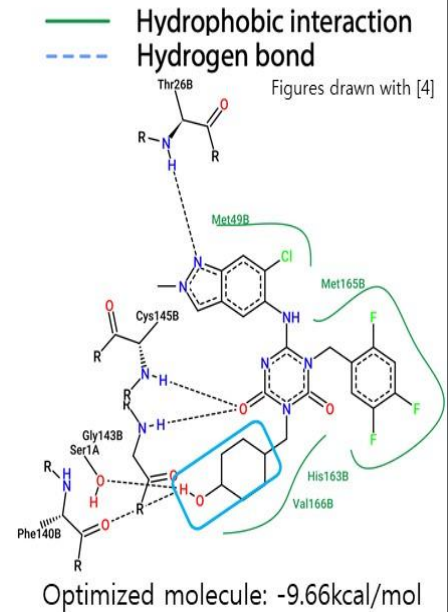
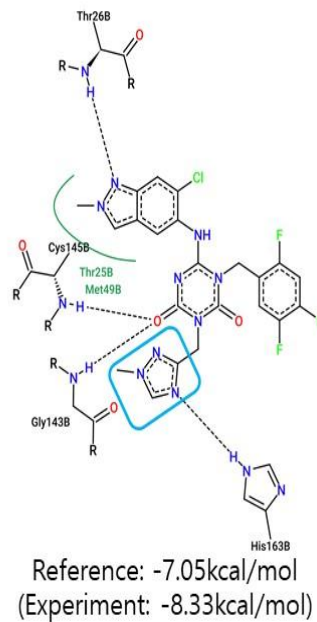
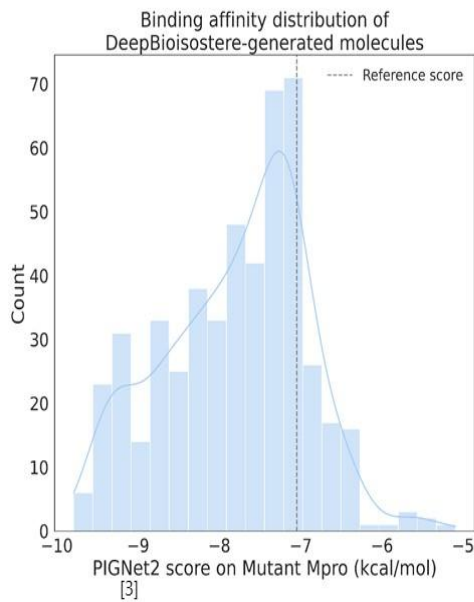
AI for Bioisostere replacement



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Drug optimization for a mutant with resistance

By optimizing *Ensitrelvir*(reference) with DeepBioisostere, 129 out of 500 molecules showed 10-fold better binding affinity in terms of inhibitory concentration on the E166V mutant.



[3] Moon, Seokhyun, et al. "PIGNet2: a versatile deep learning-based protein-ligand interaction prediction model for binding affinity scoring and virtual screening." *Digital Discovery* (2024): 1-7

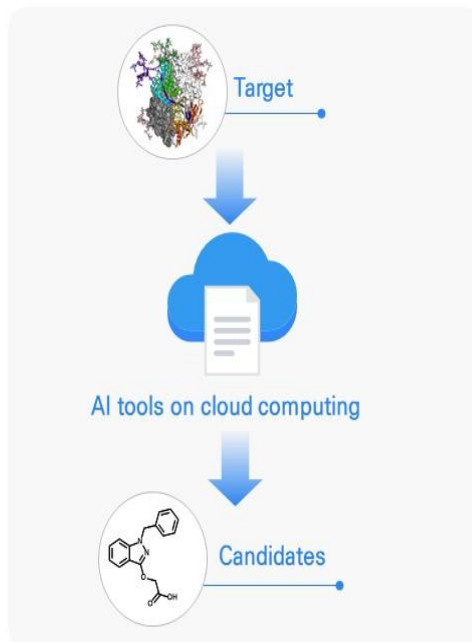
[4] Sterland, Katrin, and Matthias Rarey. "PoseView--molecular interaction patterns at a glance." *Journal of cheminformatics* 2.1 (2010): 1-11.



AI Drug Discovery
SaaS Platform

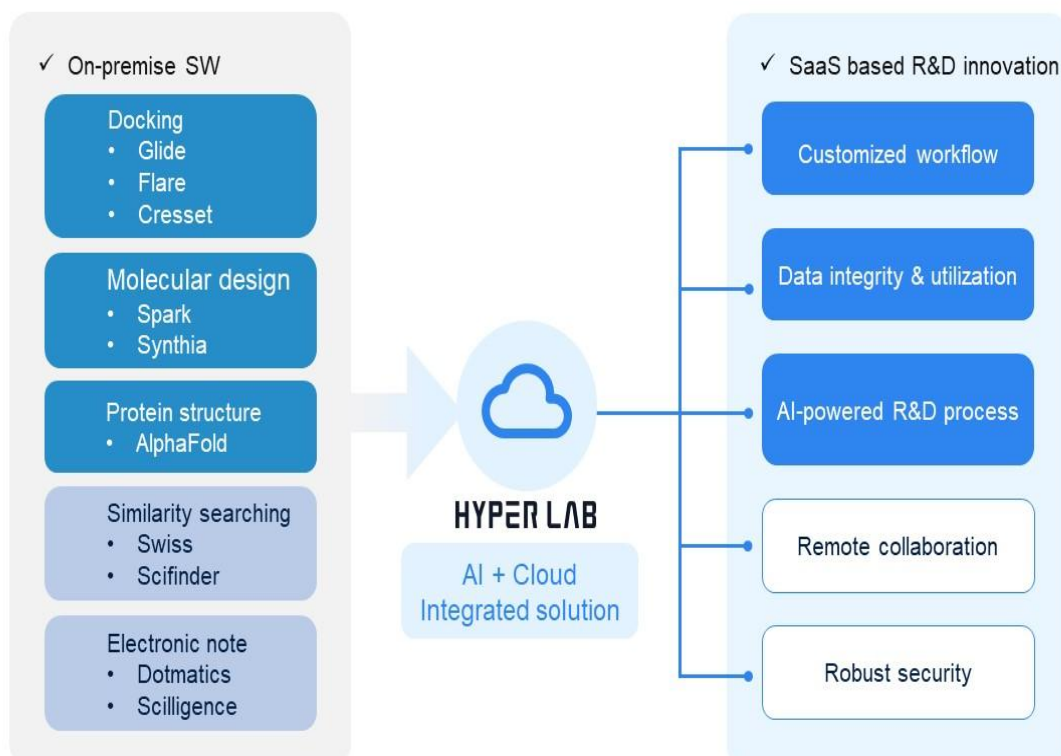
Advantages of SaaS

- **Accessibility & Collaboration:** easily accessible to researchers worldwide and democratizing advanced AI tools with remote collaboration capability for accelerated drug discovery
- **Flexibility & Customization:** offering specific needs and preferences of end users, allowing for customized workflows to support diverse projects
- **Integrity & Security:** leveraging robust integrity & security to protect sensitive research data from various projects
- **Cost-Effective & Scalability:** cost-effective alternative to on-premise infrastructure by eliminating the need for significant upfront investments in hardware and individual software tools and offering scalable computing power on demand



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Hyper Lab as AI SaaS platform



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Acknowledgements



4 weeks free trial

- NRF-Korea
- Samsung
- Hanwha
- MFDS
- <https://wooyoun.kaist.ac.kr/>
- <https://hits.ai/>
- <https://hyperlab.ai/>

세션 3.

신종감염병 백신개발 우수성과

Chair



Baik-Lin Seong

- ✓ Yonsei University College of Medicine
- ✓ Distinguished Professor & Director General, Vaccine Innovative Technology Alliance (VITAL)-Korea

Q EDUCATION:

- 1988 Massachusetts Institute of Technology, PhD
- 1979 Korea Advanced Institute of Science and Technology, MS
- 1977 Seoul National University, BS

Q PROFESSIONAL EXPERIENCE:

- 2022 ~ Present Chair, Division of Biotechnology, Science & Technology Advisory Board, MoFA, Korean Government
- 2020 ~ Present Distinguished Professor, Yonsei University College of Medicine
- 2020 ~ Present Director General, Vaccine Innovative Technology Alliance (VITAL)-Korea
- 2020 ~ 2022 Chair, COVID-19 Vaccine Pan-Government Strategic Plan, Korean Government
- 2020 ~ 2021 Member, Presidential Advisory Council on Science & Technology, Korean Government
- 2000 ~ 2009 CEO, Protheon
- 1998 ~ 2020 Professor, Department of Biotechnology, Yonsei University
- 1993 ~ 1998 Director, Institute of Biological Sciences, Hanhyo Institute of Technology
- 1992 ~ 1993 Scientist, Aviron, USA
- 1988 ~ 1992 Postdoctoral Scientist, University of Oxford, UK

01

COVID-19 백신 연구개발 및 성과

변재철 교수
연세대학교



Speaker



Jae-Chul Pyun

- ✔ Yonsei University
- ✔ Professor

🔍 EDUCATION:

- 2001 Saarland University (Dr.rer.nat)
- 1994 Dept. Chemistry, Seoul National Univeristy (M.S)
- 1992 Dept. Chemistry, Seoul National Univeristy (B.S)

🔍 PROFESSIONAL EXPERIENCE:

- 2007 ~ present Professor, Yonsei University
- 1999 ~ 2007 Team leader, KIST Europe GmbH
- 1996 ~ 1999 Investigator, Fraunhofer Institute for Biomedical Engineering
- 2018 ~ present Editor-in-Chief, BioChip Journal
- 2019 ~ present Editor-in-Chief, Journal of the Korean Ceramic Society

Q Topic

Rapid screening of target antigenic sites for SARS-CoV-2 vaccine development using Fv-antibody library

Q Abstract

The rapid screening of target antigenic sites for SARS-CoV-2 is presented and the application of screened antigenic sites is demonstrated for the vaccine development against SARS-CoV-2. The Fv-antibody represented the antigen binding site of immunoglobulin G (IgG) and the Fv-antibody library was prepared by randomizing the CDR3 through the site-directed mutagenesis. So prepared Fv-antibody library was surface-expressed on the outer membrane of E.coli with the diversity of more than 10⁶ clones/library. From the Fv-antibody library screening, effective immunogenic antigen sequences for the vaccine development could be analyzed within a few weeks. The vaccine development based on the Fv-antibody library was carried out according to the following procedure: (1) Screening of Fv-antibodies against spike protein of SARS-CoV-2 with a high binding affinity (nanomolar KD), (2) Analysis of amino acid sequence of antigenic sites (epitopes) of the screened Fv-antibodies using computer simulation, (3) Vaccine development using protein particles (ferritin) with co-expressed epitopes, (4) Analysis of neutralization efficiency of anti-sera against SARS-CoV-2 infection.

Development of SARS-CoV-2 vaccine using Fv-antibody library

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보건복지부
Ministry of Health and Welfare

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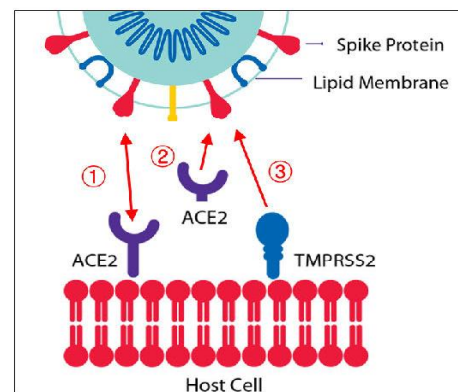
Problems of vaccines against virus

■ Prevention of viral infection

- ① **Antibodies to prevent from binding of virus to host**
- ② Expressed receptor (fragments) of host cells
- ③ Inhibition of protease (host cells) for viral infection

■ Problems

- Mutations on viral proteins binding to host receptors
- Difficulties to find immunogenic sequence for vaccines
- Stability of vaccines (including mRNA vaccines)



■ Platforms for vaccine development:

- (1) **Fv-antibody library** ⇒ Platform to search immunogenic sequences for vaccines (< 2-3 weeks)
- (2) **Ferritin complex** ⇒ Platform of (protein particle) vaccines with high neutralizing efficiency

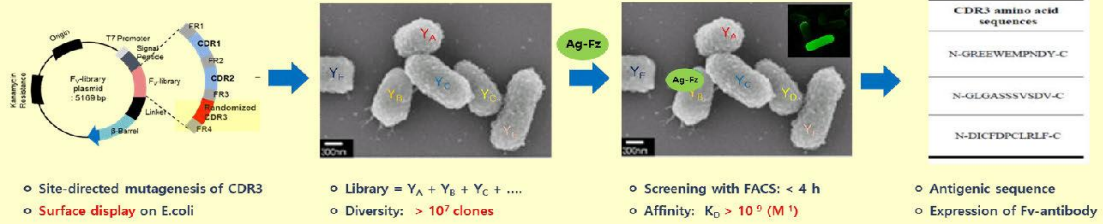
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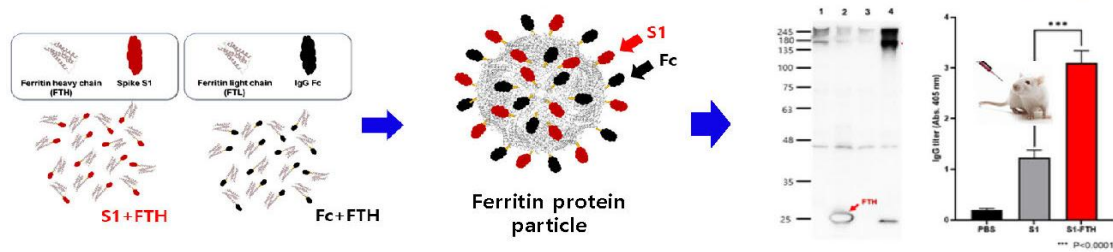
Platforms for vaccine development



(1) Fv-antibody library: searching platform of immunogenic sequences



(2) Ferritin protein particle: efficient vaccine platform



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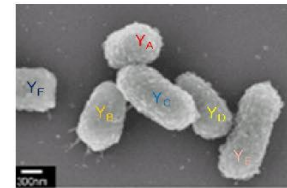
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Fv-antibody library

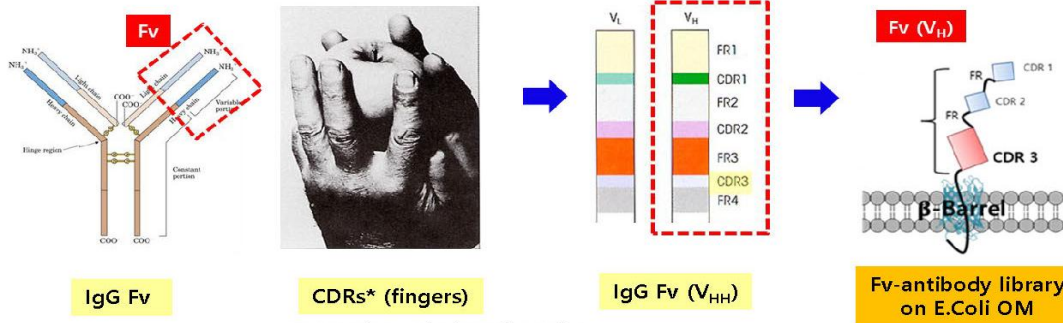


■ Fv-antibody library

- **Fv-antibody**: antigen binding site of IgG (3 CDR's + 4 FR's)
 - **Fv-antibody library**: randomizing amino acid sequences of CDR3
 - **Surface display**: expression of Fv-antibodies on the outer membrane (OM) of E.coli with high surface density
 - **Surface density**: $> 10^5$ (Fv/E.coli cell), **Expression yield**: $> 95\%$
- (비교) Bacteriophage: Surface density > 10 (Fv/phage), yield $< 10\%$



- 항체라이브러리 = $Y_A + Y_B + Y_C + \dots$
- 최종 항체다양성: $> 10^7$ clones



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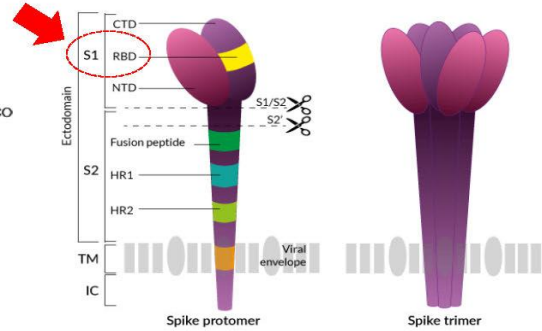
Screening of anti-RBD(SARS-CoV-2)-Fv



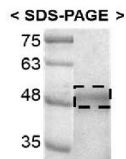
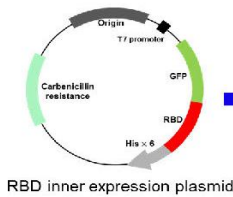
■ Spike protein RBD (SARS-CoV-2)



- RBD (319-541 a.a.): ACE2 receptor binding domain
- SP (1,273 mer): RBD (222 mer, 24.9 kDa)
- Fluorescence label: sfGFP



■ RBD (SARS-CoV-2) antigen (searching probe)



RBD of spike protein (319-541)

```

1 MFVFLVLLPL VEGCVNLTIT RTQLPRAYTH SFRGQVYVFD KVRSSVLHG TQDLFLPFFS NVTFHAIHV SGTNGTKRFD NPVLPFNDGV YFASGTEKSHI
101 IRGWIGFTIL DSKTGSLIV NNAWVWIKV CEFDQNDPF LGVYYHKNK SWMESEFRVY SSAANTCFEY VSGPFLNDLE GKGQNFPMKR EYFKNDQGY
201 FKYBKHTPI NLRDLPGGF SALEPLVLP IGNIITRFQT LLALHRSYLT PGDSSGOWTA GAAYTVGYL QPRTFLKYN ENGTITDAVD CALDPLSETK
301 CTXKSTVEK GIYQTSNFRV QRTESIVRFP NITNLCPFGE VFNATRFASV YAWNRKRISN CVADYSVLVN SASFSTKCY GVSPTKLADL CFTNVVYDSF
401 VIRGDEVRFQI APGQTGKIAD VNYKLPDDPT GCVIAWNSNI LDSKVGQNYN YLYSLFRKSN LKPFERDIST EYQAGSTPC NGVEGFNCFY PLGSEYGFQPT
501 NGVYGPYRV VVLSPELLHA PATVCSPPKIS TNLVANKQVN ENFNLTGTG VLTESEKFLF PFGQGRDIA DTTDAVRDPG TLEILDTPC SFGQSVVTP
601 GTNTGQNAV LYGDVNGTEV PVAINADQLT PTWRVYVSTG NVFSTRAGOL ICAEHNNSY EDDIPQAGI CABYQQTAS PRARQVBSQ GIAYTMSLG
701 AENSVAYSNN SIAIPTNFTI SVTTELPVS MTKTSVQDTM YICGCESTEC NLLQYGSFC TQLNRALTIQ AVEQDKTQE VFAQVQVQK TPKKDFGGF
801 NPSQLPDS KPKRSFIED LFNKVTLD AGFKIDYGDG LGDIAARDLI CADKFNGLTV LPPLLDEMI ADYTSALLAG TITSGWTFGA GAALQPFAM
901 QMAYRFNDS VYQNVLYNG KLIANQFNSA IGIKQDLSG TABALQKLD VVQVQADLV TLVQLQSNV GAISVLNDI LSRLDKVAE VOIDRLTGR
101 LOGLQTVTC QURAEIRA SANLAATKMS ECVLGGKRV DFCGKIYLM SFGQAPGVV VFLNVTYVA QEKNIPTA ICHGQAMP REGVPSNGT
1101 HWFVTVRNFY EPDITDNT PVSGNCDVH GIWNTVYDP LGPELDSPKE ELDKYFNHT SPDVLDGDS GINASVNGV KEIDRLNEVA KNLNERIDL
1201 QELGKYEQYI KWPVYVWLFIAGLAVMVTMLCCMTSC CSGLKGCSCGSCCKFDEDD SEVPLKQVLYHT
    
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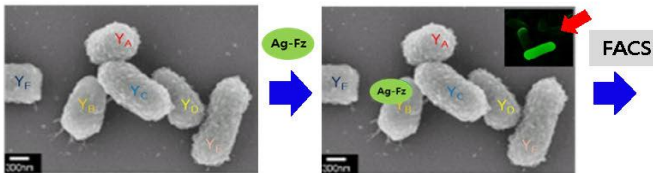
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Screening of anti-RBD(SARS-CoV-2)-Fv

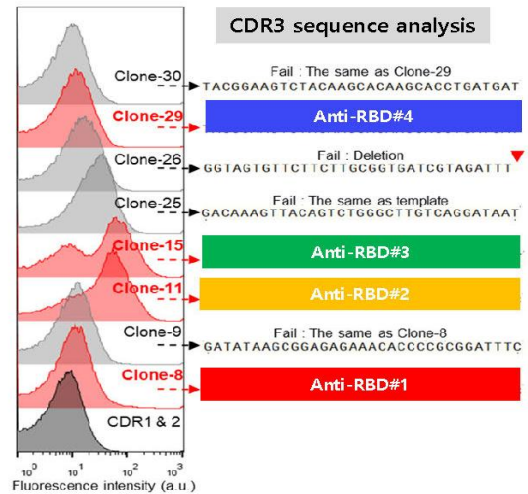


■ Screening with RBD probe (GFP labeled)



- Library = Y_A + Y_B + Y_C +
- Diversity: > 10⁷ clones
- Screening with FACS: < 4 h
- Affinity: K_D > 10⁻⁹ (M⁻¹)

Anti-RBD (Clone#)	Oligonucleotide sequence (33 nucleotides)	CDR3 amino acid sequence (11 aa)
1 (8)	3'-GCT CGT GXX AXX AXX GXX GXX AXX CXX CXX GXX GXX TXX TGG GGT-5'	1DXXXX 6KXXXX 11F
2 (11)	3'-GCT CGT GXX GXX AXX CXX AXX GXX CXX AXX AXX GXX TXX TGG GGT-5'	1DXXXX 6GXXXX 11F
3 (15)	3'-GCT CGT GXX CXX CXX AXX GXX AXX AXX GXX AXX GXX TXX TGG GGT-5'	1DXXXX 6TXXXX 11F
4 (29)	3'-GCT CGT TXX GXX AXX CXX CXX GXX CXX GXX CXX GXX TXX TGG GGT-5'	1YXXXX 6AXXXX 11D

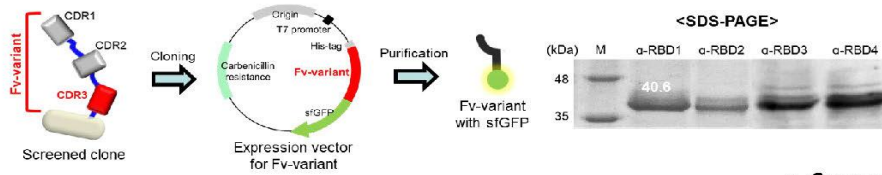


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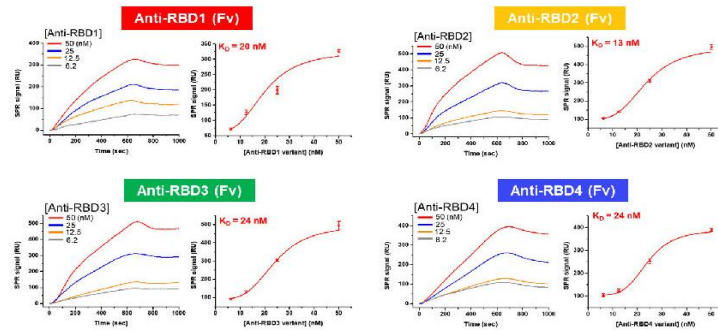
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Binding affinity of anti-RBD(SARS-CoV-2)-Fv

■ Expression of Fv-antibody (soluble)



■ Estimation of binding affinity (SPR biosensor, K_D)



< Comparison of binding affinity >

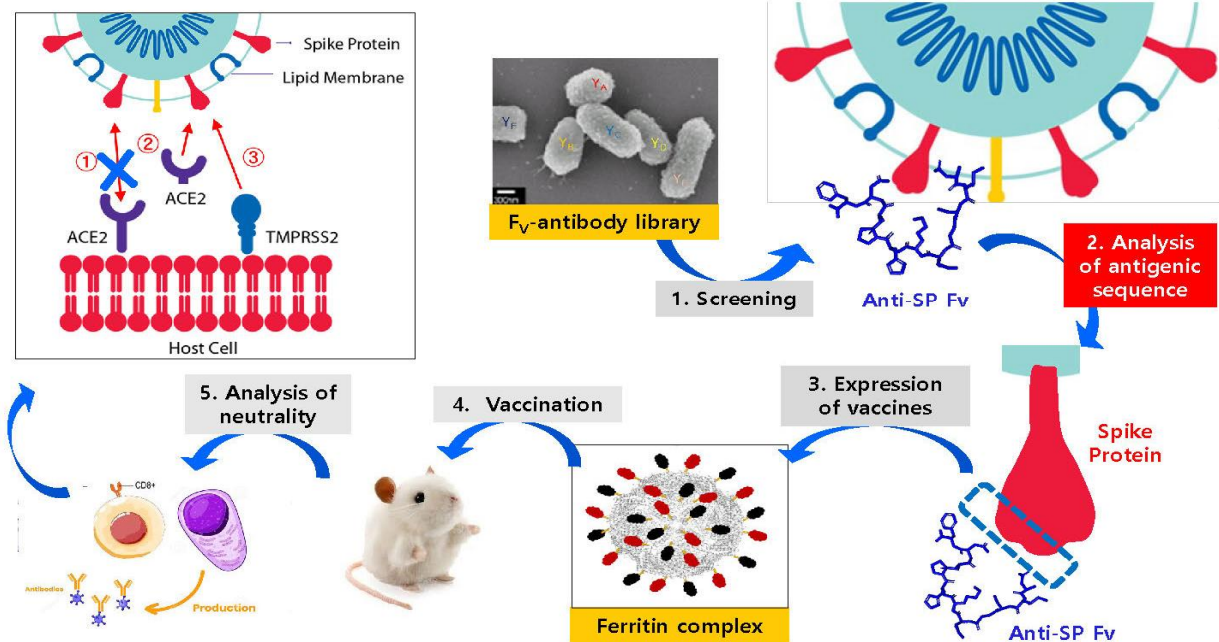
α -RBD#	LOD (nM)	K_D (nM)
SP (SARS-CoV-1) to ACE2 receptor		31 – 100*
SP (SARS-CoV-2) to ACE2 receptor		4.7 – 10*
α -RBD#1	7.7	20
α -RBD#2	7.7	13
α -RBD#3	8.7	24
α -RBD#4	13.73	24

* Nature, 581 (2020) 215–220

IDIRC (2024.03.08)

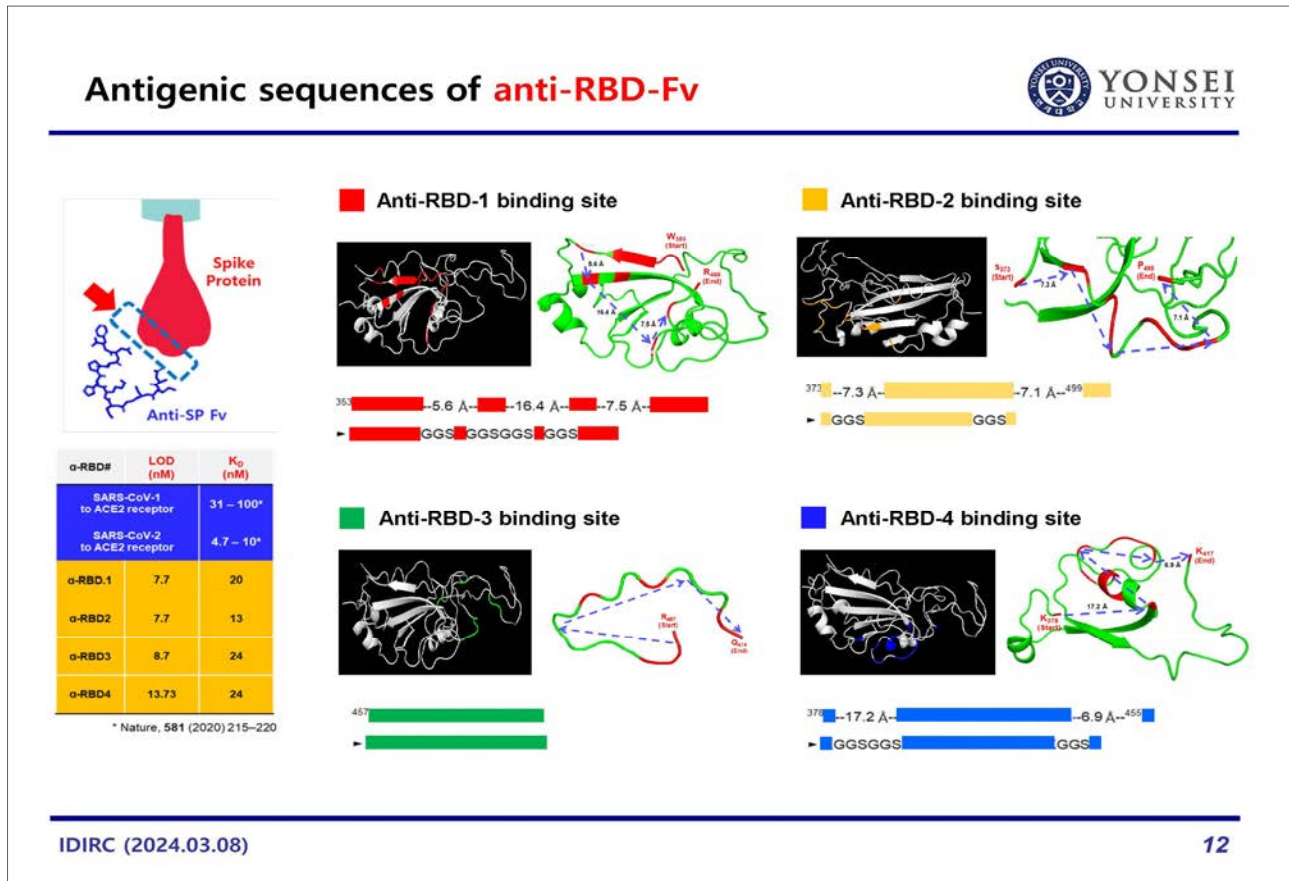
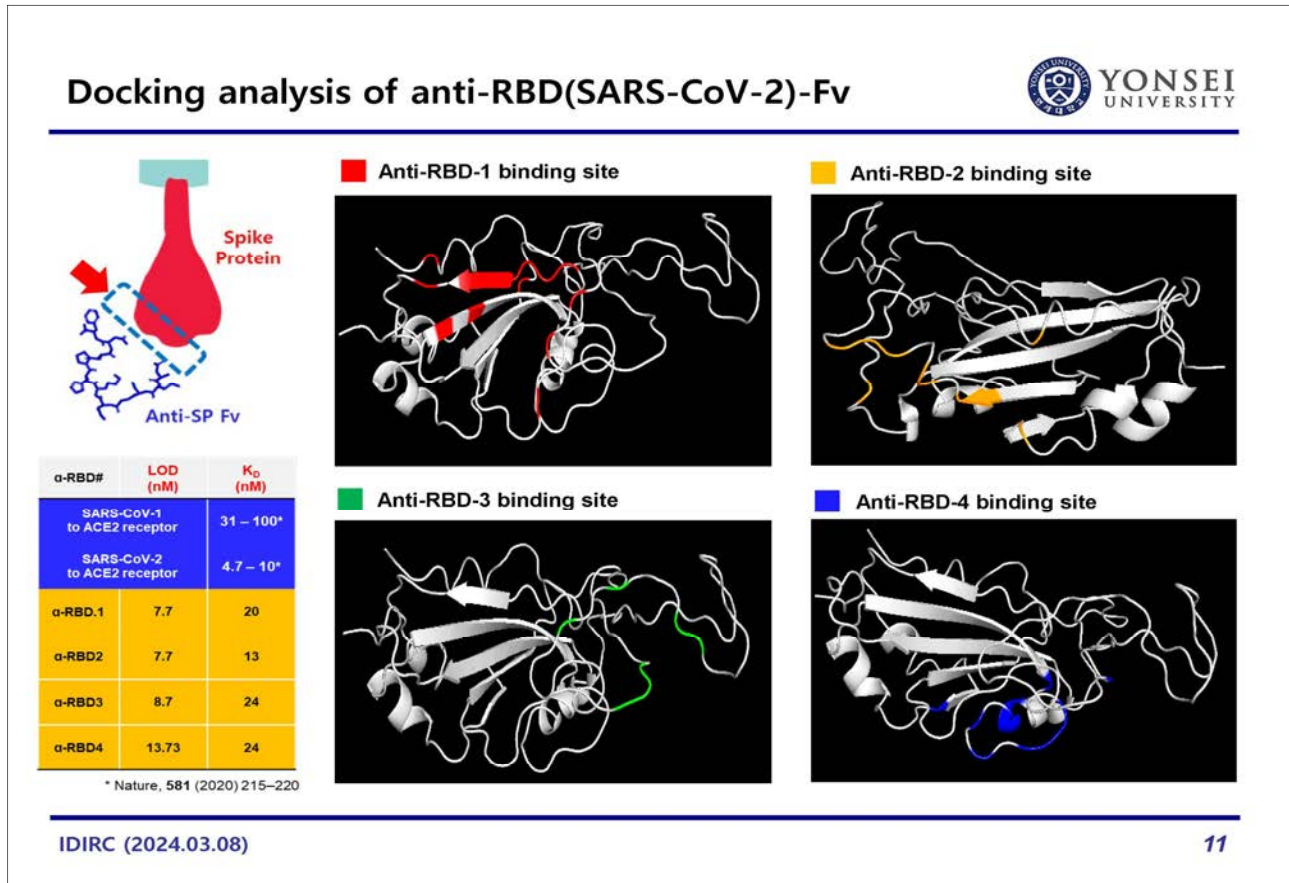
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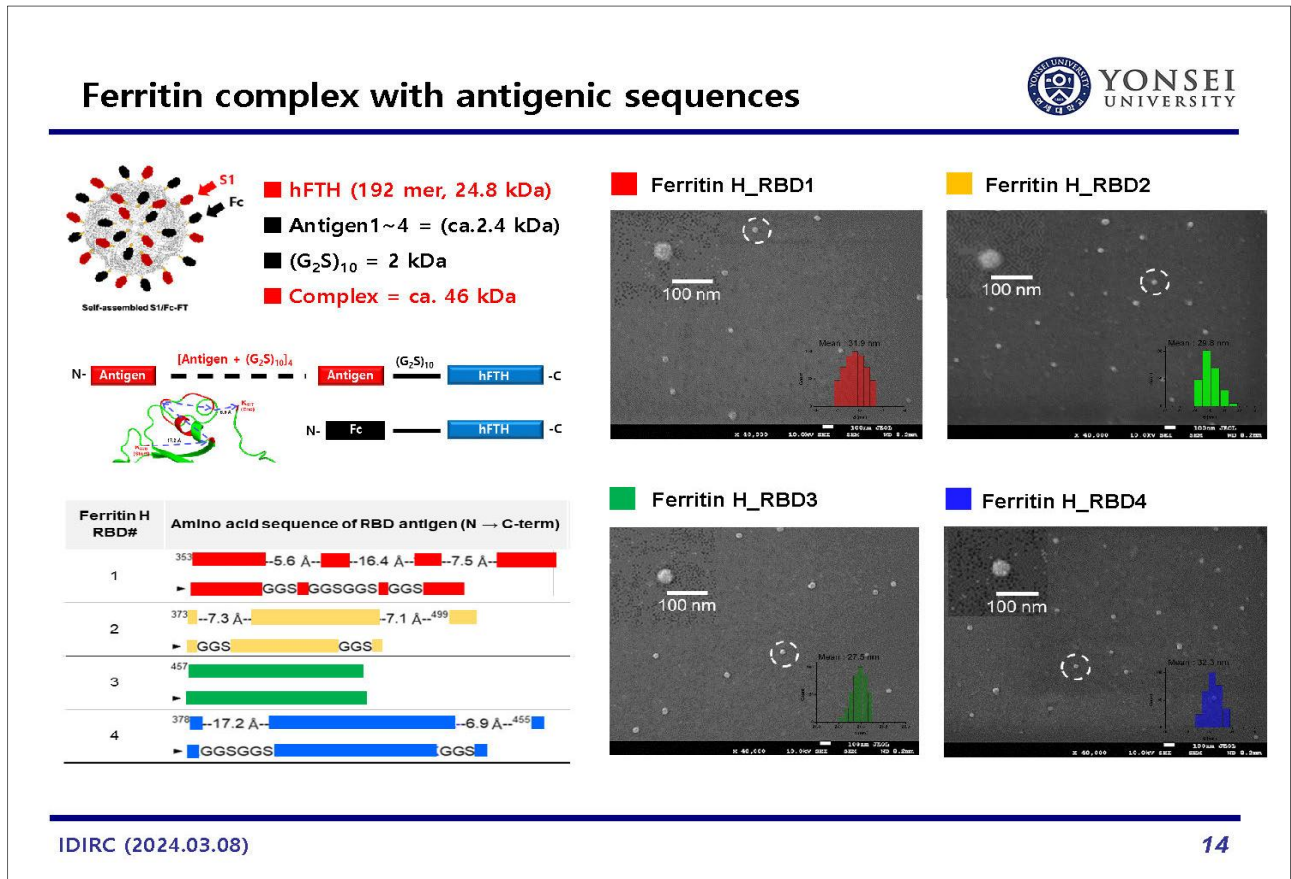
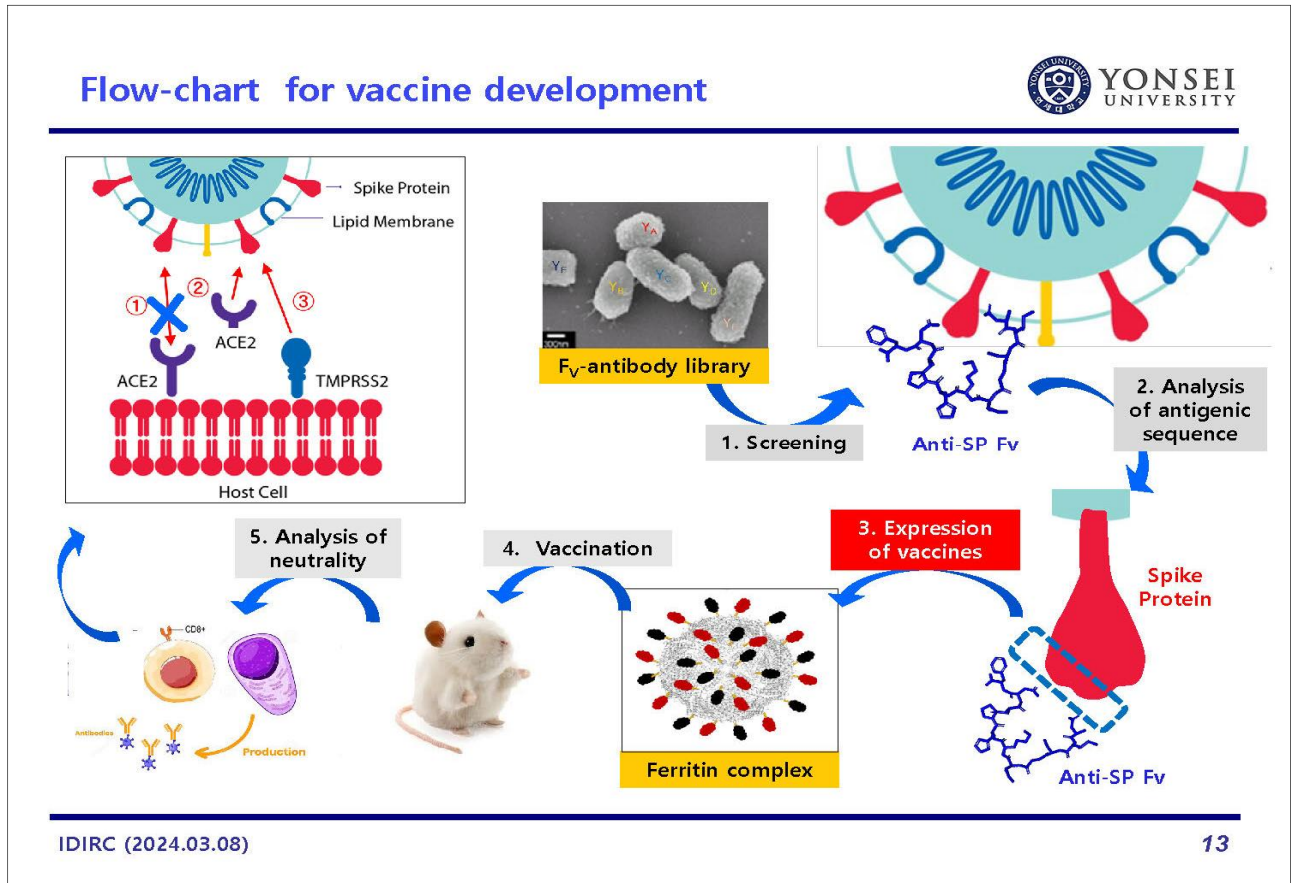
Flow-chart for vaccine development

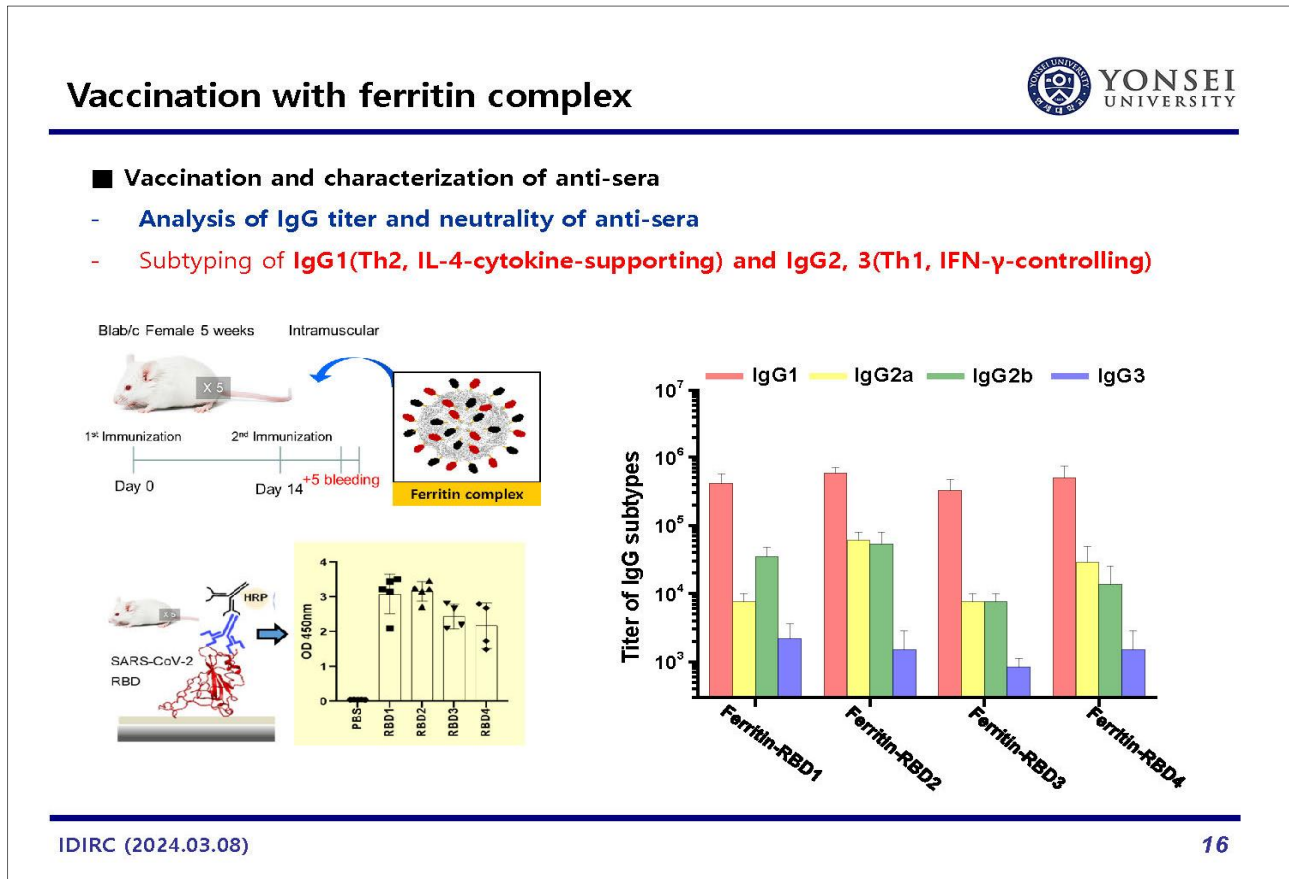
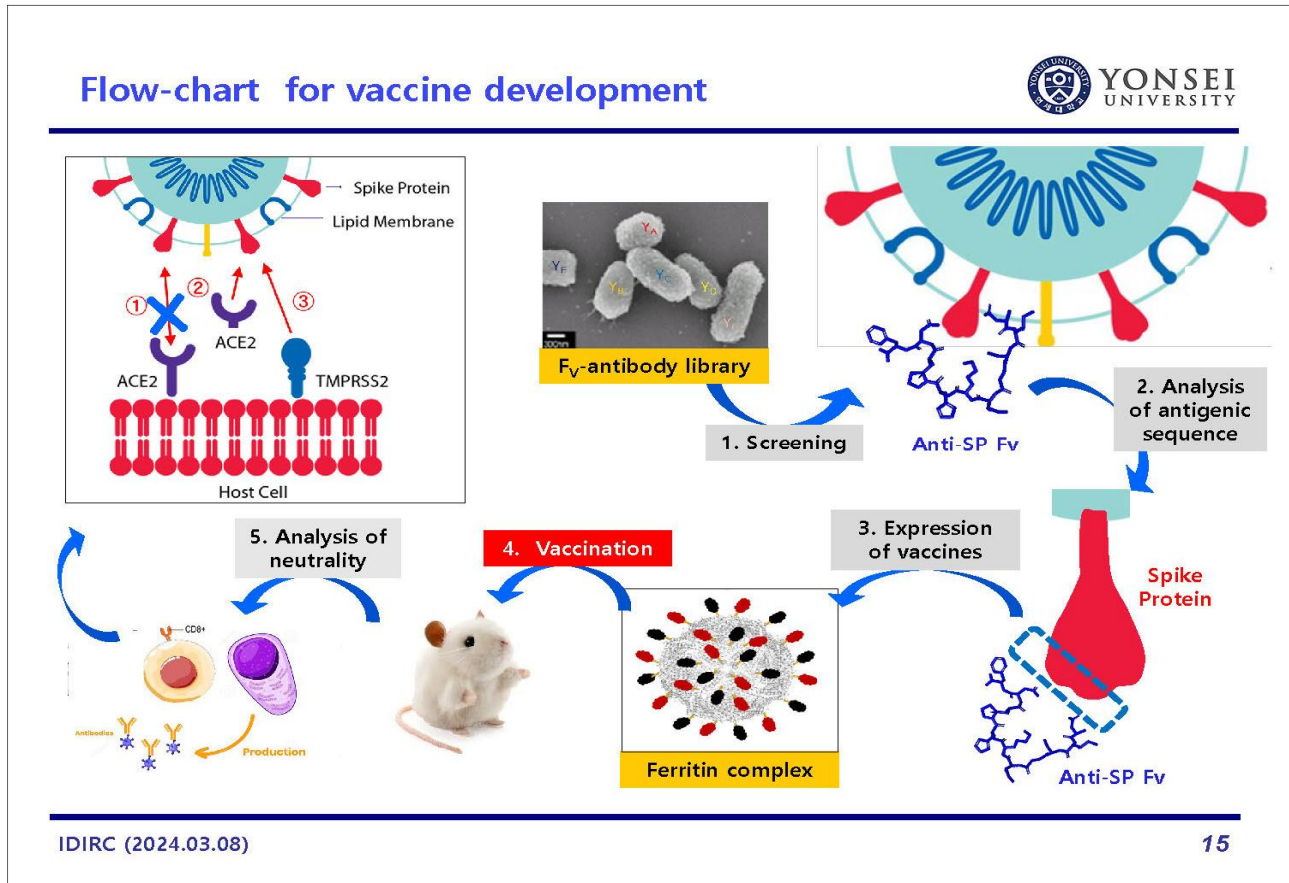


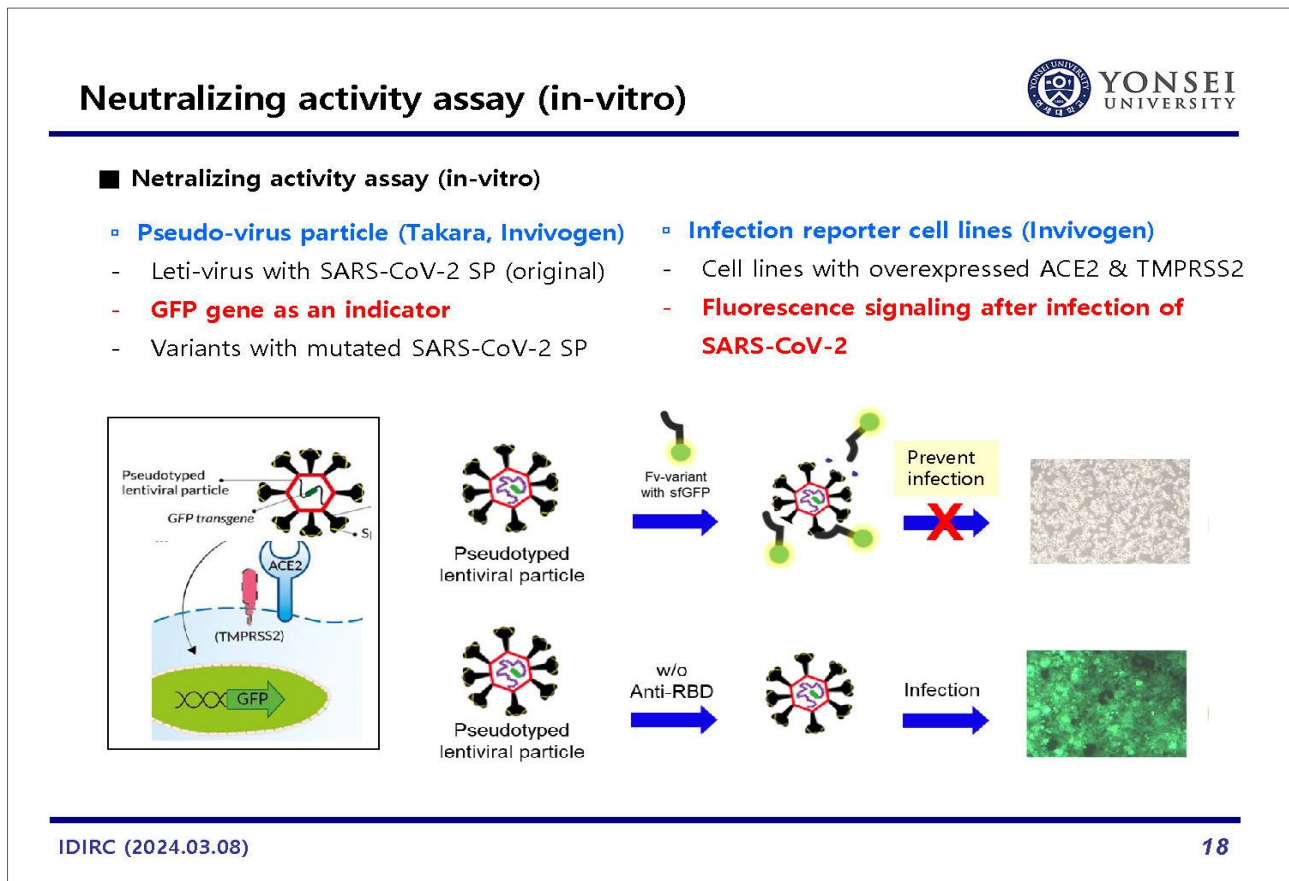
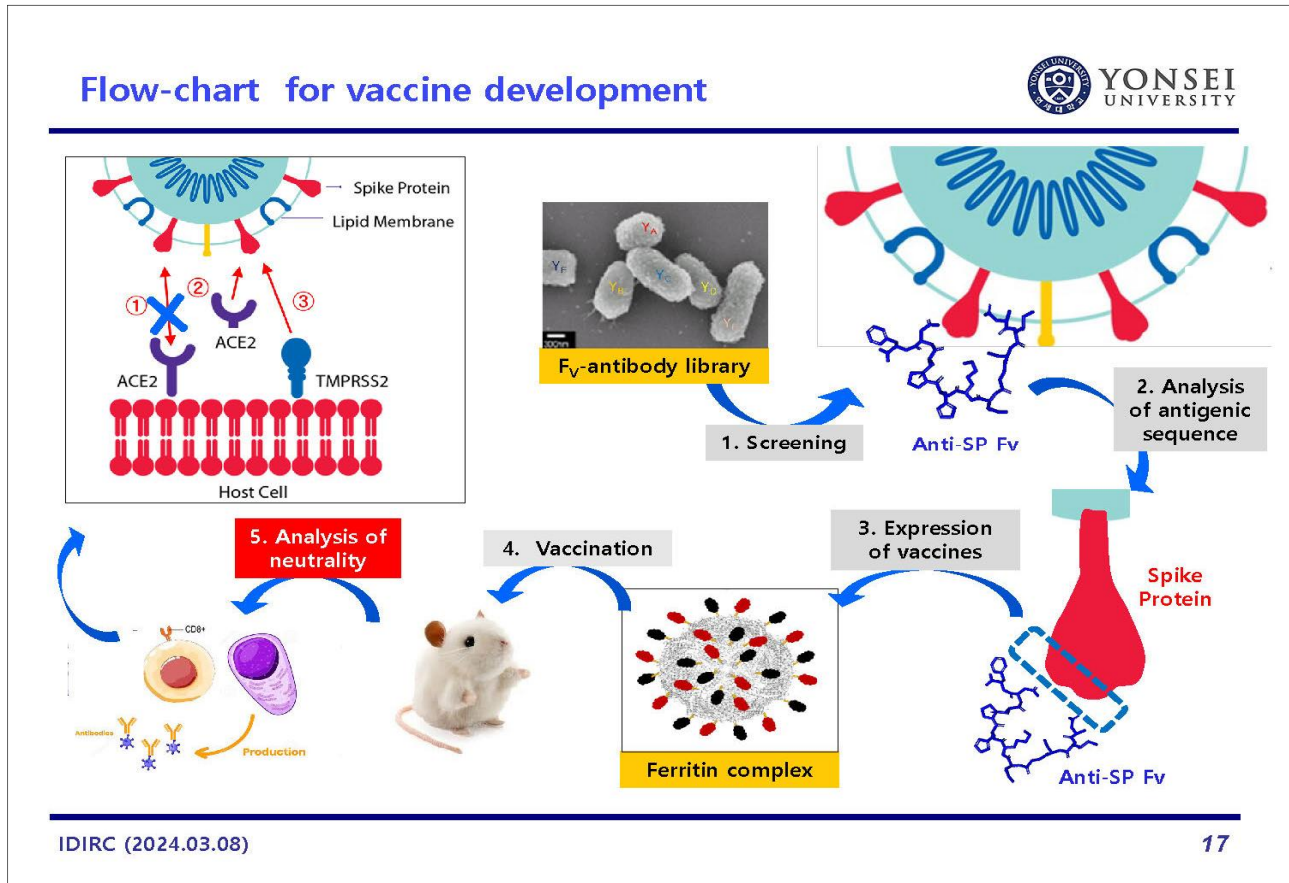
IDIRC (2024.03.08)

10

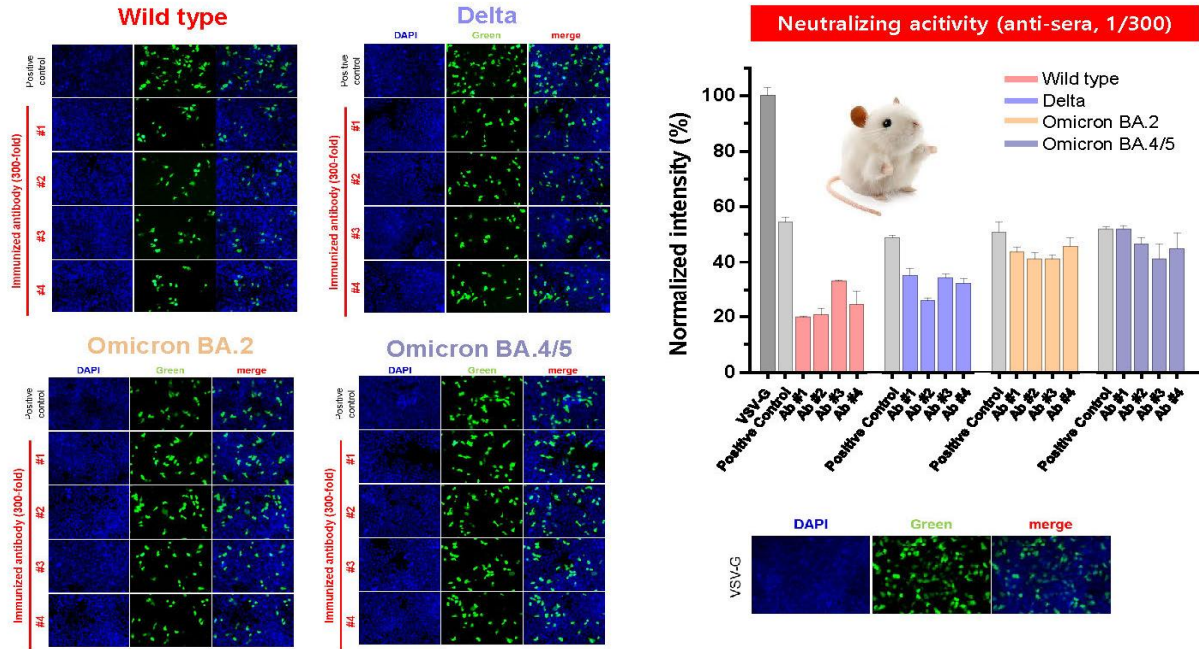








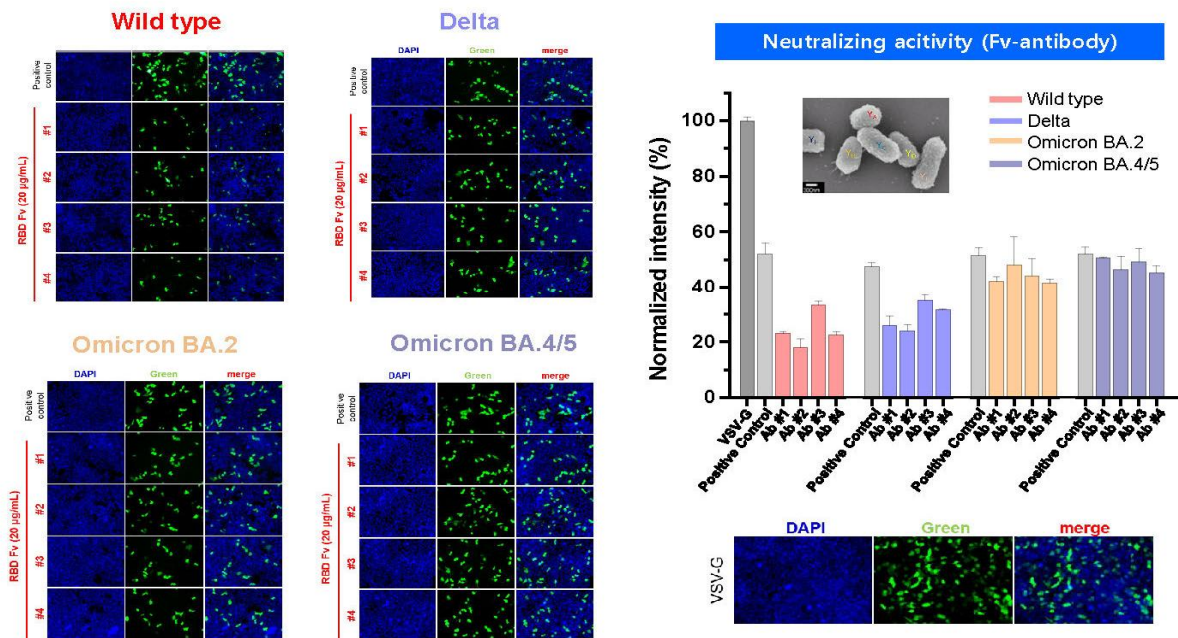
Neutralizing activity (anti-sera to variants)



IDIRC (2024.03.08)

19

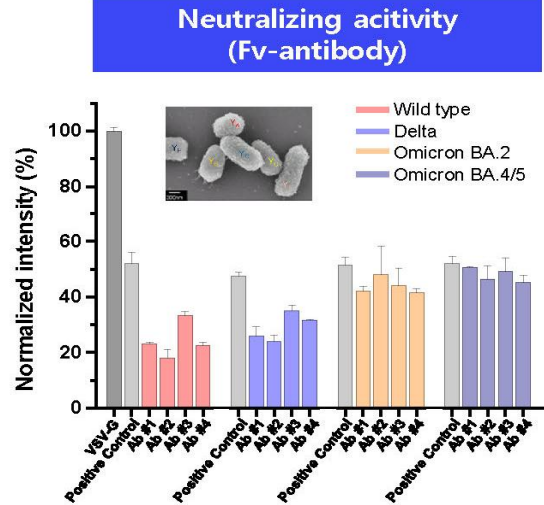
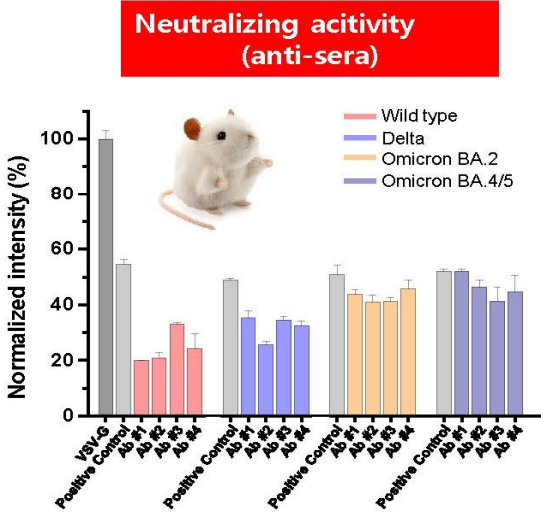
Neutralizing activity (Fv-antibodies to variants)



IDIRC (2024.03.08)

20

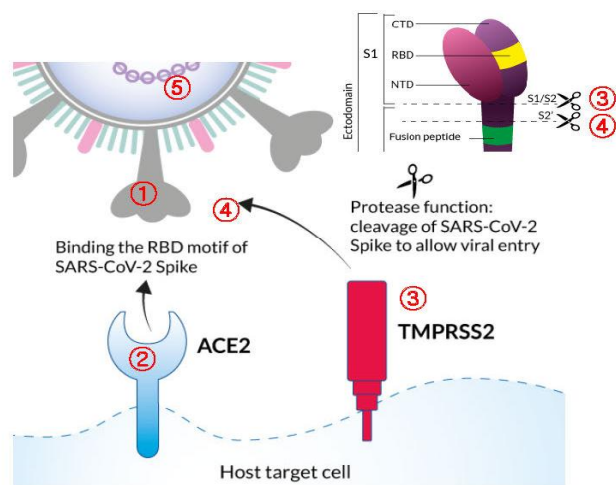
Comparison with neutralizing activity (Anti-sera vs. Fv-antibodies)



Screening of Fv-antibodies against SARS-CoV-2



1. Anti-RBD(SP)-Fv
2. Anti-ACE2-Fv
3. Anti-TMPRSS2 Fv
(to inhibit protease activity)
4. Anti-PPC site-Fv
5. Anti-NP-Fv
6. RNase Inhibitors
(to stabilize mRNA vaccines)



Acknowledgement

This work was supported by **Global Vaccine Leading Technology Center Program** through the Korea Health Industry Development Institute (KHIDI) and by **Basic Science Research Program** through the National Research Foundation (NRF) of Korea.

Development of SARS-CoV-2 vaccines using Fv-antibody library

Jae-Chul Pyun

Materials Science & Engineering
Yonsei University

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보건복지부
Ministry of Health and Welfare

02

인플루엔자 백신 연구개발 및 성과

김진일 교수
고려대학교



Speaker



Jin-II Kim

- ✓ Korea University College of Medicine
- ✓ Associate Professor

🔍 EDUCATION:

- 2016 Visiting Scholar, Rega Institute
KU Leuven – University of Leuven (Leuven, Belgium; Prof. Philippe Lemey)
- 2018 Research professor, Institute for Viral Diseases
Korea University College of Medicine
- 2014 Doctor, Virology
College of Medicine, Hallym University
- 2012 Master, Virology
College of Medicine, Hallym University
- 2009 Bachelor, Veterinary Medicine
College of Veterinary Medicine, Chungnam National University

🔍 PROFESSIONAL EXPERIENCE:

- 2021 ~ Current Associate Professor
Department of Microbiology, Korea University College of Medicine (Seoul, Republic of Korea)
- 2018 ~ 2021 Assistant Professor
Department of Microbiology, Korea University College of Medicine (Seoul, Republic of Korea)
- 2020 ~ 2021 Chair, International Relations, the Korea Society of Virology (KSV; Republic of Korea)
- 2018 ~ Current Member, the Councilor Board, the Korea Society of Virology (KSV; Republic of Korea)
- 2014 ~ Current Member, the American Society for Virology (ASV; USA)

Q Topic

HAs-NAu strategy for the development of better influenza vaccines

Q Abstract

Even though we have managed our lives by dealing with pandemic viruses, another will come to test what we have prepared against it. Highly pathogenic avian influenza A(H5Nx) viruses may be on top of potential pandemic viruses in the future. As we may know, the influenza A virus (IAV) can infect various animal hosts, and the IAV goes through genetic drift and shift. Hence, different subtypes and antigenic IAVs are circulating simultaneously in nature. It will be one of the reasons that we need a universal influenza vaccine. However, it is difficult that subdominant but cross-reactive epitopes found in the stem region of hemagglutinin (HA), one of the two major surface glycoproteins in the viral envelope, are utilized sufficiently in any conventional influenza vaccine platform. To this end, mRNA or recombinant protein strategies of COVID-19 vaccines can be a breakthrough for developing universal influenza vaccines because, using either vaccine strategy, vaccine antigen contents can be manipulated. The HA antigen may deliver protection against seasonal influenza viruses, and neuraminidase (NA), another surface glycoprotein of IAVs, may work as a universal vaccine antigen because the NA evolves genetically slower than the HA. In this regard, a universal NA vaccine antigen can be designed even for avian H5Nx viruses.



HAs-NAu Strategy **for the development of** **better influenza vaccines**

Jin Il Kim, D.V.M./Ph.D.

Lab of Viral Molecular Epidemiology
Department of Microbiology
Institute for Viral Diseases
Vaccine Innovation Center
Korea University College of Medicine



Influenza

Influenza

human seasonal virus

highly pathogenic avian influenza virus

Seasonal human influenza virus



Seasonal human influenza virus

Inactivated 4-valent
(A/H1N1, A/H3N2, B/Vc, B/Ym)



Seasonal human influenza virus

Inactivated 4-valent
(A/H1N1, A/H3N2, B/Vc, B/Ym)



VE = 40.44% (10-60)
[2004-2023; US CDC]



Seasonal human influenza virus



Inactivated 4-valent
(A/H1N1, A/H3N2, B/Vc, B/Ym)



VE = 40.44% (10-60)
[2004-2023; US CDC]

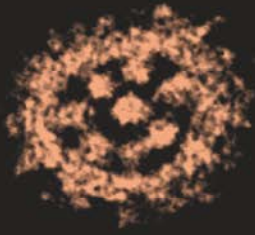


A/H3N2 lowers VE almost every season.

Frequent changes of A/H3N2 vaccine antigens

Season	A/H1N1	A/H3N2	B
1976-1977	A/New Jersey/76	A/Victoria/3/75	
1977-1978			
1978-1979	A/USSR/90/77		B/Hong Kong/5/72
1979-1980	A/USSR/90/77 or A/Brazil/11/78	A/Texas/1/77	
2000-2001			B/Beijing/184/93
2001-2002			B/Sichuan/379/99
2002-2003		A/Moscow/10/99	
2003-2004	A/New Caledonia/20/1999		B/Hong Kong/330/2001
2004-2005		A/Fujian/411/2002	
2005-2006		A/California/7/2004	B/Shanghai/361/2002
2006-2007		A/Wisconsin/67/2005	B/Malaysia/2506/2004
2007-2008	A/Solomon Islands/3/2006		B/Florida/4/2006
2008-2009	A/Brisbane/59/2007	A/Brisbane/10/2007	
2009-2010			B/Brisbane/60/2008
2010-2011		A/Perth/16/2009	
2011-2012			
2012-2013		A/Victoria/361/2011	B/Wisconsin/1/2010 (and B/Brisbane/60/2008 for quadrivalent vaccine)
2013-2014	A/California/7/2009		Massachusetts/2/2012 (and B/Brisbane/60/2008 for quadrivalent vaccine)
2014-2015		A/Texas/50/2012	B/Phuket/3073/2013 (and B/Brisbane/60/2008 for quadrivalent vaccine)
2015-2016		A/Switzerland/9715293/2013	
2016-2017			B/Brisbane/60/2008 (and B/Phuket/3073/2013 for quadrivalent vaccine)
2017-2018		A/Hong Kong/4801/2014	
2018-2019	A/Michigan/45/2015	A/Singapore/INF16H-16-0019/2016	B/Colorado/06/2017 (and B/Phuket/3073/2013 for quadrivalent vaccine)
2019-2020	A/Brisbane/02/2018	A/Kansas/14/2017	
2020-2021	A/Guangdong-Maonan/SWL1536/2019	A/Hong Kong/257/2019	B/Washington/02/2018 (and B/Phuket/3073/2013 for quadrivalent vaccine)
2021-2022	A/Victoria/2570/2019	A/Cambodia/e0826360/2020	
2022-2023			B/Austria/1359417/2021 (and B/Phuket/3073/2013 for quadrivalent vaccine)
2023-2024	A/Victoria/4897/2022	A/Darwin/9/2021	
Total	17 vaccine antigens	30	24

Highly pathogenic avian influenza virus (H5 subtype)



Highly pathogenic avian influenza virus (H5 subtype)

1997..... H5N1



Highly pathogenic avian influenza virus (H5 subtype)



1997 H5N1
2008 H5Nx
 H5N2
 H5N6
 H5N8



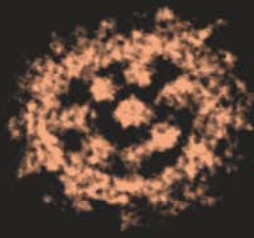
Highly pathogenic avian influenza virus (H5 subtype)



1997 H5N1
2008 H5Nx
 H5N2
 H5N6
 H5N8
2021 H5N1



Highly pathogenic avian influenza virus (H5 subtype)

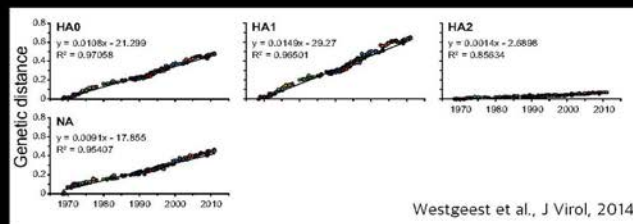


1997 H5N1
 2008 H5Nx
 H5N2
 H5N6
 H5N8
 2021 H5N1

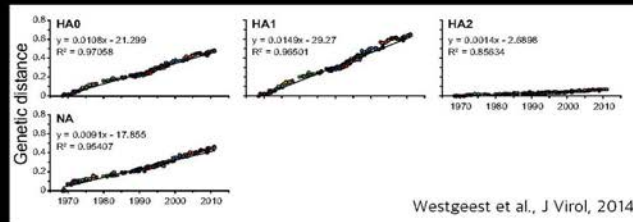


H5 vaccine should be also updated.

NA mutates less frequently than HA does.

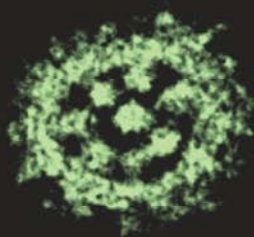


NA mutates less frequently than HA does.

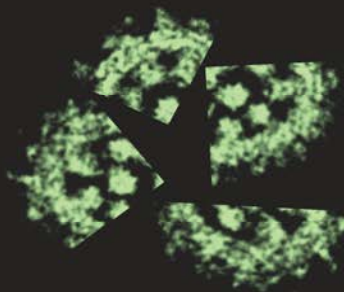


▶ **NA** exhibits better **universal antigen** candidacy.

Conventional seasonal influenza vaccine



Viral particles



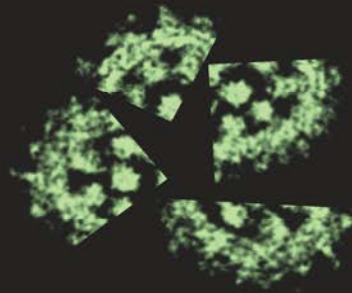
Inactivated vaccine antigen
(15 μ g, HA protein)

Conventional influenza vaccine induces mostly HA Abs

HA-specific Abs

NA-specific Abs

Others



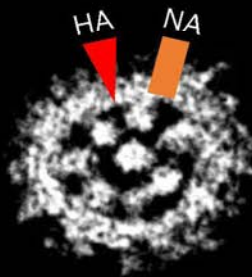
Inactivated vaccine antigen
(15 µg, HA protein)

More HAs are incorporated on the viral surface membrane

HA-specific Abs

NA-specific Abs

Others



HA : NA ≐ 3 : 1

IF,

IF,

focus on the A/H1N1 vaccine antigens

-> A/H1N1

-> HPAI H5N1

IF,

focus on the A/H1N1 vaccine antigens

-> A/H1N1

-> HPAI H5N1

focus on the A/H3N2 vaccine antigens

-> various genetic clades of A/H3N2

Then, the vaccine candidates may be:

focus on the A/H1N1 vaccine antigens

-> A/H1N1

-> HPAI H5N1

=> **inter-subtype universal vaccine**

focus on the A/H3N2 vaccine antigens

-> various genetic clades of A/H3N2

=> **cross-clade (intra-subtype) vaccine**

Each HA and NA vaccine antigen may present;

HA -> **S**pecificity

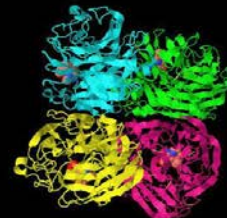


Each HA and NA vaccine antigen may present;

HA -> **S**pecificity



NA -> **U**niversality



Each HA and NA vaccine antigen may present;

HA -> **S**pecificity



NA -> **U**niversality



The optimized HAS-NAU strategy for better vaccine efficacy

The HAS-NAU strategy;

- protects from **seasonal influenza** and **variants**.
- may provide efficacy against **H5N1 viruses**.



Seasonal influenza virus

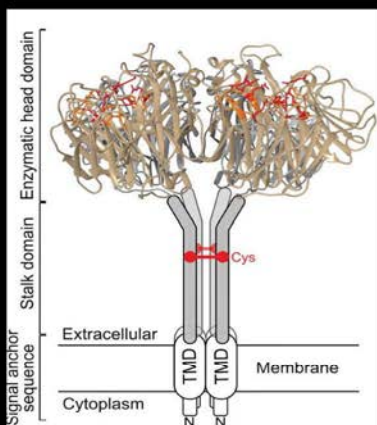


HPAI H5N1 virus

hH1N1 key mutations per clade

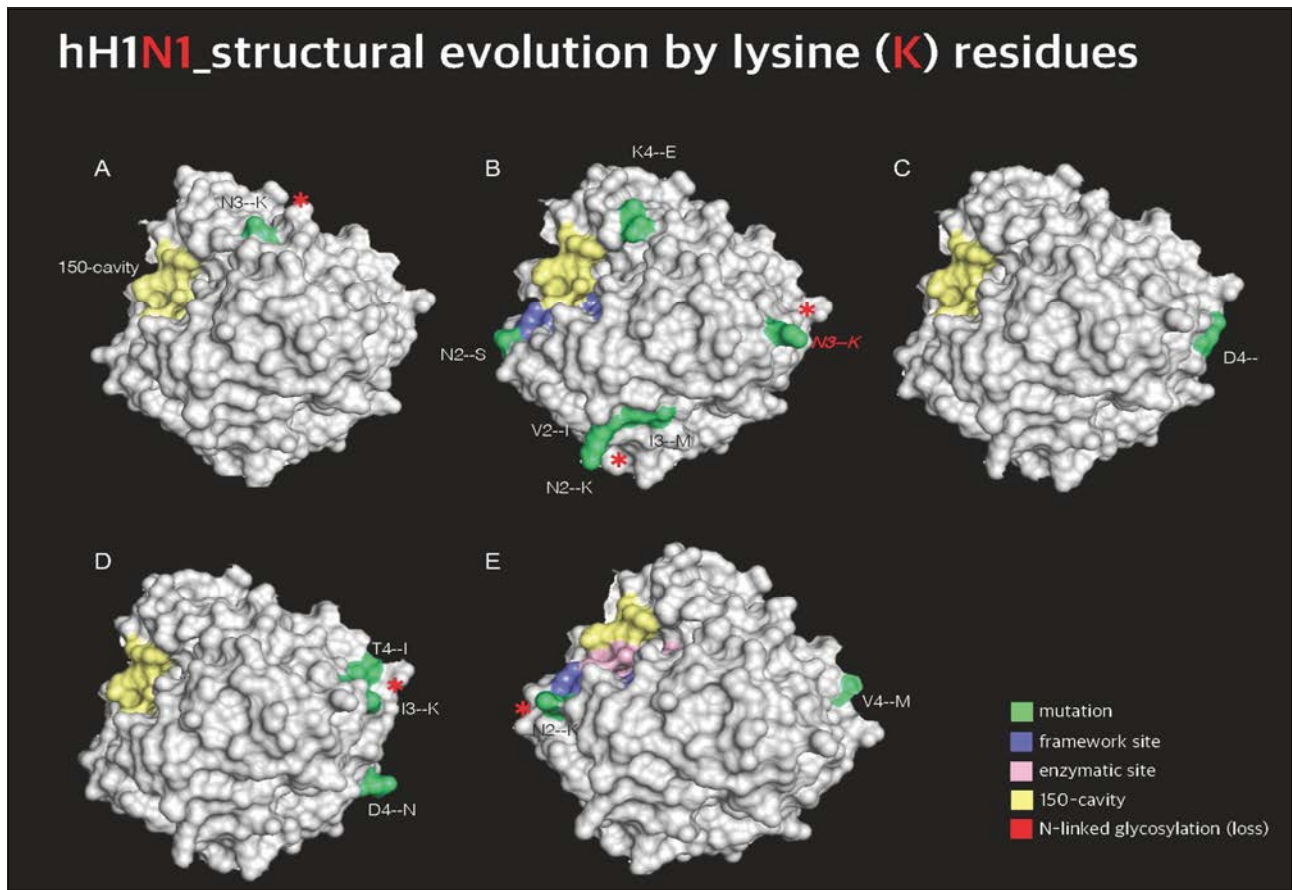


hH1N1 key mutations per clade

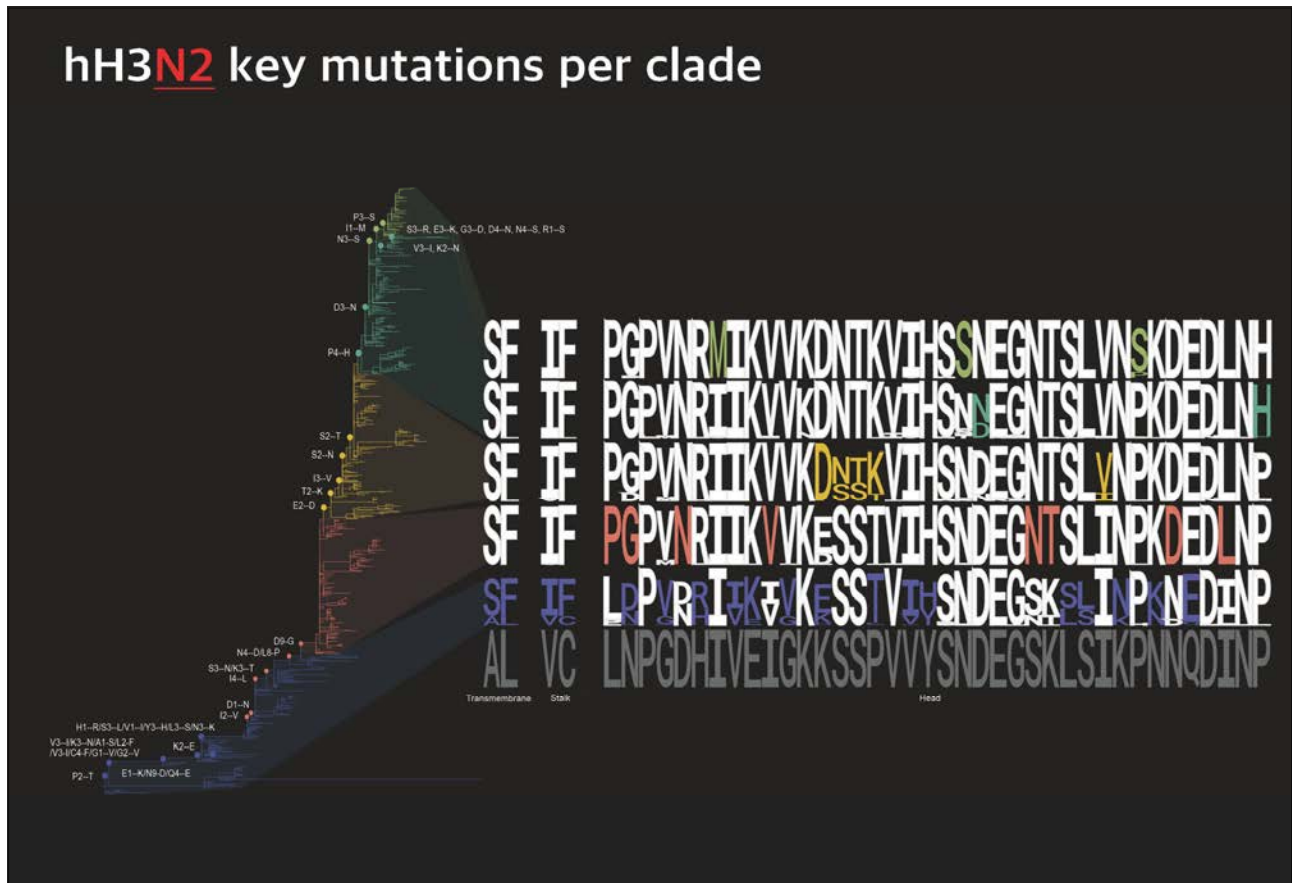


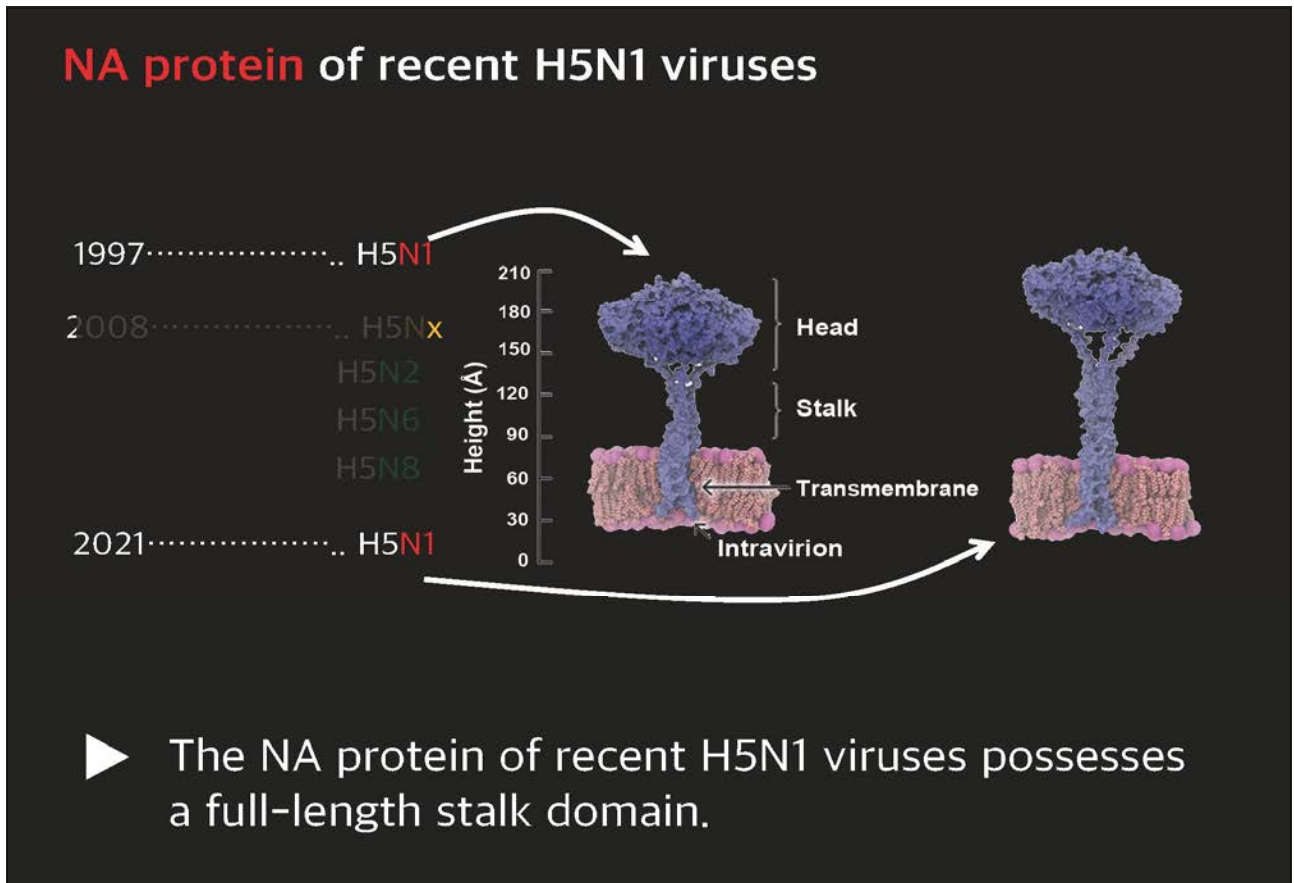
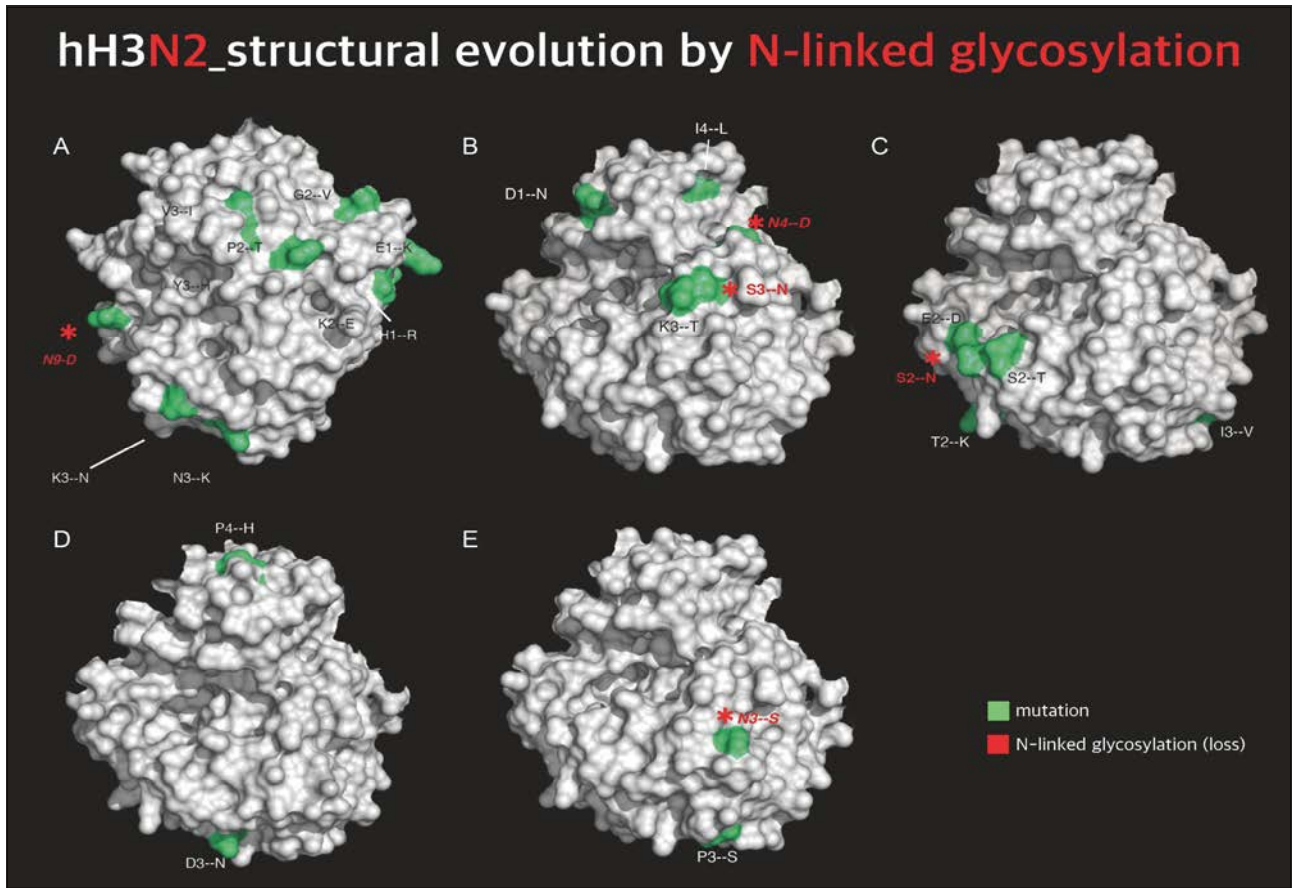
	NA1	NA2
Framework site	E119, R156, W178, S179, D198, I222, E227, H274, E277, N294, E425	
Enzymatic site	R118, D151, R152, R224, E276, R292, R371, Y406	
150-cavity	145-150 (N1 numbering) 147-152 *1149 (N2 numbering)	Lack of 150 cavity V149: salt bridge between D147-H150 (D199 participates)
430-loop	429-437	
Epitope	81, 93, 147, 150-156, 197-199, 218-230, 249-251, 292-300, 328-336, 339-347 367-375, 383-389, 398-405, 428-435	
Ca binding site	• Formed by the oxygen of main chain residue 297, 345, 348 and side chain of N324 Additional a.a. 293, 347, 111-115, 139-143	
Disulfide bond	8 conservative disulfide bond (additional bond in N2, N8, N9) Cys(C)161 of N1	

hH1N1_structural evolution by lysine (K) residues

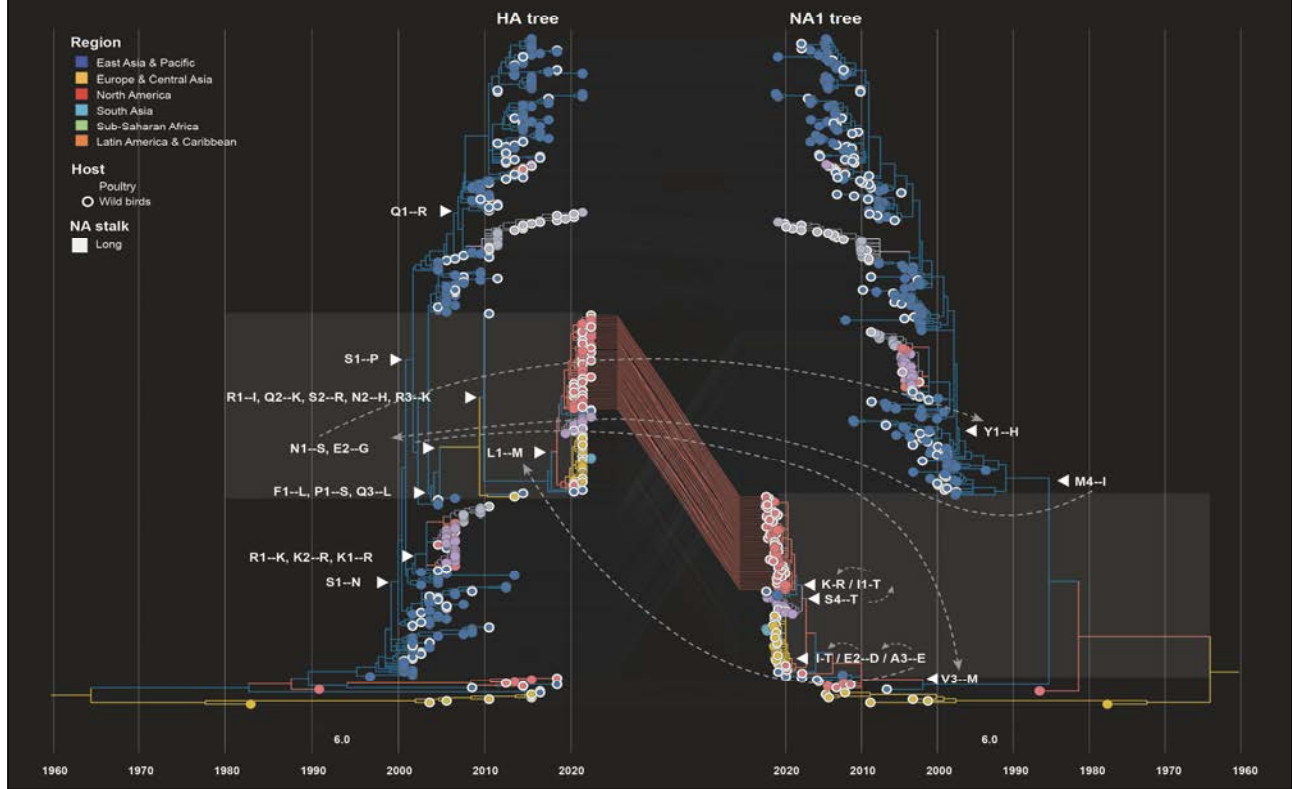


hH3N2 key mutations per clade

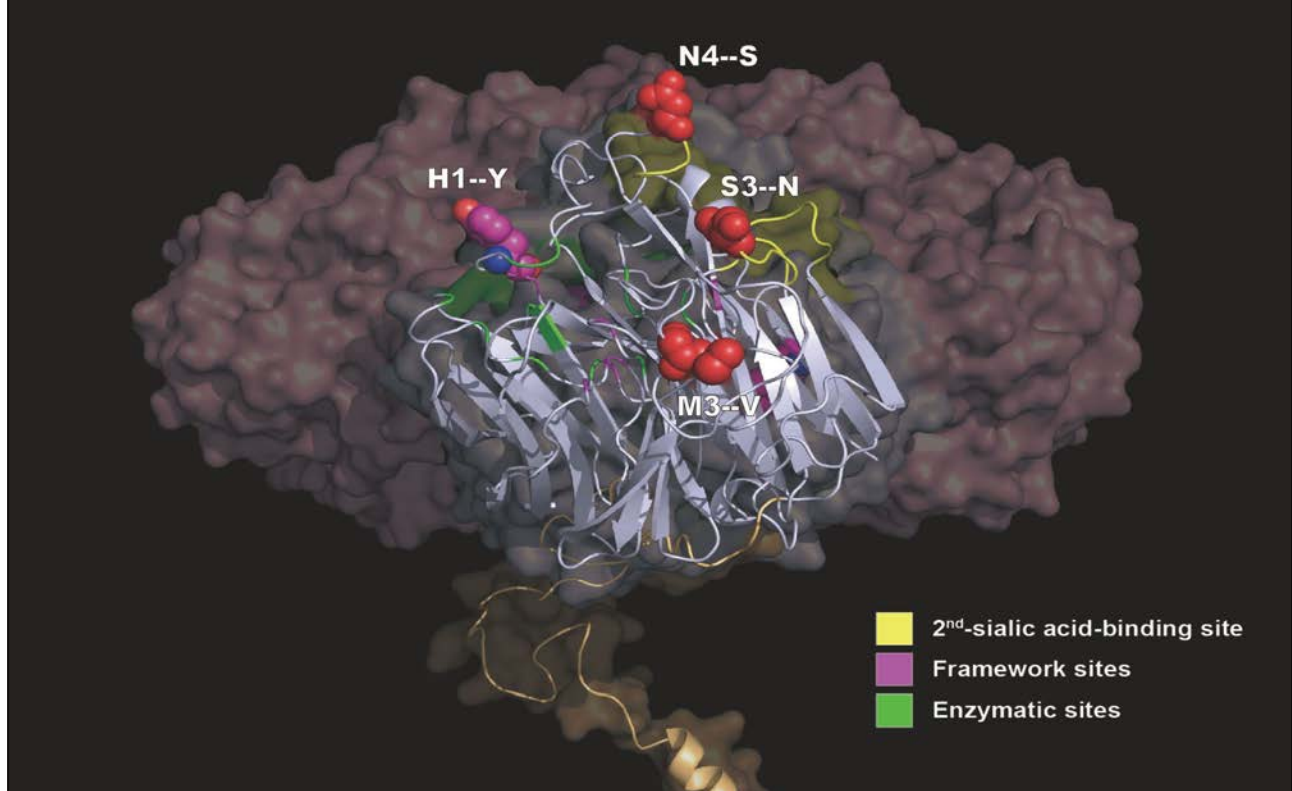




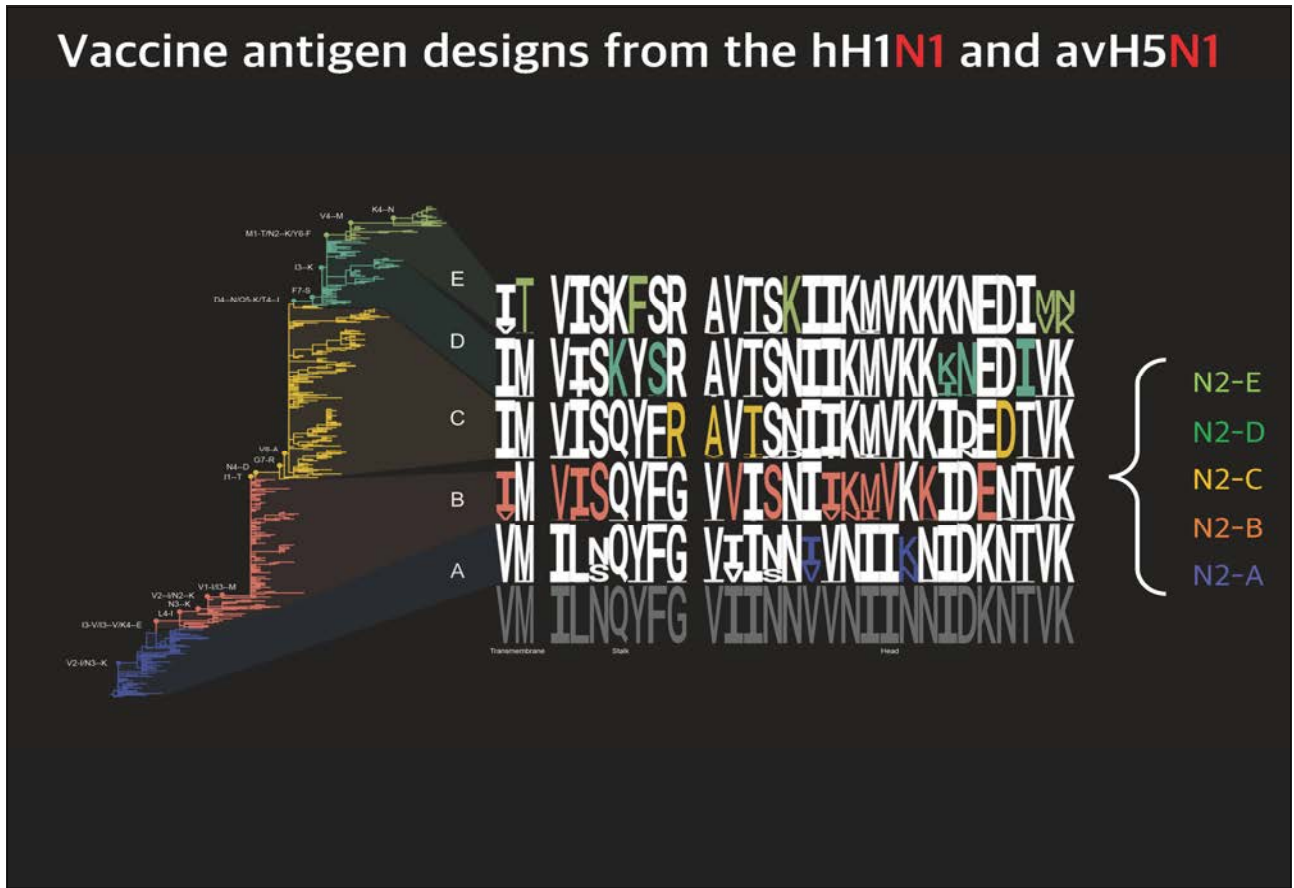
Also, the NA protein harbors several critical mutations



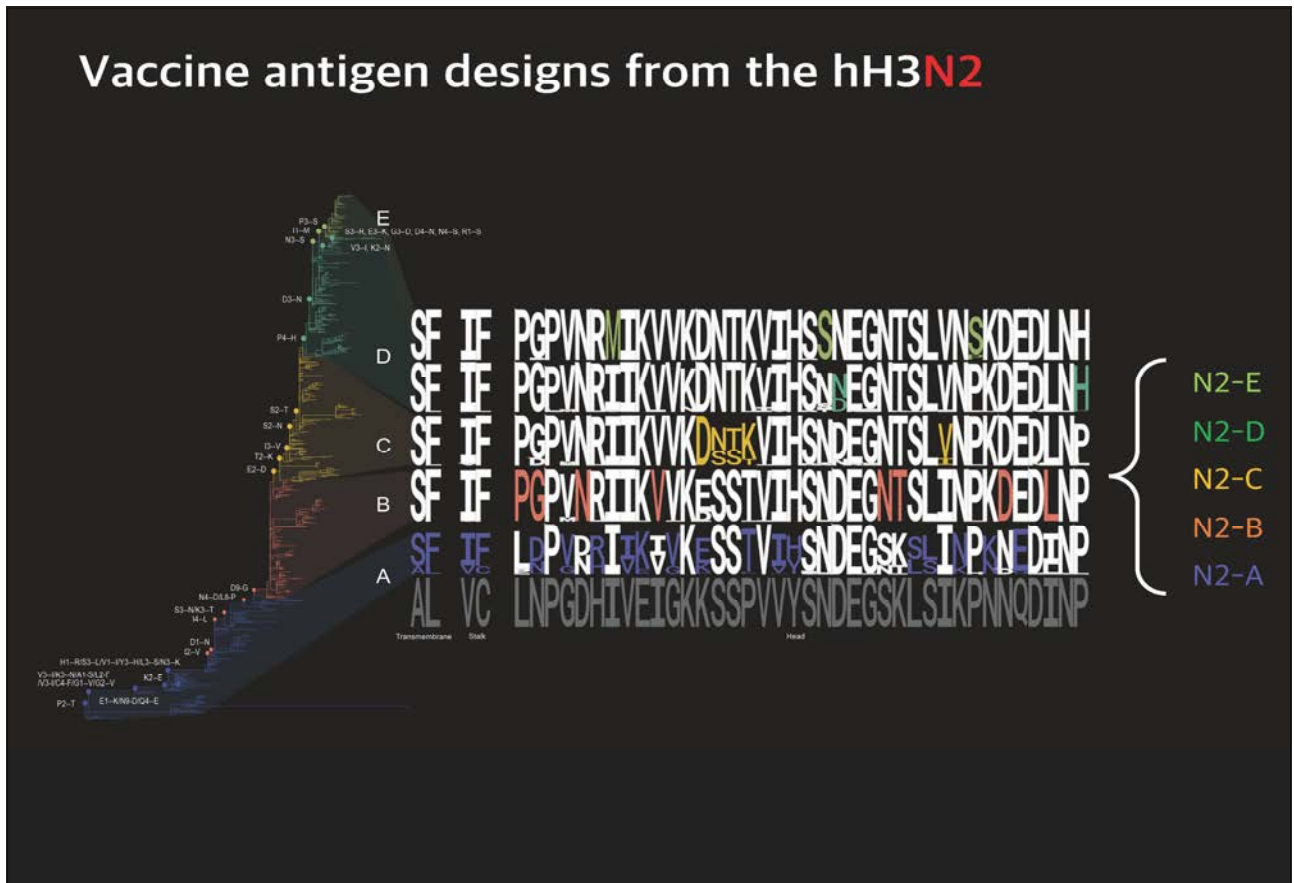
Critical mutations at key targeting sites



Vaccine antigen designs from the hH1N1 and avH5N1



Vaccine antigen designs from the hH3N2



The HAS-NAU strategy is set up for the next steps.

- H1, H3 HA vaccine design: WHO recommended HAs
- N1 vaccine designs: to cover hH1N1 and avH5N1
- N2 vaccine designs: to cover various clades of hH3N2



Seasonal influenza virus



HPAI H5N1 virus

Acknowledgement



고려대학교 미생물학교실

바이러스 분자역학 연구실

이규영 박사, Atanas Demirev 박사

이상아, 박세직, 김현빈, 조승혜, 신우진 대학원생

박만성 교수

김기순 교수

Park's lab 연구진



KU LEUVEN

Evolutionary and
Computational Virology

Philippe Lemey 교수

Guy Baele 교수

Bram Vrandken 박사



Thank you



03

SFTS mRNA 백신 연구 개발 및 성과

김현국 연구관
국립감염병연구소 감염병백신연구과



Speaker



KIM, Hyeon-Guk

- ✓ Korea National Institute of Health
- ✓ Senior staff Scientist

Q EDUCATION:

- 2008 Korea University Graduate School, Ph.D.
- 2002 Korea University Graduate School, Ms.
- 2000 KonKuk university,

Q PROFESSIONAL EXPERIENCE:

- 2021 ~ presents Senior staff Scientist, Division of infectious disease vaccine research, Korea National Institute of Health
- 2015 ~ 2021 Staff Scientist, Division of Biologics, Ministry of Food and Drug Safety
- 2010 ~ 2015 Staff Scientist, Division of vaccine, Ministry of Food and Drug Safety
- 2009 ~ 2010 Senior researcher, Korea National Institute of Health
- 2008 ~ 2009 Research Professor, Korea university

Topic

SFTS mRNA Vaccine Research and Development

Abstract

Severe fever with thrombocytopenia syndrome (SFTS) is a tick-borne emerging infectious disease and caused by Dabie bandavirus also known as SFTS virus (SFTSV) belonging to the genus Bandavirus. Since SFTS first reported in China in 2012, subsequently confirmed cases in recent years have been reported in South Korea and Japan with high mortality rate of over 20%. Despite the wide distribution and high fatality of SFTS, there is no licensed vaccine. Therefore, we evaluated immunogenicity and protective efficacy of SFTSV mRNA vaccine with research collaboration of Korea NIH and Moderna in mice.

As a result of our study, the selected candidates showed more humoral and cellular immune responses as well as stimulating protective immunity than others. It indicated that these candidates have possibility as the most promising candidates for protection against SFTSV infections

04

Sarbecoviruses에 대한 단일클론항체 및 범용 백신연구개발 및 성과

Wang Linfa Professor

DUKE-NUS, Singapore Executive Director for the Programme
for Research in Epidemic Preparedness and Response



Speaker



Wang Linfa

- ✔ Professor in the Programme in Emerging Infectious Diseases at DUKE-NUS Medical School, Singapore
- ✔ Executive Director for the Programme for Research in Epidemic Preparedness and Response (PREPARE), Singapore
- ✔ Professor

🔍 EDUCATION:

- 1986 Ph.D. Biochemistry (Molecular Biology), University of California, Davis.
- 1982 B.S. (Honour) Biology (Biochemistry), East China Normal University, Shanghai, China

🔍 PROFESSIONAL EXPERIENCE:

- 2021 ~ Present Director, BMGF Asia Pathogen Genomics Initiative (PGI) Center
- 2021 ~ Present Executive Director, PREPARE (Programme for Research in Epidemic Preparedness and Responses), Singapore
- 2020 ~ Present Professor, Program in Emerging Infectious Diseases, Duke-NUS Medical School, Singapore
- 2012 ~ 2020 Director and Professor, Program in Emerging Infectious Diseases, Duke-NUS Medical School, Singapore
- 2008 ~ 2015 OCE Science Leader, CSIRO Australian Animal Health Laboratory, Geelong, Vic.

🔍 Topic

Broad spectrum vaccine and mAbs for sarbecoviruses

🔍 Abstract

Although the public health emergency is over for the COVID-19 pandemic, the virus variants are continuously circulating and mutating. It is therefore necessary for us to continue our effort to develop better and more effective vaccines and other countermeasures. In this presentation, we will focus on our approach for cross-clade boosting vaccine development as well as our latest data on broad-spectrum neutralizing human monoclonal antibodies for SARS-CoV-2, SARS-CoV-1 and animal sarbecoviruses.

세션 4.

신종감염병 백신개발 현황 및 전략

Chair



Kevin Kee-Jong Hong

- ✔ Gachon Univ. School of Medicine
- ✔ Professor, Gachon Univ. School of Medicine & Director General, Korea mRNA Vaccine initiative (KmVAC)

🔍 EDUCATION:

- 2001 Texas Tech University, TX, U.S.A.(Ph.D.)
- 1991 Seoul National University, Seoul.(M.S.)
- 1988 Seoul National University, Seoul, Korea.(B.S.)

🔍 PROFESSIONAL EXPERIENCE:

- 2022 ~ Present Professor, Research related to vaccine development, Gachon Univ. School of Medicine, Incheon, Korea
- 2022 ~ Present Director General, Korea mRNA Vaccine initiative (KmVAC), Seongnam, Korea
- 2023 ~ Present Member, Selection Committee, RIGHT Foundation, Seoul, Korea
- 2020 ~ 2022 Professor, General R&D planning for establishment of the infectious disease graduate school of KU-KIST program, Konkuk Univ., Seoul, Korea
- 2017 ~ 2019 Executive Director, Launching newly opened industrial R&D center, Interpark Bio-Convergence, Seoul, Korea
- 2016 ~ 2017 Scientific Consultant for the Director General, Vaccine preparedness strategy, International Vaccine Institute, Seoul, Korea
- 2014 ~ 2015 Executive Director, R&D Planning & Business Development, Institut Pasteur Korea, Seongnam, Korea
- 2012 ~ 2014 Director, Molecular imaging development for vaccine development, nano-medicine and convergent technology group, Korea National Institute of Health, Osong, Korea

Q PROFESSIONAL EXPERIENCE:

- 2013 ~ 2014 Governmental Representative, “Able Response (Korea–U.S.A. annual joint planning practice for the biothreat preparedness)”, Ministry of Health and Welfare, Sejong, Korea
- 2011 ~ 2014 Deputy Director, Dept. high-risk pathogen research, Anthrax and Tularemia Vaccine development, Korea Center for Disease Control and Prevention, Osong, Korea
- 2011 ~ 2012 Deputy Director, Taskforce for institutional vaccine research (VRC planning team), Korea National Institute of Health, Osong, Korea
- 2009 ~ 2011 Deputy Director, Dept. of Influenza viruses, Universal Vaccine development, Korea National Institute of Health, Seoul, Korea
- 2007 ~ 2009 Senior Scientist, Dept, of AIDS and oncological viruses, AIDS therapeutics development, Korea National Institute of Health, Seoul, Korea
- 2004 ~ 2006 Research Associate, Dept. of Microbiology, AIDS and Tularemia pathogenesis, Univ. of Kansas Medical Center, Kansas City, Kansas, U.S.A.
- 2003 ~ 2004 Research Associate, Clinical Oncology Lab, Southwest Cancer and Research Center, Lubbock, TX, U.S.A.
- 2002 ~ 2004 Postdoc, Dept of Pathology, Texas Tech Health Sci. Center, Lubbock, TX, U.S.A.

01

백신 면역증강기술

염정선 대표
차백신연구소



Speaker



Jung-Sun Yum

- ✓ CHA Vaccine Institute
- ✓ CEO

🔍 EDUCATION:

- 1992 Syracuse University, Ph.D.
- 1985 Seoul National University, BS

🔍 PROFESSIONAL EXPERIENCE:

- 2014 ~ present CEO, CHA Vaccine Institute
- 2011 ~ 2014 Head of R&D center, CHA Vaccine Institute
- 2000 ~ 2011 Director, Dobeel Corp.
- 1993 ~ 2000 Principal investigator, Mogam Biotechnology Research Institute

🔍 Topic

Vaccine adjuvant platform

🔍 Abstract

CHA Vaccine Institute is a “clinical stage biotech company” focused on the vaccines, both prophylactic and therapeutic for infectious disease, as well as cancer immunotherapy.

Our core technology is vaccine adjuvant platform, which is based on TLR2 and TLR3 agonists. Vaccine adjuvant is a substance that increases or modulates the immune response to a vaccine. By using adjuvant technology, we can improve the efficacy of the current vaccines and also develop novel vaccines.

In this presentation, I will introduce functional advantages of our adjuvant L-pampo and Lipo-pam and explain the current status of our vaccine pipelines using this platform.



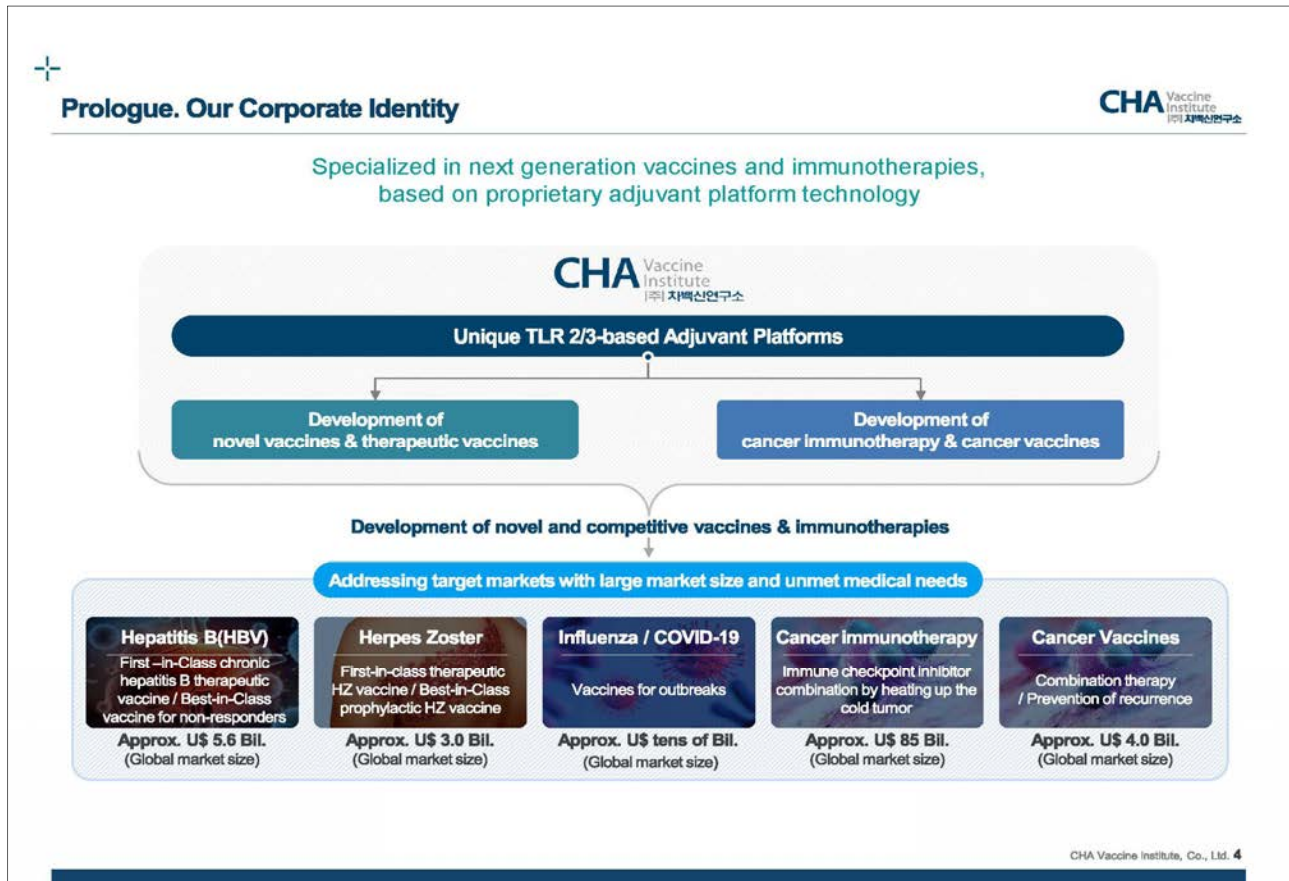
Executive Summary

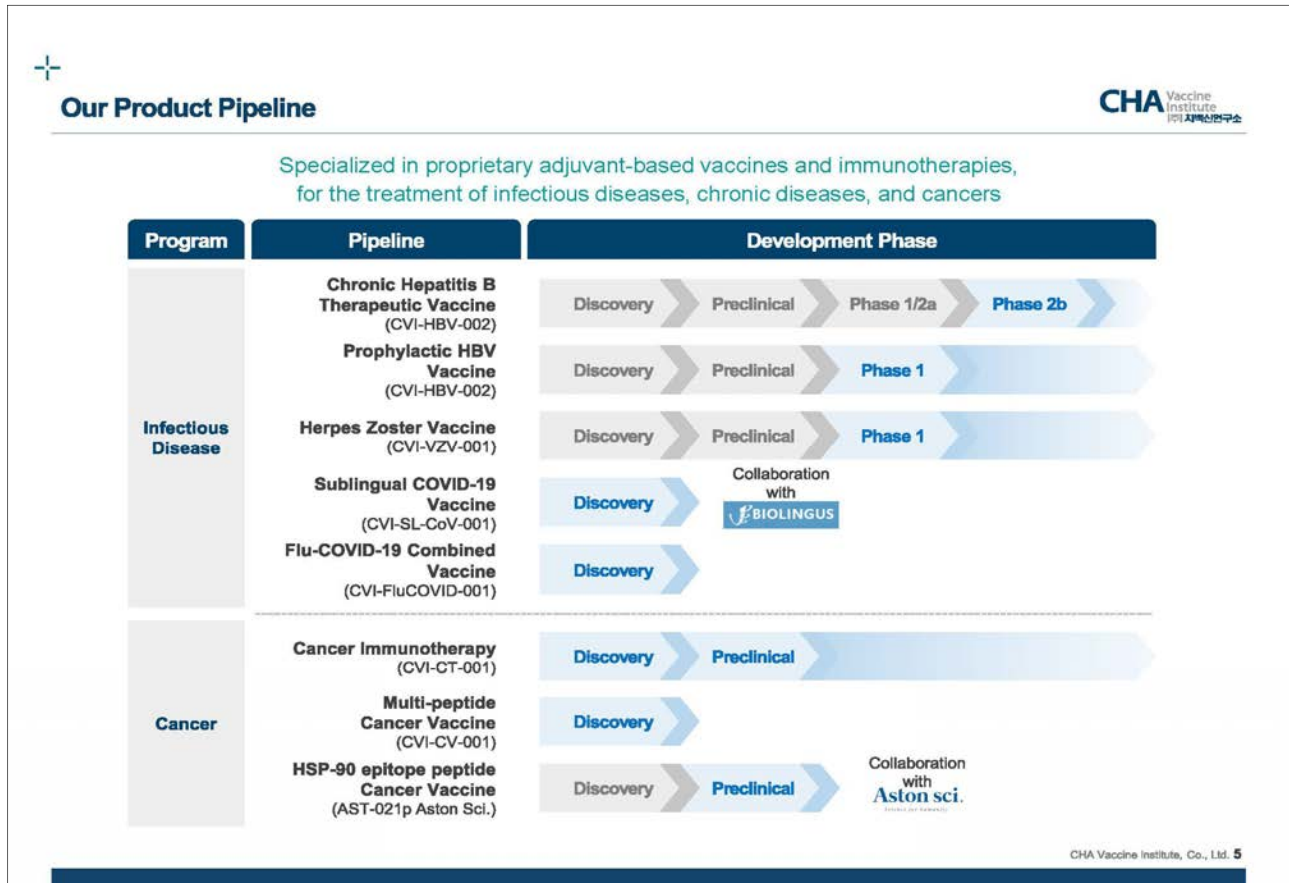


CHA Vaccine Institute (KOSDAQ: 261780) is a dynamic biotechnology company that specializes in the development of groundbreaking therapeutic and prophylactic vaccines, along with innovative cancer immunotherapies.

Key Points

- **Cutting-Edge Adjuvant Platforms:** Our TLR2/TLR3 agonist combination significantly improves vaccine and anti-cancer efficacy.
- **Tackling Urgent Medical Needs:** We address critical medical needs, including Chronic Hepatitis B (\$5.6 billion) and Herpes Zoster (\$5.0 billion).
- **Advancing Clinical Trials:** We have three ongoing trials, including a Phase 2b vaccine and two Phase 1 prophylactic vaccines.
- **Strong Intellectual Property:** With 40 worldwide patents, we ensure robust protection for our innovative solutions.
- **Experienced Leadership:** Our team provides expert guidance in the biotech field.
- **Seeking Partnerships:** We actively seek partnerships to co-develop and out-license our revolutionary adjuvant platforms, vaccines, and cancer immunotherapies. Join us in revolutionizing healthcare and making a lasting global impact.





CVI's Adjuvant Platforms Offer Advantages Over Conventional Adjuvants


CHA Vaccine Institute
백신 면역증강연구소

- L-pampo™ & Lipo-pam™: Innovative adjuvant platforms utilizing TLR2 and TLR3 agonists that demonstrate excellent synergistic effects in inducing robust humoral & cellular immune responses**
 - Superior performance in diverse vaccines targeting infectious diseases and cancers
 - Proven clinical safety for over 200 patients (up to phase 2b)
 - Diverse formulations capable of delivering peptides, proteins, and nucleic acids as antigens
 - Not derived from natural products; a combination of synthesized materials
 - Scalable manufacturing process
 - Long-term stability in liquid vaccine formulation: 36 months at 2~8°C

Superior performance, Safety, Stability

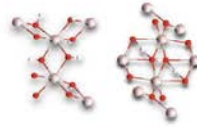
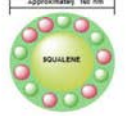
CHA Vaccine Institute, Co., Ltd. 6

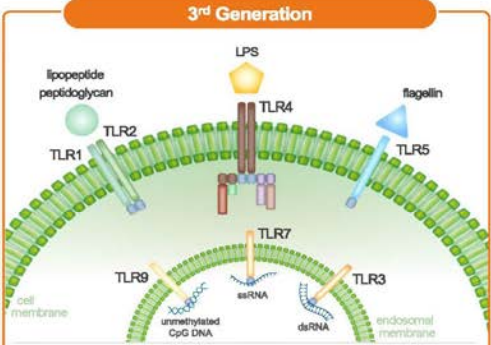
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Innovative TLR-based Adjuvant Platforms: L-pampo™ & Lipo-pam™ (1)

L-pampo™ & Lipo-pam™ are innovative adjuvant platforms that utilize TLR2 and TLR3 agonists to demonstrate excellent synergistic effects in inducing robust T cell activation

	1 st Generation	2 nd Generation	
Components	Alum 	Non-TLR Composition of MF59* Approximately 100 nm  □ Squalene ■ Span 65 ■ Tween 80	
Major immune effects	<ul style="list-style-type: none"> Acts as antigen delivery vehicle - slowly releases antigen and results in prolonged immune response 		
Adjuvants	<ul style="list-style-type: none"> Aluminum salts 	<ul style="list-style-type: none"> MF59 AS03 Emulsion, liposome 	



Harnesses innate immunity to promote adaptive immunity

Unique adjuvant platforms with TLR 2/3 agonists, L-pampo™ & Lipo-pam™


Therapeutic vaccine for chronic hepatitis B

Prophylactic vaccine for HBV

Prophylactic vaccine for Herpes Zoster

CHA Vaccine Institute, Co., Ltd. 7

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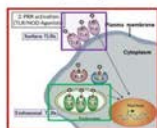


Innovative TLR-based Adjuvant Platforms: L-pampo™ & Lipo-pam™ (2)

Scalable platforms from infectious diseases, to chronic diseases, to oncology

L-pampo™

Complex of TLR2 & TLR3 agonists



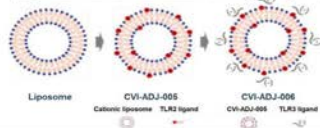
TLR2 agonist (cell memb.)
+

TLR3 agonist (endosomal memb.)

- **Excellent immune-boosting effect of L-pampo™**
 - 100x higher antibody induction than Alum
 - Excellent adjuvanticity over MPL, CpG, and MF59
 - Inducing mucosal immunity
 - **Robust T cell activation and antibody induction**
- Clinical safety proven: phase 2b ongoing
- **Vaccine pipeline using L-pampo™:**
Chronic hepatitis B therapeutic vaccine, Prophylactic HBV vaccine for non-responders, COVID-19 vaccine, Cancer vaccines

Lipo-pam™

Liposomal formulation of L-pampo™



- **Complex of TLR2 and/or TLR3 agonists formulated in liposomes**
 - Dual effect: Immune response booster + Ag delivery vehicle
 - Applicable to peptide, protein, DNA and RNA vaccines
- Designed to induce **stronger cell-mediated immunity**
- Inducing mucosal immunity
- **Vaccine pipeline using Lipo-pam™:**
Herpes Zoster vaccine, Norovirus vaccine, Cancer vaccines

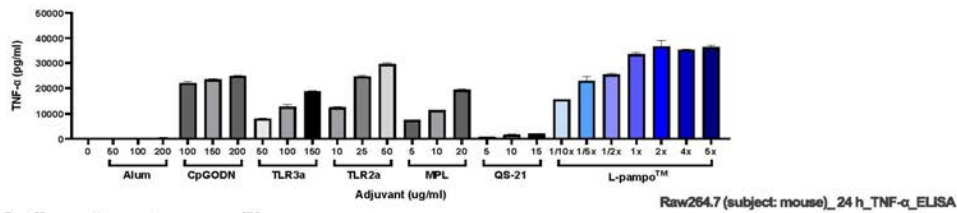
CHA Vaccine Institute, Co., Ltd. 8



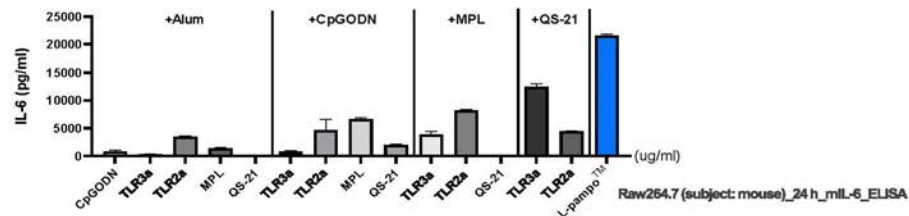
L-pampo™ Induces Higher Production of Pro-inflammatory Cytokines (*in vitro*)



Single adjuvants vs. L-pampo™



Combination of adjuvants vs. L-pampo™



L-pampo™ exhibits a superior capability for inducing pro-inflammatory cytokines compared to conventional TLR-based adjuvants such as TLR2, TLR3, TLR4, TLR9 agonists, as well as Alum and QS-21, whether used alone and in combination.




L-pampo™ & Lipo-pam™ Enhance Cellular & Humoral Immunity (*in vivo*)



Target vaccines	Head-to-head comparisons	Animal strains	Summary
HBV vaccine	<ul style="list-style-type: none"> Alum AddaVax™ CpG ODN (TLR9 agonist) 	<ul style="list-style-type: none"> C57BL/6 mice BALB/c mice HBsAg/HLA-A2 Tg mice 	L-pampo™ induces the strongest humoral and cellular immune responses.
Influenza vaccine	<ul style="list-style-type: none"> Alum AddaVax™ 	<ul style="list-style-type: none"> BALB/c mice (Young, Aged) 	L-pampo™ induces superior protection efficacies in terms of HI titers and IgG GMT, and the highest cell-mediated immunity.
H7N9 avian influenza Vaccine	<ul style="list-style-type: none"> Alum AddaVax™ 	<ul style="list-style-type: none"> BALB/c mice Ferret 	L-pampo™ induces superior protection efficacies in terms of HI titers, IgG GMT, and lung virus titers, as well as the highest cell-mediated immunity.
SARS-CoV-2 vaccine	<ul style="list-style-type: none"> Alum AddaVax™ AddaS03™ (AS03-like) CpG 	<ul style="list-style-type: none"> Ferret BALB/c mice 	L-pampo™ induces the highest neutralizing antibody titers and strongest cell-mediated immunity.
Peptide cancer vaccine (breast cancer)	<ul style="list-style-type: none"> Incomplete Freund's Adjuvant (IFA) & Complete Freund's Adjuvant (CFA) TLR4 agonist (MPL) 	<ul style="list-style-type: none"> C57BL/6 mice FVB/N-Tg (MMTVneu) mice 	L-pampo™ induces the strongest Th1 immune response.
Japanese encephalitis vaccine	<ul style="list-style-type: none"> Alum Alum+TLR4 agonist (AS04-like) 	<ul style="list-style-type: none"> BALB/c mice 	L-pampo™ induces the highest antigen-specific antibody production and cell-mediated immunity.
Acellular pertussis vaccine	<ul style="list-style-type: none"> M. Tuberculosis derived TLR4 agonist Cholera toxin-based adjuvant Alum 	<ul style="list-style-type: none"> BALB/c mice 	L-pampo™ induces the strongest humoral immune response and enhances the production of class-switched IgG antibodies.
HIV vaccine	<ul style="list-style-type: none"> Alum IFA 	<ul style="list-style-type: none"> BALB/c mice 	L-pampo™ induces the highest humoral immune response.
Herpes Zoster vaccine	<ul style="list-style-type: none"> AS01: liposome+MPL+QS-21 AS02: MF59+MPL+QS-21 QS-21 only 	<ul style="list-style-type: none"> C57BL/6 mice 	Lipo-pam™ induces the most effective humoral and cellular immune responses.
Mucosal vaccine (OVA – model Ag)	<ul style="list-style-type: none"> Alum 	<ul style="list-style-type: none"> BALB/c mice 	L-pampo™ induces the most potent mucosal, humoral, and cellular immune responses.
Norovirus vaccine	<ul style="list-style-type: none"> Alum Alum+TLR4 agonist (AS04-like) Cholera toxin-based adjuvant 	<ul style="list-style-type: none"> BALB/c mice 	L-pampo™ & Lipo-pam™ induce the most effective humoral (IgG Ab, IgA Ab, HBGA Blocking Ab) and cellular immune responses.

+




Innovative TLR-based Adjuvant Platforms: L-pampo™ & Lipo-pam™ (3)

Effective & Versatile Adjuvants for Vaccine Development

<div style="border: 1px solid #008080; border-radius: 50%; width: 20px; height: 20px; margin-bottom: 5px; display: flex; align-items: center; justify-content: center;">+</div> <div style="background-color: #4b4b9b; color: white; padding: 5px; border-radius: 5px;">Breaking immune tolerance with a strong immune response</div>	<ul style="list-style-type: none"> • Chronic hepatitis B therapeutic vaccine
<div style="border: 1px solid #008080; border-radius: 50%; width: 20px; height: 20px; margin-bottom: 5px; display: flex; align-items: center; justify-content: center;">+</div> <div style="background-color: #4b4b9b; color: white; padding: 5px; border-radius: 5px;">Enhancing cell-mediated immune response (Th1)</div>	<ul style="list-style-type: none"> • Chronic hepatitis B therapeutic vaccine • Recombinant Herpes Zoster vaccine
<div style="border: 1px solid #008080; border-radius: 50%; width: 20px; height: 20px; margin-bottom: 5px; display: flex; align-items: center; justify-content: center;">+</div> <div style="background-color: #4b4b9b; color: white; padding: 5px; border-radius: 5px;">Therapeutic T cell vaccine</div>	<ul style="list-style-type: none"> • Cancer Immunotherapy • Anti-cancer vaccine
<div style="border: 1px solid #008080; border-radius: 50%; width: 20px; height: 20px; margin-bottom: 5px; display: flex; align-items: center; justify-content: center;">+</div> <div style="background-color: #4b4b9b; color: white; padding: 5px; border-radius: 5px;">Boosting immune response in the elderly</div>	<ul style="list-style-type: none"> • Influenza vaccine
<div style="border: 1px solid #008080; border-radius: 50%; width: 20px; height: 20px; margin-bottom: 5px; display: flex; align-items: center; justify-content: center;">+</div> <div style="background-color: #4b4b9b; color: white; padding: 5px; border-radius: 5px;">Inducing long-lasting immune response</div>	<ul style="list-style-type: none"> • Influenza vaccine
<div style="border: 1px solid #008080; border-radius: 50%; width: 20px; height: 20px; margin-bottom: 5px; display: flex; align-items: center; justify-content: center;">+</div> <div style="background-color: #4b4b9b; color: white; padding: 5px; border-radius: 5px;">Sparing antigen dose</div>	<ul style="list-style-type: none"> • Influenza vaccine
<div style="border: 1px solid #008080; border-radius: 50%; width: 20px; height: 20px; margin-bottom: 5px; display: flex; align-items: center; justify-content: center;">+</div> <div style="background-color: #008080; color: white; padding: 5px; border-radius: 5px;">Inducing mucosal immunity</div>	<ul style="list-style-type: none"> • Norovirus vaccine • Sublingual COVID-19 vaccine

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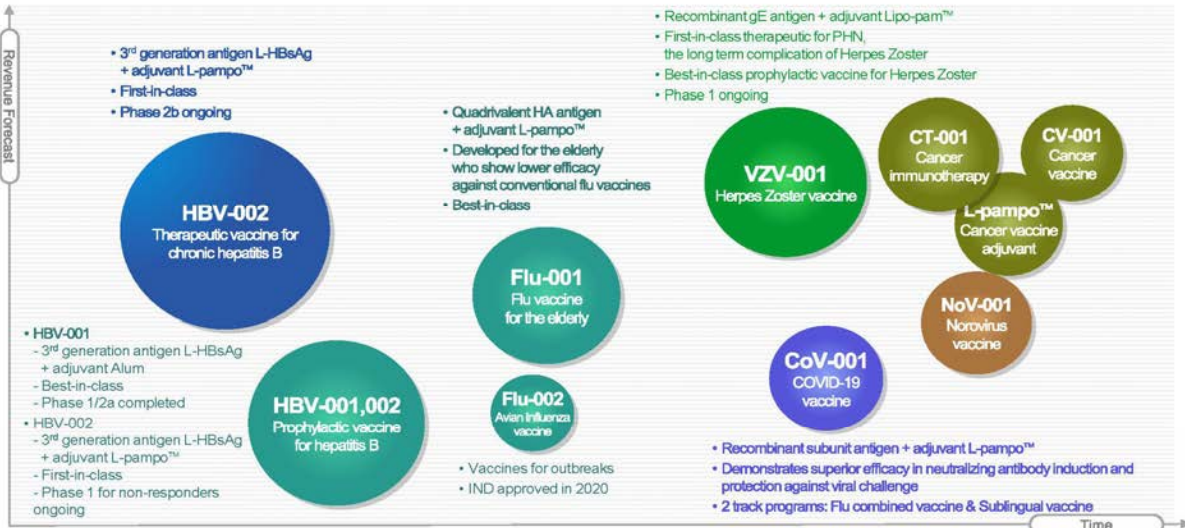
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Portfolio Scalability Using CVI's Adjuvants

With its unique and competitive adjuvant platforms, CVI will build a strategic portfolio and generate a solid revenue

Revenue Forecast



- 3rd generation antigen L-HBsAg + adjuvant L-pampo™
- First-in-class
- Phase 2b ongoing

HBV-002
Therapeutic vaccine for chronic hepatitis B

- Quadrivalent HA antigen + adjuvant L-pampo™
- Developed for the elderly who show lower efficacy against conventional flu vaccines
- Best-in-class

Flu-001
Flu vaccine for the elderly

Flu-002
Avian Influenza vaccine

- Vaccines for outbreaks
- IND approved in 2020

VZV-001
Herpes Zoster vaccine

CT-001
Cancer immunotherapy

CV-001
Cancer vaccine

L-pampo™
Cancer vaccine adjuvant

NoV-001
Norovirus vaccine

CoV-001
COVID-19 vaccine

- HBV-001
- 3rd generation antigen L-HBsAg + adjuvant Alum
- Best-in-class
- Phase 1/2a completed
- HBV-002
- 3rd generation antigen L-HBsAg + adjuvant L-pampo™
- First-in-class
- Phase 1 for non-responders ongoing

- Recombinant gE antigen + adjuvant Lipo-pam™
- First-in-class therapeutic for PHN, the long term complication of Herpes Zoster
- Best-in-class prophylactic vaccine for Herpes Zoster
- Phase 1 ongoing

- Recombinant subunit antigen + adjuvant L-pampo™
- Demonstrates superior efficacy in neutralizing antibody induction and protection against viral challenge
- 2 track programs: Flu combined vaccine & Sublingual vaccine

Time

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+

CVI-HBV-002: adjuvanted HBV vaccine, very potent vaccine

Therapeutic potential was confirmed using HBsAg/HLA-A2 Tg mouse model
To overcome immune tolerance and eradicate HBV antigens*

- 3rd generation antigen including preS and S Ag
- Highly immunogenic
- Glycosylated VLP (Virus Like Particle) Ag

CVI-HBV-002

Therapeutic vaccine for chronic hepatitis B
- Phase 2b on-going

Prophylactic vaccine for non-responders
- Phase 1 on-going

Overcome immune tolerance

Th1 response

Functional cure

Rapid protection

High Ab titers

- Complex of TLR2 & TLR3 agonists
- Synergistic effects in inducing immune responses (both humoral & cellular)
- Th1 immune response induced

*published in Clinical Vaccine and Immunology in 2012

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CVI-HBV-002: Therapeutic Potential in HBsAg/HLA-A2 Tg Mouse Model*

CVI-HBV-002 enhances immune responses & reduces blood HBsAg in the immune-tolerant model

Ab titers: anti-S, anti-preS

- Highest Ab titers in the L-HBsAg + L-pampo™ group (CVI-HBV-002)
- No Ab response in the HBsAg + Alum group (conventional 2nd gen. HBV vaccine)

Ab isotypes

- Ab isotype switching observed in the L-HBsAg + L-pampo™ group (CVI-HBV-002)
- **Inducing strong Th1 response**

HBsAg reduction in the blood

HBV vaccine	Antigen + Adjuvant	Decrease rate of HBsAg	# of cured mouse (%)
CVI	L-HBsAg + Alum	58.8 %	1/7(14.29)
	L-HBsAg + L-pampo™	81.9%	5/7(71.43)
2 nd Gen.	HBsAg + Alum	12.2%	0/7(0.00)


- HBsAg reduced in the L-HBsAg + L-pampo™ group (CVI-HBV-002)
- **Complete disappearance of HBsAg in 5/7 mice (71%)**

Proved the potential to achieve functional cure by overcoming immune tolerance and inducing immune response in CHB patients

* A model for T cell tolerance to hepatitis B surface antigen in chronic hepatitis B virus infection developed by Institut Pasteur

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CVI-VZV-001: Recombinant Herpes Zoster Vaccine in Phase 1

Preclinical studies of CVI-VZV-001 have demonstrated tolerability and higher immunogenicity.

Advantages

-  **Inducing strong CMI**
-  **First-in-Class (Therapeutic)**
-  **Best-in-Class (Prophylactic)**




CVI-VZV-001 with improved immunogenicity, safety & productivity

- **Liposome formulation with adjuvant L-pampo™**
- **Dual acting (Ag delivery & Immune booster)**
- **Robust CMI response**
- **Safety proven by CVI adjuvanted vaccine studies**

Excellent adjuvant "Lipo-pam™"

Recombinant antigen "gE Ag"




CVI-VZV-001

- **Recombinant antigen produced in CHO cells**
- **Truncated with a deletion of 77 a.a anchor domain**
- **B cell and CD4+ T cell epitopes**

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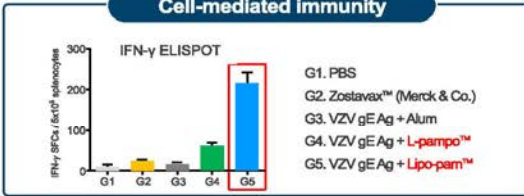


CVI-VZV-001: Superior Efficacy Over Existing Herpes Zoster Vaccines

CVI-VZV-001, a Lipo-pam™-adjuvanted vaccine, demonstrates higher efficacy, with higher cell-mediated immunity and polyfunctional T cells

CVI-VZV-001 vs. a live-attenuated vaccine (Zostavax™, Merck & Co.)

Cell-mediated immunity

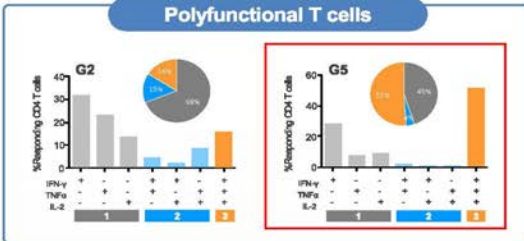


IFN-γ ELISPOT

iFN-γ SFCs / 1x10⁶ splenocytes

G1. PBS
G2. Zostavax™ (Merck & Co.)
G3. VZV gE Ag + Alum
G4. VZV gE Ag + L-pampo™
G5. VZV gE Ag + Lipo-pam™

Polyfunctional T cells

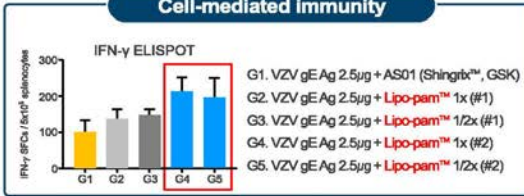


% Responding CD4+ T cells

IFN-γ TNF-α IL-2

CVI-VZV-001 vs. a recombinant vaccine (Shingrix™, GSK)

Cell-mediated immunity

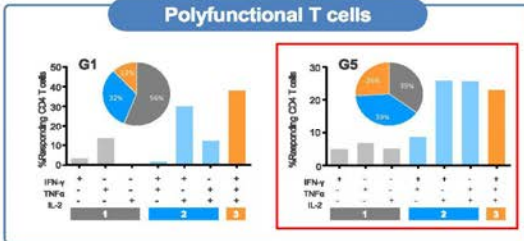


IFN-γ ELISPOT

iFN-γ SFCs / 1x10⁶ splenocytes

G1. VZV gE Ag 2.5µg + AS01 (Shingrix™, GSK)
G2. VZV gE Ag 2.5µg + Lipo-pam™ 1x (#1)
G3. VZV gE Ag 2.5µg + Lipo-pam™ 1/2x (#1)
G4. VZV gE Ag 2.5µg + Lipo-pam™ 1x (#2)
G5. VZV gE Ag 2.5µg + Lipo-pam™ 1/2x (#2)

Polyfunctional T cells



% Responding CD4+ T cells

IFN-γ TNF-α IL-2

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CVI-Flu-001: An Influenza Vaccine for the Elderly in Preclinical Studies

CHA Vaccine Institute 제주 차백신연구소

L-pampo™ adjuvanted CVI-Flu-001 is designed to induce higher Ab production and long-lasting responses in the elderly

- Quadrivalent flu vaccine (split virion, inactivated)
- Two A subtypes & Two B types
- Collaboration program

Seasonal Flu vaccine "HA Antigenes from 4 flu viruses"

Potent Adjuvant "L-pampo™"

Enhanced Flu vaccine efficacy for elderly

Advantages

- Higher HI Titers and CMI
- Long Lasting Response
- Sparing Antigen Dose

- Complex of TLR2 & TLR3 ligands
- Synergistic effects in inducing both humoral & cellular immune responses
- Strong Th1 immune response

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CVI-NoV-001: L-pampo™ Adjuvanted Norovirus VLP Vaccine Program

CHA Vaccine Institute 제주 차백신연구소

Multivalent Norovirus VLP vaccine platform: Robust humoral, cellular, and mucosal immunity able for cross-protection against various genotypes

Advantages

- Inducing neutralizing Ab
- Inducing mucosal immune response
- Inducing strong CMI

Potent adjuvant "L-pampo™" "Lipo-pam™"

Various Ag types "Norovirus VLP"

Prevention of Norovirus-derived gastroenteritis


CVI-NoV-001

- Inducing mucosal immunity
- Dual acting (Ag delivery & Immune booster)
- Robust CMI response
- Proven safety by CVI adjuvanted vaccine studies

- Multivalent VLP antigens produced by Baculovirus expression systems
- GI.1, GI.3, GII.2, GII.4 consensus sequences

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CVI-SL-CoV-001: Sublingual COVID-19 Vaccine

A subunit vaccine targeting mucosal immunity,
which is safer, more effective, and more convenient than existing COVID-19 vaccines

Advantages

-  Needle-free administration
-  Reducing distribution cost
-  Inducing mucosal immune response




Prevention of COVID-19 disease in LMICs

- Inducing humoral & cellular immune responses
- Respiratory mucosal immunity

Potent adjuvant "L-pampo™"

Sublingual delivery system


Ag types "RBD of VOCs"



- SARS-CoV-2 delta variant RBD antigen
- Sublingual delivery system provided by BioLingus

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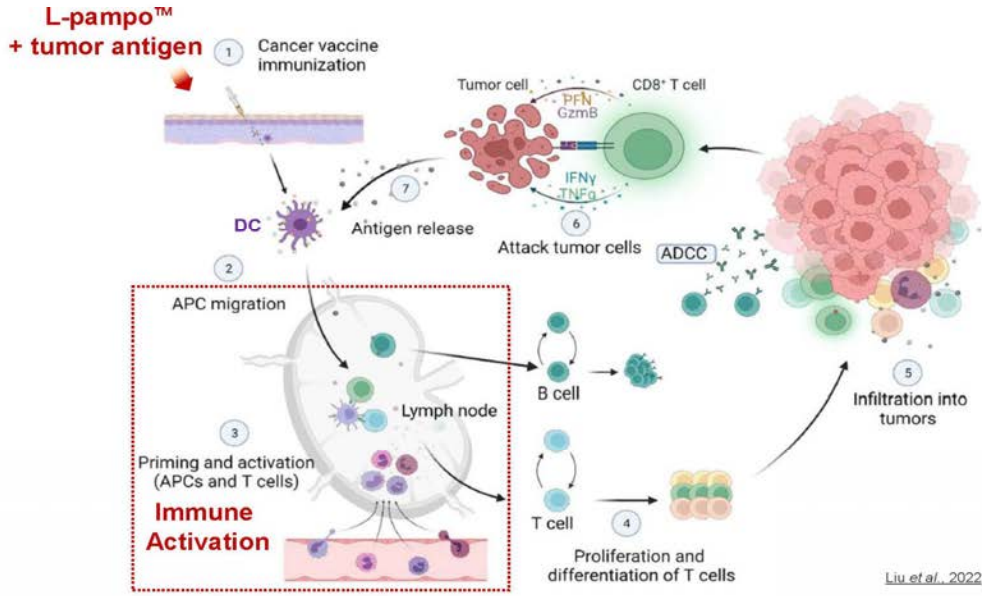
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L-pampo™, a Potent Cancer Vaccine Adjuvant

L-pampo™, a potent cancer vaccine adjuvant, promotes robust tumor antigen-specific T-cell immune responses in the Tumor-Immunity Cycle induced by cancer vaccines

L-pampo™ + tumor antigen



The diagram illustrates the Tumor-Immunity Cycle. It starts with cancer vaccine immunization (1) where a dendritic cell (DC) captures tumor antigens. The DC then migrates to a lymph node (2) for priming and activation (3) of T cells. This leads to the proliferation and differentiation (4) of T cells. The activated T cells then infiltrate the tumor (5) and attack tumor cells (6) through ADCC, releasing cytotoxic molecules like PFN and GzmB, and cytokines like IFNγ and TNFα. Finally, the attack results in antigen release (7) from the tumor cells.

Liu et al., 2022

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Collaboration Opportunity Summary



- 1 L-pampo™ & Lipo-pam™ Platform Technology**

 - Synergistically Induces Humoral and Cellular Immune Responses
 - Therapeutic Potential by Eliciting a Strong Th1 Immune Response
 - Platform Clinically Proven Mature: Phase 2b

- 2 Huge Market Potential with Disruptive Approaches**

 - First-in-Class Therapeutic Vaccine for Chronic Hepatitis B
 - Best-in-Class Prophylactic Vaccine for Hepatitis B Virus
 - Best-in-Class Prophylactic Vaccine for Herpes Zoster
 - Best Immune Checkpoint Inhibitor Combination Therapy to Overcome Resistance to ICI Therapy

- 3 CHA Vaccine Institute is Seeking Collaboration Partners**

 - Co-development & Out-licensing of CVI's Existing Pipelines
 - Co-development of Combination Therapy with CVI's Pipelines
 - Collaboration to Develop Novel Immunotherapies with CVI's Platform Technologies



THANK YOU

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 Homepage: <http://en.chavaccine.com/>

02

**감염병 백신 개발을 위한
SKY mRNA 플랫폼**

신진환 실장
SK바이오사이언스



Speaker



Jinan Shin

- ✔ SK bioscience
- ✔ Vice President

🔍 EDUCATION:

- 2020 Ph.D. in Pharmacy, School of Pharmacy, Sungkyunkwan University
- 2004 M.S. Biological Science, KAIST
- 2002 B.S. Genetic Engineering, Korea University

🔍 PROFESSIONAL EXPERIENCE:

- 2018 ~ Present SK bioscience
- 2008 ~ 2018 SK Chemicals
- 2004 ~ 2008 Hanmi Pharmaceutical

Q Topic

SKY mRNA Platform for Prophylactic Vaccine Development

Q Abstract

Introduction: SK initiated research into mRNA vaccines in response to the COVID-19 pandemic. In a relatively short period, the company secured its mRNA platform and undertook research and development for infectious diseases such as Covid, Japanese Encephalitis Virus (JEV*) and Respiratory Syncytial Virus (RSV). The SKY mRNA platform incorporated proprietary UTR combinations and poly A-tail modifications to enhance antigen expression, mRNA stability, and process convenience. With improved protein expression and process convenience, the platform now encompasses clinical-scale GMP production processes and analytical methods.

Methods: Using the SKY mRNA platform, antigens for JEV and RSV were introduced to generate vaccine candidates. These candidates were administered to mice or rats to induce in vivo immune responses. Total antibody levels were assessed through ELISA, while neutralizing antibodies were evaluated using Focus Reduction Neutralization Test (FRNT) and Plaque Reduction Neutralization Test (PRNT). T-cell activity was examined through Intracellular Cytokine Staining (ICS) and Enzyme-Linked ImmunoSpot (ELISPOT). The efficacy of the vaccines was validated through a Challenge study.

Results: In all groups administered with the JEV vaccine candidate, effective total antibody and neutralizing antibody formation were confirmed through ELISA and FRNT analyses. T-cell activity was verified through cytokine analysis. Ultimately, in the Challenge study using a lethal dose of JEV virus, all groups vaccinated with the JEV mRNA vaccine candidate showed no pathological signs, confirming the efficacy of the vaccine candidate.

For the RSV vaccine candidate, analysis using ELISA and PRNT confirmed the induction of total antibodies and neutralizing antibodies in the vaccinated groups. Ongoing research is focused on developing a vaccine utilizing a novel form of prefusion antigen for RSV. **Conclusions:** By applying antigens of diverse infectious diseases such as Covid, JEV, and RSV to the SKY mRNA platform, reproducibility in production processes and in vivo immunogenicity were validated. This platform technology secures the foundation for developing prophylactic vaccines. The SKY mRNA platform is poised to play a crucial role in the rapid and effective development of vaccines in response to emerging infectious diseases in the future.

(*:The Japanese Encephalitis Virus (JEV) research project is being conducted with sponsorship from CEPI.)

International Conference USJCMSP

SK Bioscience

SKY mRNA Platform for Prophylactic Vaccine Development

Jinan Shin, Ph.D. Vice President

Mar 2024

SK Group – Biopharmaceuticals Portfolio



from Prevention



Vaccine business across R&D, process dev., manufacturing, and commercialization



Pangyo R&D Center

- Diverse Vaccine Platform
- PD, Analytical, Serology
- 650 FTE



Andong L-House Plant

- High Flexible Single Use System
- Multi-Modular system
- 390 FTE

to Cure



Pharma R&D and manufacturing



Plasma fractionization and blood products



Novel biopharmaceutical therapeutics R&D



Biopharma CDMO including CGT and API

SK bioscience – Upgrading R&D/Mgf. Infra



R&D Songdo Global R&PD Center

“Global Hub for bio R&D”

- Pangyo R&D Center’s seamless R&D and process development excellence

⇓

- Global hub for R&D ecosystem for top-tier partners
- Upgraded R&D infra & scale by 1st half 2025

Mfg. Andong L House

“Vaccine/Bio Mfg. Hub Expansion”

- Diverse and agile manufacturing capacities (Bacterial suits, Vial suits and Fill & Finish)

⇓

- Globally qualified EU GMP and cGMP readiness
- Top tier technology platform (mRNA, small footprint and modular system)

CONTENT OVERVIEW

- 1 SKBS mRNA Manufacturing Platform
- 2 JEV Vaccine [CEPI]
- 3 RSV Vaccine
- 4 Further Plan



SKBS mRNA Manufacturing Platform

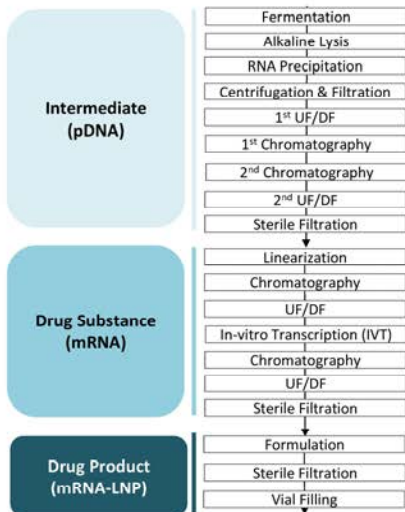
Platform for mRNA Vaccine

SKY mRNA Manufacturing Platform

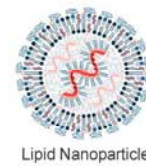
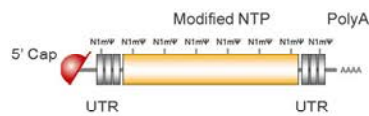


Process Development

✓ Process Diagram



✓ mRNA Platform



✓ Scaling Up from the Lab to a GMP Facility



SKY mRNA Manufacturing Platform



Analytical Method Development

✓ Analytical Methods for Drug Substance, DS (mRNA)

Category	Quality Attributes	Analytical Methods
General	Appearance	Appearance
	pH	Potentiometry
Safety	Bioburden	Bioburden
	Bacterial Endotoxin	Kinetic turbidimetric assay (LAL assay)
Purity	mRNA Integrity	Capillary Gel Electrophoresis
	dsRNA	ELISA
Contents	mRNA Content	Fluorescence assay
Integrity	% of 5' Cap	RP-UPLC
	% of Poly A Tail	RP-UPLC (TBD)
Identity	mRNA Sequence	PCR & Sanger sequencing
Process-related Impurity	Residual DNA template	RT-PCR & Sequencing

✓ Analytical Methods for Drug Product, DP (mRNA-LNP)

Category	Quality Attributes	Analytical Methods
General	Appearance	Appearance
	pH	Potentiometry
	Visible particle	Particles
Excipients	sub-visible particle	Subvisible particulate matter
	Osmolality	Osmometry
	LNP Size	Dynamic light scattering
Purity	LNP Polydispersity	Dynamic light scattering
	mRNA Encapsulation	Fluorescence assay
Content	mRNA Integrity	CGE
	mRNA Content	Fluorescence assay
Identity	Identity of encoded mRNA Sequence	
	Ionizable lipid Content	
	PEG-lipid Content	
Excipients	DSPC Content	HPLC-CAD
	Cholesterol Content	
	Lipid Identity	
Potency	In-vitro Expression	Cell based assay
	PRNT	PRNT
Safety	Bacterial Endotoxin	Kinetic turbidimetric assay (LAL assay)
	Sterility	Sterility
General	Extractable Volume	Volume of injections in containers
	Container Closure Integrity	Dye incursion

SKY mRNA Platform Development

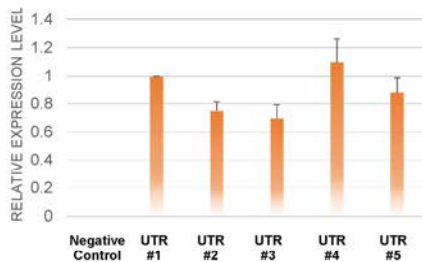


SKBS UTR System – Translation Efficiency

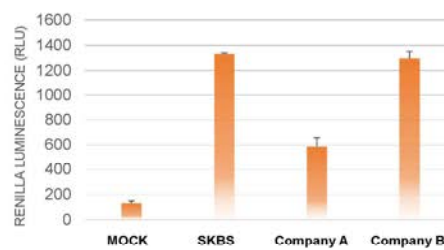


- ✓ Securing UTR platform for enhanced expression:
- ✓ Cell-Based Assay: Confirming expression levels in vitro using a reporter in cell-based assays.
- ✓ Animal Study: Validating effective efficacy in vivo for various antigens.

UTR Screening Study



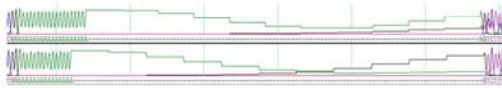
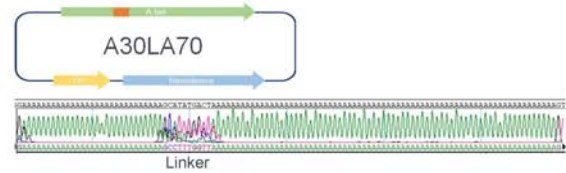
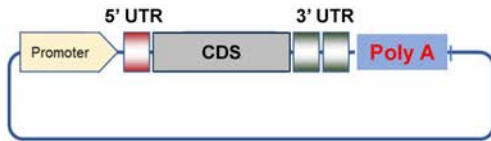
Expression Level Comparison



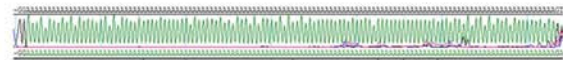
SKY mRNA Platform Development



Poly A tailing



- ✓ SKBS platform: E.coli strain, Culture media, Culture condition optimization
- ✓ Maintaining stability is possible with more than 120 consecutive A stretches in the cell stock.



- ✓ Cloning more than 100 consecutive A stretches into pDNA results in deletions, making stable maintenance challenging.
- ✓ Frequent deletion of adenine repeat during cloning and fermentation



Japanese Encephalitis Virus mRNA vaccine

CEPI-funded mRNA Vaccine Project



JEV Vaccine Development (CEPI Funding)

Japanese Encephalitis Virus

- ✓ Japanese encephalitis virus (JEV) is a flavivirus transmitted by mosquitoes, similar to dengue, yellow fever, and West Nile viruses.
- ✓ It's a leading cause of viral encephalitis in Asia, with an estimated 68,000 clinical cases annually and a high case-fatality rate of up to 30%.
- ✓ Survivors may experience permanent neurological or psychiatric issues in 30%–50% of cases.
- ✓ JEV affects 24 countries in the WHO South-East Asia and Western Pacific regions, putting over 3 billion people at risk of infection.
- ✓ While there's no cure, treatment focuses on symptom management. Vaccines are available and recommended by WHO for areas where JE is a public health concern, aiming to integrate JE vaccination into national immunization schedules.
- ✓ SK Bioscience has applied the SKY mRNA Platform to develop a JEV mRNA vaccine for public health, supported by funding from CEPI.

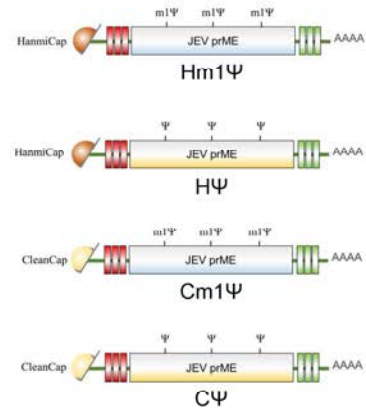
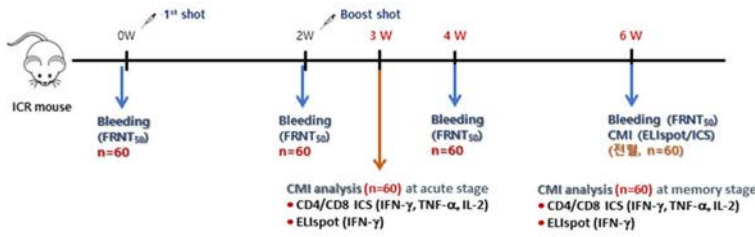
Nature Reviews | Neurology

JEV Vaccine Development (CEPI Funding)



Preclinical Animal Study (Humoral & cellular immunity)

- ✓ The test articles were manufactured using either HanmiCap or CleanCap and Modified UTP. (HanmiCap supplied by Hanmi Fine Chemical and CleanCap supplied by TriLink).
- ✓ The humoral and cellular immune responses of the vaccine candidates were evaluated using ICR mice.



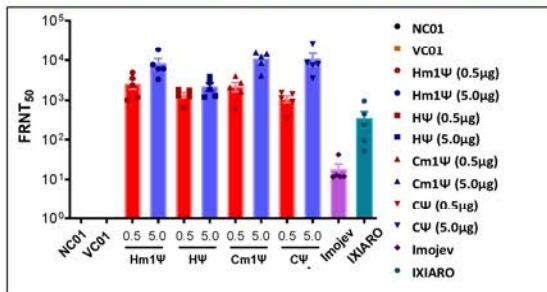
JEV Vaccine Development (CEPI Funding)



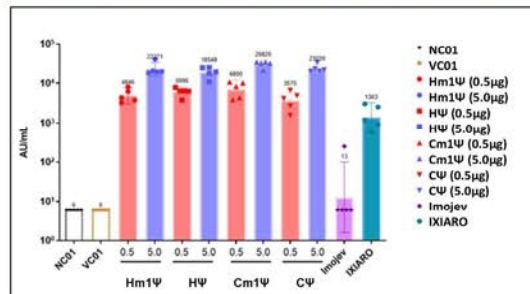
Humoral Immunogenicity - Antibody Evaluation

- ✓ FRNT and ELISA assays were conducted to assess antibody response.
- ✓ All tested mRNA JEV candidates exhibited higher antibody titers compared to comparator vaccines.
- ✓ A positive correlation was observed between neutralization and total antibody titers, indicating the potential effectiveness of mRNA JEV candidates in inducing robust immune responses.

The level of neutralization Abs result(post-boost vaccination)



The Anti-JEV prME IgG titer result(post-boost vaccination)

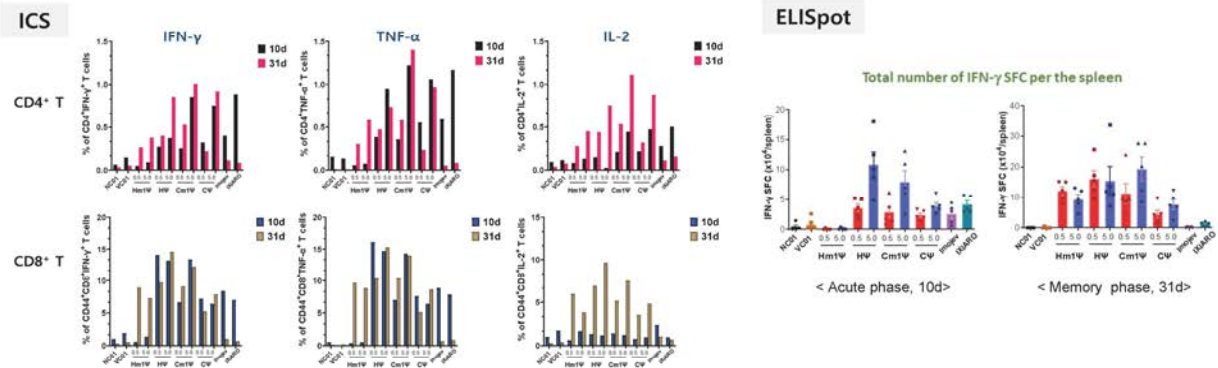


JEV Vaccine Development (CEPI Funding)



Immunogenicity Study – Cell Mediated Immunity (ICS, ELISpot)

- ✓ Intracellular Cytokine Staining (ICS) and ELISpot assays were performed to assess cellular immune response.
- ✓ SK-JEV mRNA candidates were found to elicit CD4+ and CD8+ T cell responses from 10 to 31 days post-vaccination.
- ✓ Additionally, SK-JEV mRNA exhibited prolonged T cell responses and higher levels of IFN-γ compared to comparator vaccines.

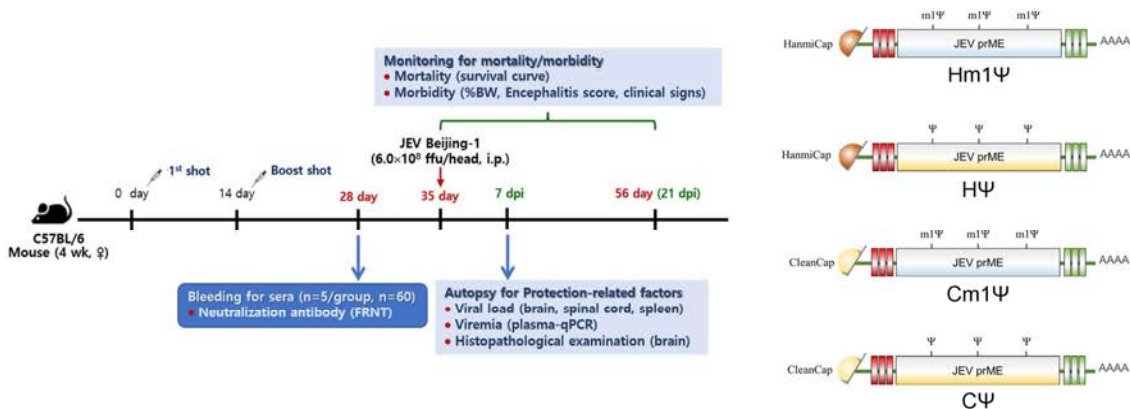


JEV Vaccine Development (CEPI Funding)



Preclinical Animal Study (Effectiveness (Protective))

- ✓ Test articles were synthesized utilizing either HanmiCap or CleanCap with Modified UTP, where HanmiCap was procured from Hanmi Fine Chemical and CleanCap from TriLink.
- ✓ Effectiveness studies were performed utilizing C57BL/6 mice and the JEV Beijing-1 strain.

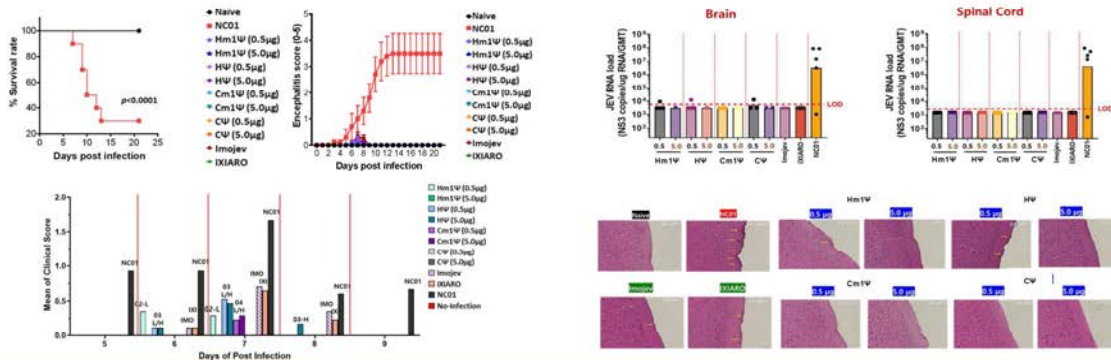


JEV Vaccine Development (CEPI Funding)



Effectiveness

- ✓ Both SK-JEV mRNA and comparator vaccines demonstrated exceptional protective efficacy, with no observed mortality at a dose of 6×10^8 ffu/head via intraperitoneal administration.
- ✓ Particularly noteworthy was the expedited recovery trend of clinical symptoms observed in the SK-JEV mRNA group compared to the comparator vaccines.
- ✓ Viral RNAs in the central nervous system (CNS) were undetectable (below the limit of detection) in both the SK-JEV mRNA and comparator vaccine groups.
- ✓ Additionally, only mild cellular infiltration was observed in a minority of individuals from both groups, suggesting the absence of actual encephalitis or significant brain tissue damage.



Respiratory Syncytial Virus mRNA vaccine

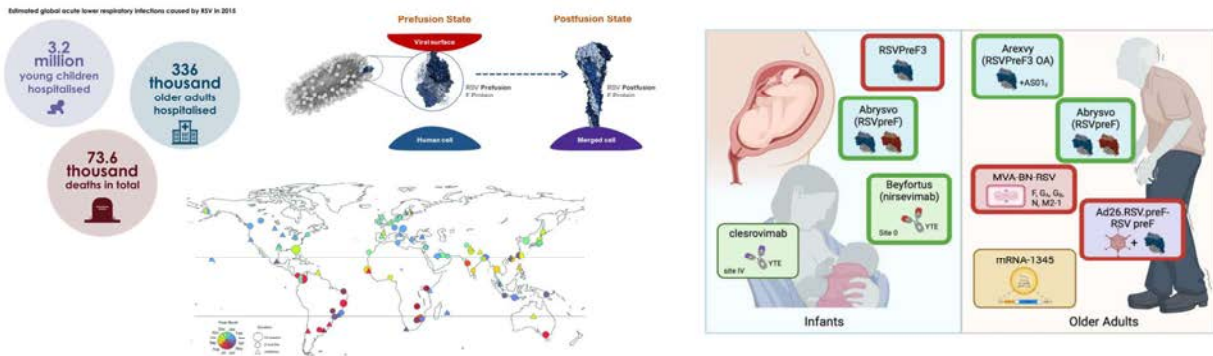
SK Bioscience mRNA Vaccine Project

RSV Vaccine Development



Respiratory Syncytial Virus

- ✓ Human respiratory syncytial virus (RSV) is a common virus that causes respiratory tract infections in people of all ages.
- ✓ In infants and young children, RSV can cause severe bronchiolitis, which can sometimes be fatal.
- ✓ Since infections do not provide complete immunity, they are usually not serious, but reinfection is common.
- ✓ Recently, GSK's Arexvy and Pfizer's Abrysvo are approved for people aged 60 years and older.
- ✓ SK bioscience applied SKY mRNA Platform and own prefusion mutation for RSV vaccine development

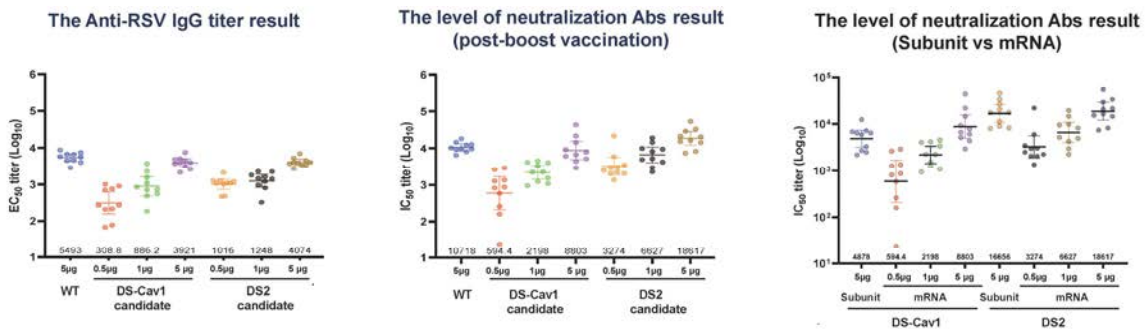


RSV Vaccine Development



Respiratory Syncytial Virus

- ✓ Previously Known Prefusion mutant forms (DS-Cav1 and DS2) were applied to SKY mRNA platform.
- ✓ FRNT and ELISA assay conducted to evaluate antibody response.
- ✓ Successful neutralization and total antibody response observed in SKY mRNA Platform.
- ✓ Neutralization antibody response of mRNA vaccine was comparable to that of subunit vaccine
- ✓ SK Bioscience will apply own prefusion mutation for preclinical test





Further Plan

mRNA therapy

Further Development

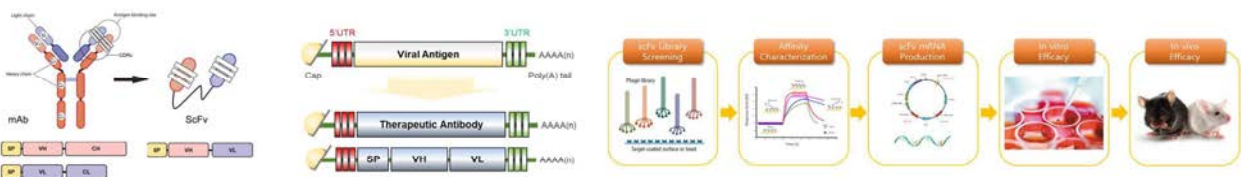


Prophylactic Vaccine

- ✓ Japanese encephalitis virus (JEV) vaccine
 - Evaluation of safety and stability of JEV vaccine candidate is underway.
 - IND filing and Phase 1 trials are scheduled for 2024.
- ✓ Respiratory syncytial virus (RSV) vaccine
 - Immunogenicity of SK's prefusion mutation will be assessed.
 - Following the selection of the RSV vaccine candidate, NCS study will be conducted.

mRNA therapies

- ✓ Antibody therapies have become an important class of therapeutics in recent years.
- ✓ SK Bioscience plans to utilize scFv (single-chain variable fragment) with its SKY mRNA platform.
- ✓ It is anticipated that mRNA antibodies will expand treatment options for a broader range of patients..



03

RSV 백신 연구개발 전략

김석규 이사
유바이오로지스



Speaker



Seok-Kyu Kim

- ✓ EuBiologics
- ✓ Director / Head of Business Development

🔍 EDUCATION:

- 2012 MBA, Korea University

🔍 PROFESSIONAL EXPERIENCE:


- 2018 ~ Present Director, EuBiologics
- 2007 ~ 2018 Professional, LG Chem

🔍 Topic

EuBiologics' Vaccine Platform & RSV Vaccine Development

🔍 Abstract

In order for effective vaccine development, there must be a distinctive vaccine platform others could not. EuBiologics is currently advancing the development of an RSV vaccine using its own TLR-4 Agonist (MPLA) adjuvant(immune enhancer) produced in-house, and SNAP (Spontaneous Nano-liposome Antigen Particle) technology, enabling the prompt antigen display in liposomes. All non-clinical trials have been successfully completed and EuBiologics obtained phase 1 IND approval from the Korean Ministry of Food and Drug Safety in January 2023. In this presentation, I aim to introduce Eubiologics' cutting-edge vaccine platform, its diverse vaccine development portfolio, and the results from the non-clinical research on the RSV vaccine.




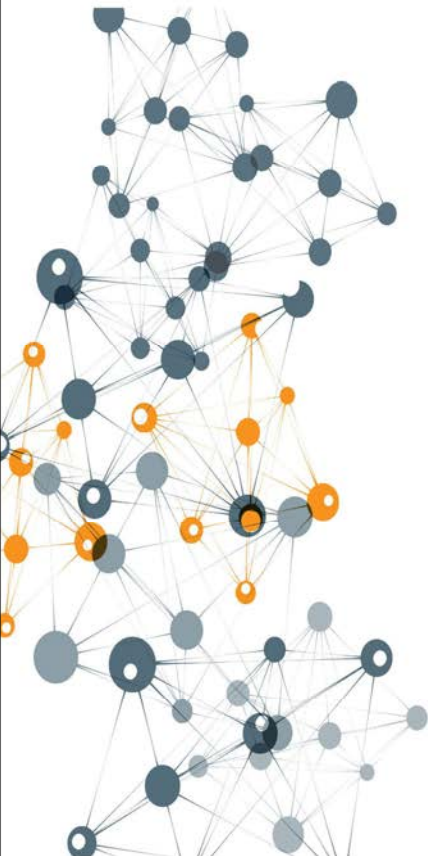
For Health that lasts a lifetime!
eubiologics

Development of Respiratory Syncytial Virus (RSV) vaccine

MAR 2024


S. K. Kim


www.eubiologics.com



For Health that lasts a lifetime!
eubiologics

- I. EuBiologics Company Overview**
- II. Business Case**
- III. Platform Technology: EuVCT™, EuIMT™**
- IV. Vaccine Pipeline**
- V. Development of RSV vaccine**
- VI. Conclusion**


www.eubiologics.com

I. EuBiologics Company Overview



EuBiologics is a publicly traded biopharmaceutical company based in South Korea focusing on vaccine development and supply, immuno-therapeutics development for global public health.

Company Profile

Establishment	10 th March, 2010
Business Place	HQ: Seoul, South Korea Facility - Two Manufacturing sites in Chuncheon - R&D Center in Chuncheon
No. of Employee	Over 320
Market Capital	USD 340M Listed in KOSDAQ since Jan 2017
Business Area	- Vaccine Development, Manufacturing & Supply - CRMO(Contract R&D and Manufacturing Organization)

Plant



[C-Plant]



[V-Plant, R&D Center]

[Facility and Capacity]

- C Plant : Oral Cholera Vaccine-DS & DP (33M doses/y)
: EuCorvac-19 Vaccine-DS (200M doses/y, 1,000L*2 lines of Animal cell culture line)
- V Plant : Bacterial Vaccine Line- DS(Total 200M doses/y)
→ rCRM197, TCV, MCV, PCV and others
: Oral Cholera Vaccine-DS & DP (32~50M doses/y)
-under construction by support of BMGF
: CMO for API ; Suite#4, 5 (50/100/200/500/1,000-L Lines)

II. Business Case: OCV & Public Vaccines



EuBiologics becomes the largest supplier of oral cholera vaccine(**EuVichol-Plus**) shipping over 110M doses to LMICs through UNICEF, as a result of successful public/private product development partnership. EuBiologics has continued to scale-up and developed programmatically suitable presentation and new vaccines at affordable pricing to meet the needs of public markets and responds to infectious diseases outbreak promptly.

Date	OCV Development History
Sep 2010	OCV License Agreement with International Vaccine Institute
Aug 2014	Non-inferiority trial (Euvichol vs Shanchol) in the Philippines
Dec 2015	Euvichol WHO PQ (6M doses per annum)
Sep 2016	PQ variation approval (600L scale-up allowing 25M & thimerosal removal)
Aug 2017	PQ variation approval (Plastic Tube)
~2024	Expects Euvichol-S (Simplified) PQ achieving cost reduction & capacity increase
~Jun 2025	Scale up for DS and DP ongoing, capacity doubled up to 80~100M funded by BMGF

Vaccine	Development Stage	Commercialization Strategy
Cholera Conjugate Vaccine	<ul style="list-style-type: none"> Phase I study started in Oct 2022 Collaboration with International Vaccine Institute and Massachusetts General Hospital 	<ul style="list-style-type: none"> Targeting children in LMICs to complement OCV



Euvichol (Glass Vial)



Euvichol-Plus (Plastic Tube)

→ **Game changer**
; Weight, Volume down
; Easy Administration

II. Business Case: Immuno-stimulants



EuBiologics engages in active research and development in the fields of immunology and life sciences, and produces a carrier protein (**rCRM197**) for the polysaccharide conjugation vaccines and various adjuvant system of recombinant TLR4 agonist (**MPLA**) for enhancing the vaccine efficacy.

[EuCRM-197]



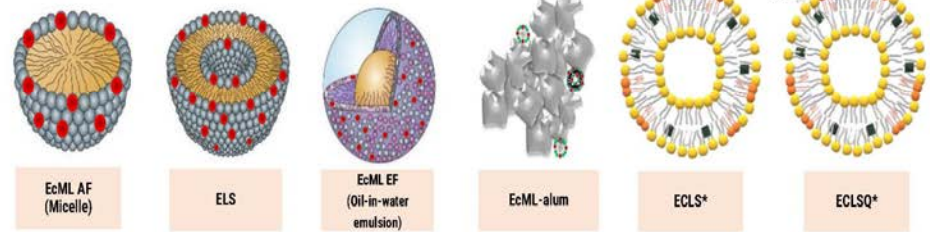
<Essential Material for conjugation with bacterial polysaccharides>

- Method for Production of rCRM197 by recombinant E. coli ; Patent No.: 10-2048456 (KR)
- Expression Method of CRM197 Protein ; Patent No.: 10-2099342 (KR)

[EcML]



<Adjuvant System, containing EcML>



*Collaboration with POP Biotechnologies, Inc.

Abbreviation:

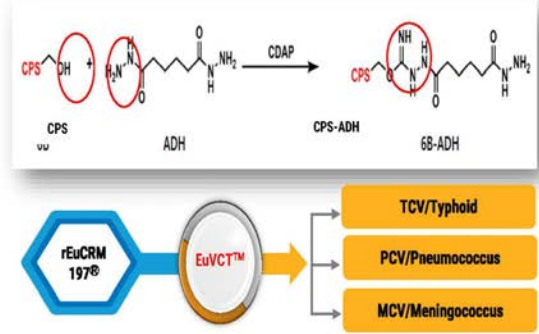
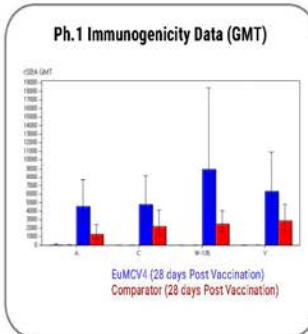
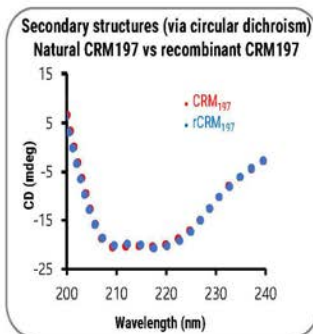
E: EcML, C: CoPoP, Q: QS21, LS: Liposome

III-1. Platform Technology: EuVCT™



EuVCT™: EuBiologics Vaccine Conjugation Technology

Development & in-house production of recombinant CRM197 and conjugation know-how leads successful development of conjugate vaccines which demonstrate higher efficacy at lower cost




Patents & Publication

- 1) Method for Production of rCRM197 by recombinant E. coli - Patent No.: 10-2048456 (KR)
- 2) Expression Method of CRM197 Protein - Patent No.: 10-2099342 (KR)
- 3) An open-label, comparative, single dose, clinical Phase I study to assess the safety and immunogenicity of typhoid conjugate vaccine (Vi-CRM197) in healthy Filipino adults.
Vaccine. 2021 May 6;39(19):2620-2627. Seuk Keun Choi et al.
- 4) Generation of a human monoclonal antibody to cross-reactive material 197 (CRM197) and development of a sandwich ELISA for CRM197 conjugate vaccines.
J. Microbiol. Biotechnol. 2018, vol.28, no.12, pp. 2113-2120. Dain Kim et al.

III-1. Platform Technology: EuVCT™



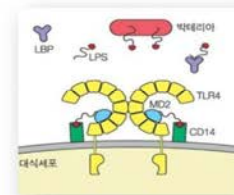
Vaccine	Development Stage	Commercialization Strategy
Typhoid conjugate vaccine (EuTYPH-C)	<ul style="list-style-type: none"> Completed Phase III study in the Philippines, non-inferiority demonstrated to Typbar TCV Additional Phase III study ongoing in Africa, funded by RIGHT Foundation 	<ul style="list-style-type: none"> Expect PQ in 2024 Targeting LMICs through UNICEF 
Quadrivalent Meningococcal Conjugate Vaccine(ACWY)	<ul style="list-style-type: none"> Phase I study completed, safety and immunogenicity to Menveo demonstrated 	<ul style="list-style-type: none"> License out
Pentavalent Meningococcal Conjugate Vaccine(ACWY + X)	<ul style="list-style-type: none"> Phase I study in progress Collaboration with PATH funded by BMGF and RIGHT Foundation 	<ul style="list-style-type: none"> Expect PQ in 2027 Targeting LMICs through UNICEF
Pneumococcal Conjugate Vaccine (15-valent)	<ul style="list-style-type: none"> Phase I study completed 	<ul style="list-style-type: none"> License out

III-2. Platform Technology: EuIMT™



EuIMT™: EuBiologics Immuno-Modulation Technology

- Monophosphoryl Lipid A produced from recombinant *E.coli* (EcML)
 - A potent vaccine adjuvant with effectiveness comparable to other MPLAs
 - Boosting immune responses by acting as a **TLR4 agonist**.
 - Recombinant *E.coli* directly producing MPLA
 - **Simple manufacturing process, low cost and scalable**



Natural form (LPS) Modified form (EcML)

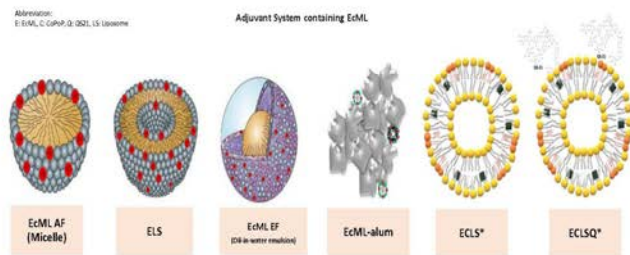
Production of EcML

Genetic engineering

1) Bacterium producing monophosphoryl lipid A and method of producing monophosphoryl lipid A by using bacterium
 - Patent No.: 10-1761348(KR) / US10308945 (US)

2) Bacteria constitutively producing monophosphoryl lipid A, and method for the production of monophosphoryl lipid A using the same
 - Patent No.: 10-2019331(KR) / US10557156 (US)

Product	Composition
MPL(GSK)	Heterogeneous; Hexa acyl 20~40%, Penta acyl 25~60%, Tetra acyl 15~35%, Hepta acyl ~ 0.5%
GLA(IDRI)	Homogeneous; Hexa acyl 100%
EcML (EuBiologics)	Nearly Homogeneous Hexa acyl ≥ 90%, Penta+Tetra acyl 10~20%



III-2. Platform Technology: EuIMT™



EuIMT™: EuBiologics Immuno-Modulation Technology

Potent Nanoliposome Vaccine Adjuvant: ECLS & ECLSQ

1. Nanoliposome based Adjuvant

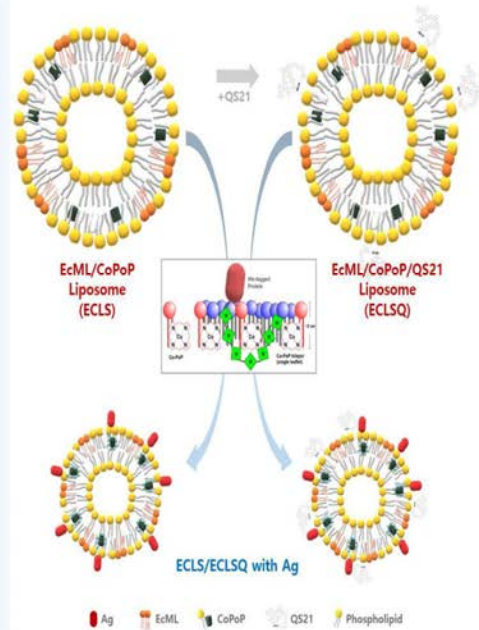
- Similar to lipid & cholesterol in human body → **No safety concern**
- Liposome DDS(Drug Delivery System) is widely applied in the field of vaccines and therapeutics.

2. Monophosphoryl Lipid A produced from recombinant *E.coli* (EcML)

- **A potent vaccine adjuvant** with effectiveness comparable to other MPLAs
→ boosting immune responses by acting as a **TLR4 agonist**.
- Recombinant *E.coli* directly producing MPLA
→ **Simple manufacturing process, low cost and scalable**

3. Versatile Antigen Display using CoPoP (SNAP platform)

- Simple nanoparticle antigen display technology using CoPoP (similar to VLP)
- Diverse antigen anchored on the liposome surface
→ **Enhanced uptake by antigen presenting cells**



IV. Vaccine Pipeline



EuBiologics has a pipeline of vaccines leveraging its platform technologies, **EuVCT™** and **EuIMT™**

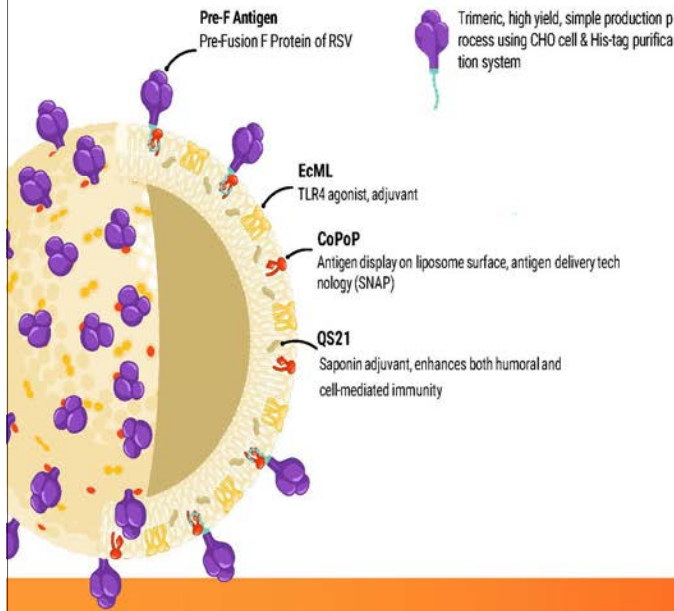
Product	Discovery	Pre-clinical	Phase I	Phase II	Phase III	NDA	Launch	Remark	
EuVichol /EuVichol-Plus	1) TCV: Typhoid Conjugate Vaccine 2) PCV: Pneumococcal Conjugate Vaccine 3) MCV: Multivalent Meningococcal Conjugate Vaccine								
EuCRM197™	4) RSV: Respiratory Syncytial Virus 5) HZV: Herpes Zoster Virus 6) AD: Alzheimer Disease								
EuVCT	TCV ¹⁾							Sponsored by RIGHT Foundation Grant	
	PCV ²⁾							Open collaboration	
	MCV ³⁾							Sponsored by Korean Gov't BMGF/RIGHT Grant	
EcML™ (MPL-A, Novel Adjuvant)									
EuIMT	COVID-19							Sponsored by Korean Gov't	
	HPV							Sponsored by Korean Gov't	
	RSV ⁴⁾							Sponsored by Korean Gov't	
	HZV ⁵⁾							Sponsored by Korean Gov't	
	AD ⁶⁾								

V. Development of RSV vaccine: EuRSV

➤ EuRSV vaccine candidate, **IND approval by MFDS(Ministry of Food and Drug Safety)** on 2 January 2024

EP-RSV: Liposome-displayed Pre-fusion F

Prefusion F protein of RSV



TPP(Target Product Profile)

Description	EuRSV vaccine (EuRSV vaccine combined with RSV F protein and nano-particle adjuvant)	
	Strain	CHO (Chinese Hamster Ovary) cell
Antigen	RSV Prefusion F	
Name	EuRSV-1	EuRSV-2
API	RSV F (Low & High ds)	RSV F (Low & High ds)
Excipient (adjuvant)	EcML CoPoP QS21 /0.5mL/dose	EcML CoPoP /0.5mL/dose
Dosage form	Lyophilized	
Indication	Prevention of lower respiratory tract disease (LRTD) caused by Respiratory Syncytial Virus (RSV) in elderly people over 60 years of age	
Dosing schedule	0.5mL, IM, twice in 4-week interval (TBD)	
Storage condition	2 ~ 8°C	

V. Development of RSV vaccine: strategy

Basic Concept of EuRSV vaccine candidate

1. RSVF-E2 Antigen: pre fusion F protein

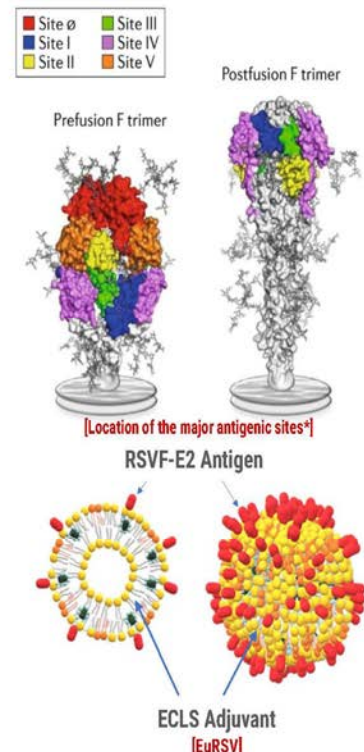
- High yield, simple production process using CHO cell & His-tag purification system

2. ECLS(+/- Q) Adjuvant (EuIMT™: EuBiologics Immuno-Modulation Technology)

- EcML: TLR4 agonist, Adjuvant
- CoPoP: Antigen display on liposome surface
- QS-21: saponin, Adjuvant

→ Leveraging adjuvant ECLS(+/- Q), only a small amount of antigen required

3. Presentation & Storage → Lyophilized, 2-8°C



*Ref. Respiratory syncytial virus entry and how to block it, NATURE Reviews | Microbiology, VOLUME17, APRIL 2019

VI. CONCLUSION



➤ Efficacy Study

- The efficacy study of EuRSV vaccine candidate was evaluated in cotton rat, mouse animal models.
- EuRSV vaccine candidate demonstrated **excellent humoral and cellular immunity**.

➤ Toxicity Study

- There is **no toxicity** caused by EuRSV vaccination, suggesting its safety profile.
- EuRSV vaccine candidate has **low risk of Vaccine-Associated Enhanced Disease(VAERD)**

➤ In summary, the non-clinical outcomes have led to the approval of the Phase I clinical trial by MFDS.

➤ Future plan

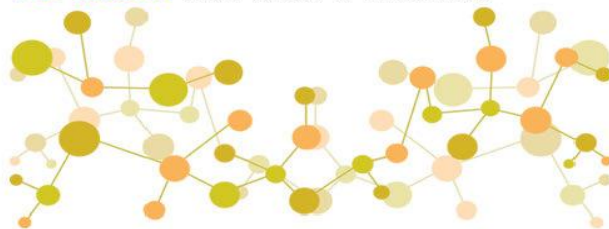


Premium vaccine development FROM 'EUPOP Life Sciences'

	Year	2024	2025	2026	2027
EuRSV Vaccine Development	Phase I	In KOREA			
	Phase II & III		In USA or AUS (EUPOP)		

Thank You

일생 동안 지속하는 **인류의 건강**에 기여
For health that lasts a lifetime!



eubiologics

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04

신종변이 대응 코로나19 다가백신 개발 전략

강창울 대표
셀리드



Speaker



Chang-Yuil Kang

- ✔ Cellid Co., Ltd.
- ✔ Chief Executive Officer

🔍 EDUCATION:

- 1987 Ph.D.in Immunology(State University of New York at Buffalo, USA)
- 1981 M.S.in Microbiology/Pharmacy (SeoulNational University, Seoul, Korea)
- 1977 B.S.in Pharmacy (Seoul National University, Seoul, Korea)

🔍 PROFESSIONAL EXPERIENCE:

- 2014 ~ Present Chief Executive Officer, Cellid Co., Ltd.
- 2020 ~ Present Professor Emeritus, College of Pharmacy, Seoul National University
- 2020 ~ Present Non-Executive Director, Handok Co., Ltd.
- 1994 ~ 2020 Professor, College of Pharmacy, Seoul National University
- 2009 ~ 2010 Team Leader of T/F, Bio-Medical Dep, Presidential Council for Future & Vision
- 2005 ~ 2005 Secretary-General, International Society of Cytokines.
- 2003 ~ 2004 President, Korean Society of Immunizations
- 1987 ~ 1994 Scientist, IDEC Pharmaceutical Corporation(Currently, Biogen-IDEC), USA

🔍 Topic

Strategy to develop effective multivalent COVID-19 vaccines against emerging variants based on adenovirus vector platform

🔍 Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron strain has evolved into highly divergent variants. We developed chimeric adenoviral vector (Ad5/35)-based coronavirus disease 2019 (COVID-19) vaccines, which are replaced with a serotype 35 fiber based on the backbone of serotype 5 adenovector for better antigen delivery. Our vaccine can effectively deliver spike genes to antigen-presenting cells through CD46 binding, which leads to effectively stimulating CD4+ T cells, CD8+ T cells, and B cells in either direct or indirect ways. Our AdCLD-CoV19-1 OMI vaccine, encoding the spike protein of the BA.1 variant, is currently in Phase 3 clinical trials. Additionally, we developed multivalent Omicron variant-specific vaccines using phylogenetic trees and antigenic cartography and demonstrated their superior ability to neutralize a wide range of variants in mice and macaques. These data suggest that the developed multivalent vaccines enhance immunity against circulating Omicron subvariants and effectively elicit neutralizing antibodies across a broad spectrum of SARS-CoV-2 variants. Our ongoing research explores combinations of next-generation multivalent vaccines to confer broad protection against newly emerging subvariants.

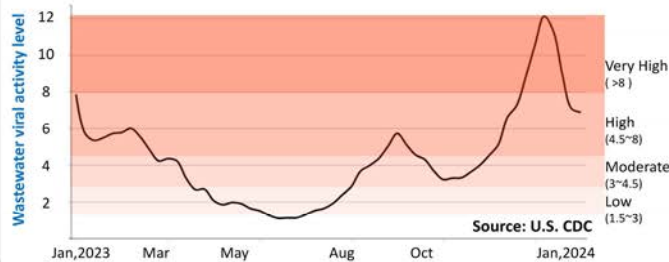


Strategy to develop effective multivalent COVID-19 vaccines against emerging variants based on adenovirus vector platform

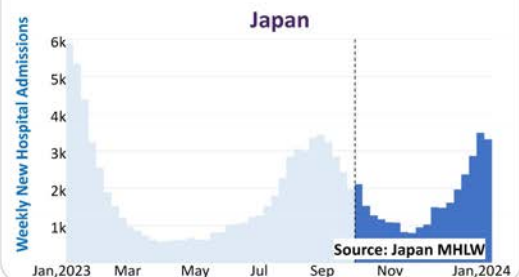
Chang-Yuil Kang, Ph.D.
Cellid Co., Ltd.

Prolonged COVID-19 Pandemic

• COVID-19 Wastewater Viral Level

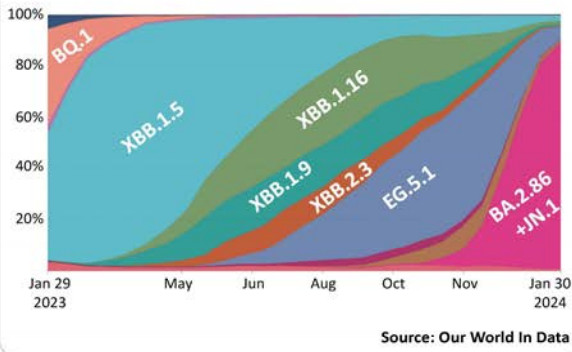


• COVID-19 new hospital admissions

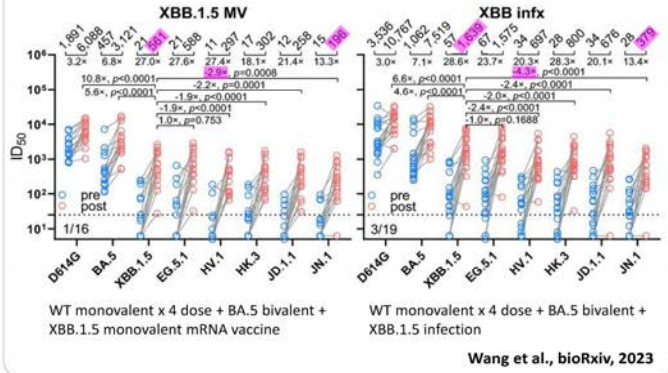


Limitations of Current Vaccines

- Evolution of SARS-CoV-2 Variants (2023-2024, United States)



- Immune evasion of novel COVID-19 variants

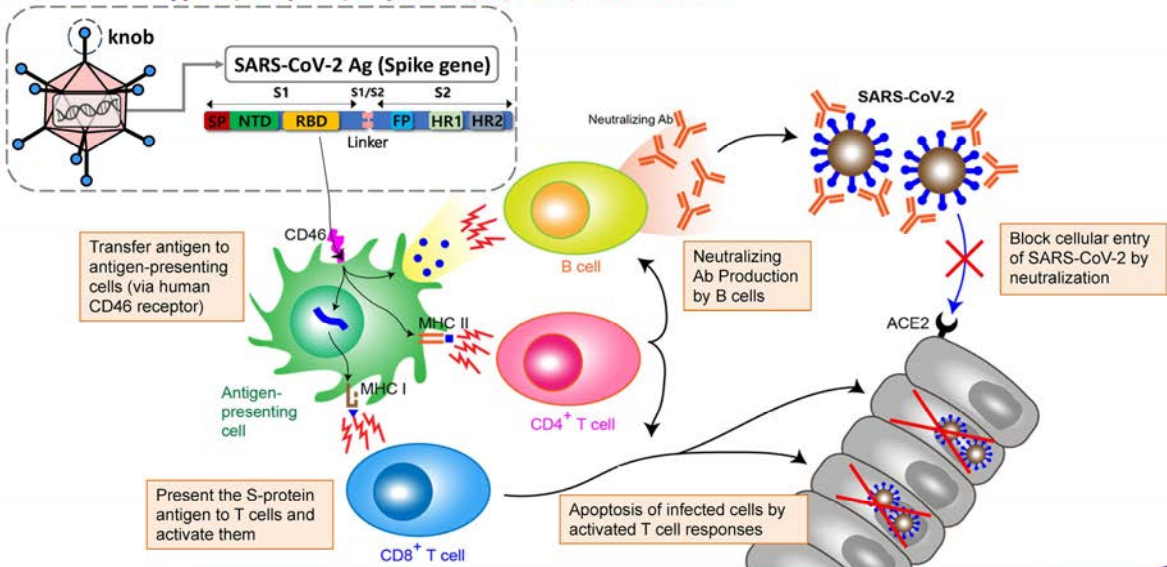


Emerging variants such as JN.1 may reduce the efficacy of current vaccines.

→ New vaccine development strategy that can defend against emerging variants is essential.

CELLID's COVID-19 vaccine platform

Adenovirus type 5/35 (Ad5/35) Cellid's proprietary vector backbone



Response to variants: Variant Vaccine Library

Table 1. Variant-specific vaccine library

Variant	Vaccine Plasmid	Immunogenicity study	Variant	Vaccine Plasmid	Immunogenicity study
Wild type	Completed	Completed	XBB.1.5.1	Completed	Standby
Beta	Completed	Completed	XBB.1.16	Completed	Standby
Gamma	Completed	Completed	XBB.2.3	Completed	Completed
Delta	Completed	Completed	FD.2	Completed	Standby
Lambda	Completed	Completed	EG.1	Completed	Standby
Mu	Completed	Completed	XBB.1.5.10	Completed	Standby
BA.1	Completed	Completed	XBB.1.16.1	Completed	Standby
BA.2	Completed	Completed	EG.5	Completed	Standby
BA.2.12.1	Completed	Completed	XBB.1.5.68	Completed	Standby
BA.4.1	Completed	Completed	XBC	Completed	Standby
BA.5	Completed	Completed	XBC.1.6	Completed	Standby
BA.2.75	Completed	Completed	EU.1.1	Completed	Standby
BA.4.6	Completed	Standby	EG.5.1	Completed	Completed
BA.2.75.2	Completed	Standby	XBB.1.16.6	Completed	Standby
BF.7	Completed	Standby	FL.1.5.1	Completed	Standby
BQ.1	Completed	Standby	BA.2.86	Completed	Completed
BQ.1.1	Completed	Completed	JN.1	Completed	Completed
XBB	Completed	Completed	HK.3	Completed	Standby
BN.1	Completed	Completed	DV.7.1	Completed	Standby
BA.2.3.20	Completed	Standby	HV.1	Completed	Standby
XBB.1.5	Completed	Completed	HF.1	Completed	Standby
BA.2.3.20	Completed	Standby	GK.1.1	Completed	Standby
CH.1.1.1	Completed	Standby	JD.1.1	Completed	Standby
XBF	Completed	Standby	XCU	Completed	Standby

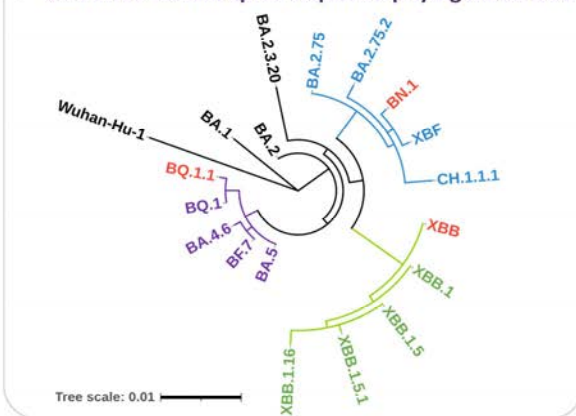
Table 2. Pseudovirus library for neutralization test

Variants	Pseudovirus	Manufacturing	Evaluation	Variants	Pseudovirus	Manufacturing	Evaluation
-	Wild type	Completed	Completed	Omicron subvariant	BN.1	Completed	Completed
Common	B.1.1.7/B.1.351/P.1/B.1.617.2	Completed	Completed		XBB	Completed	Completed
α/βγ common	B.1.1.7/B.1.351/P.1	Completed	Completed		XBB.1.5	Completed	Completed
βγ common	B.1.351/P.1	Completed	Completed		BA.2.3.20	Completed	Completed
Beta (partial)	B.1.351 (Partial)	Completed	Completed		CH.1.1.1	Completed	Completed
Delta (partial)	B.1.617.2 (Partial)	Completed	Completed		XBF	Completed	Completed
Delta (partial)	B.1.617.2 (Partial)	Completed	Completed		XBB.1.5.1	Completed	Completed
Alpha	B.1.1.7	Completed	Completed		XBB.1.16	Completed	Completed
Beta	B.1.351	Completed	Completed		XBB.2.3	Completed	Completed
Gamma	P.1	Completed	Completed		FD.2	Completed	Completed
Delta	B.1.617.2	Completed	Completed		EG.1	Completed	Completed
Delta plus (Delta subtype)	AY.1 AY.4 AY.4.2 AY.43 AY.69	Completed	Completed		XBB.1.5.10	Completed	Standby
Lambda	C.37	Completed	Completed		XBB.1.16.1	Completed	Standby
Mu	B.1.621	Completed	Completed		XBC	Completed	Standby
IHU	B.1.640.2	Completed	Completed		XBC.1.6	Completed	Completed
Omicron	B.1.1.529	Completed	Completed		EG.5.1	Completed	Completed
Stealth Omicron	BA.2	Completed	Completed		EU.1.1	Completed	Standby
	BA.2.12.1	Completed	Completed		FL.1.5.1	Completed	Completed
	BA.4.1	Completed	Completed		EG.5	Completed	Standby
	BA.4/BA.5	Completed	Completed		XBB.1.16.6	Completed	Standby
	BA.2.75	Completed	Completed		XBB.1.5.68	Completed	Standby
	BA.4.6	Completed	Completed		BA.2.86	Completed	Completed
Omicron subvariant	BA.2.75.2	Completed	Completed		HK.3	Completed	Completed
	BF.7	Completed	Completed		DV.7.1	Completed	Standby
	BQ.1	Completed	Completed		HV.1	Completed	Completed
	BQ.1.1	Completed	Completed		HF.1	Completed	Ongoing
					JN.1	Completed	Completed
					GK.1.1	Ongoing	Ongoing
					JD.1.1	Ongoing	Ongoing
					XCU	Ongoing	Ongoing

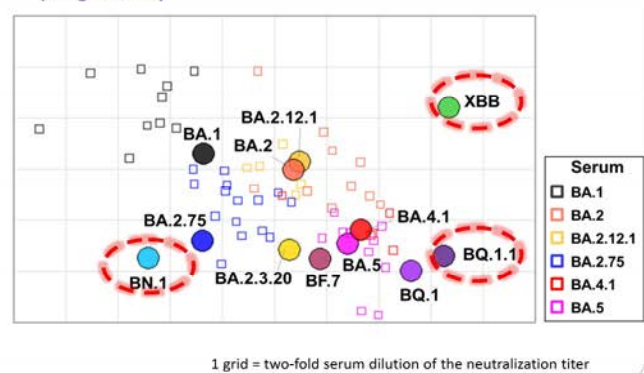
Ad5/35 platform can be easily modified to respond variants by replacing antigen to that of VOCs.

Clustering based on the variant sequence and the immunogenicity of the vaccine

COVID-19 variant spike sequence phylogenetic tree



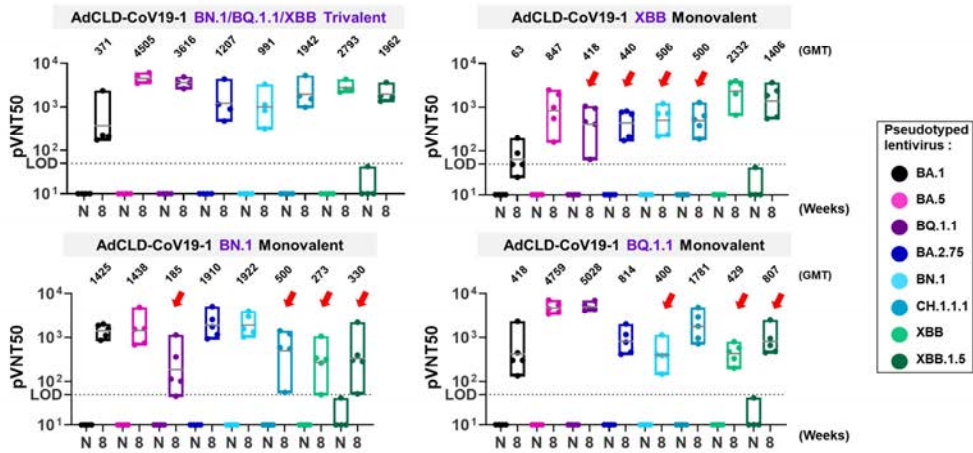
COVID-19 variant spike antigenic cartography map (Single shot)



Through the variant sequence and antigenic cartography map-based clustering produced by cross-neutralization activity, we selected **XBB, BN.1, and BQ.1 trivalent vaccines as the candidate for the multivalent vaccine.**

Next-generation COVID-19 vaccine development strategy: Multivalent Vaccine

- Immunogenicity of Omicron subvariant vaccines **after single administration**

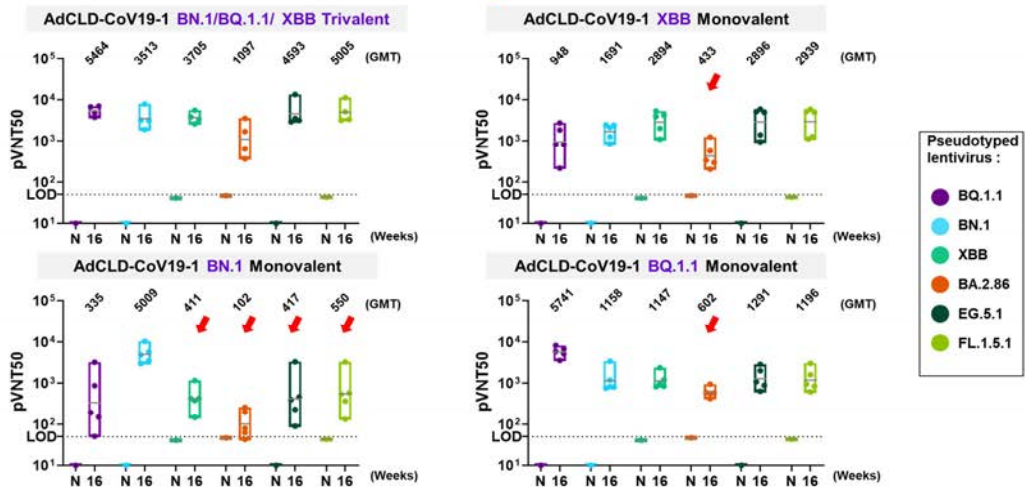


- AdCLD-CoV19-1 XBB/BN.1/BQ.1.1 trivalent vaccine enhanced cross-neutralizing activities.

Chang et al., 2024, Proc Natl Acad Sci U S A. (in press)

Next-generation COVID-19 vaccine development strategy: Multivalent Vaccine

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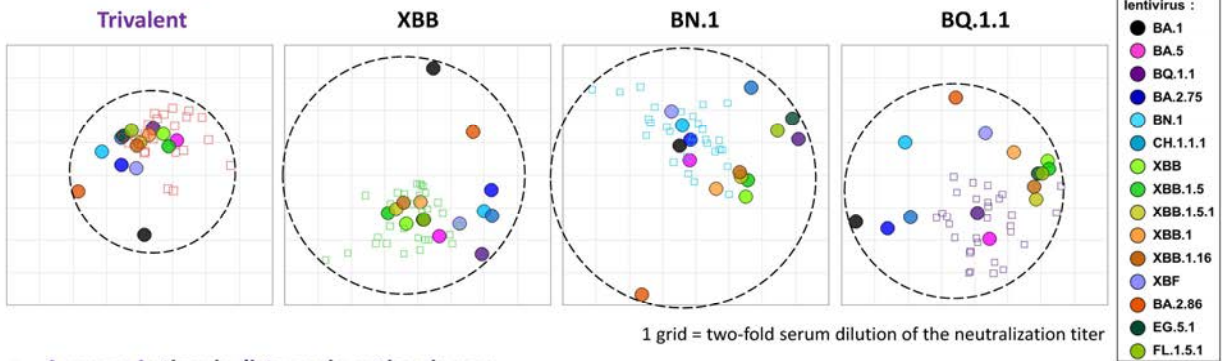


- AdCLD-CoV19-1 XBB/BN.1/BQ.1.1 trivalent vaccine enhanced cross-neutralizing activities.

Chang et al., 2024, Proc Natl Acad Sci U S A. (in press)

Next-generation COVID-19 vaccine development strategy: Multivalent Vaccine

• Antigenic cartography map



1 grid = two-fold serum dilution of the neutralization titer

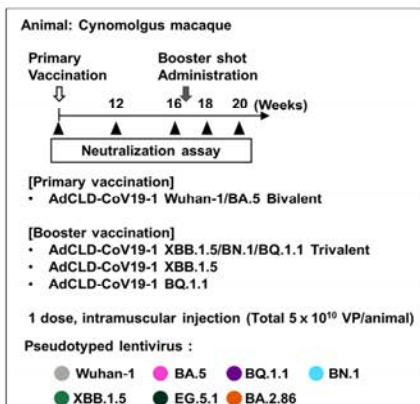
• Average Antigenic distance in antigenic map

	Trivalent	XBB	BN.1	BQ.1.1
Variant-Variant	1.6	2.4	2.3	3.2
Serum-Variant	1.2	1.6	1.9	2.4

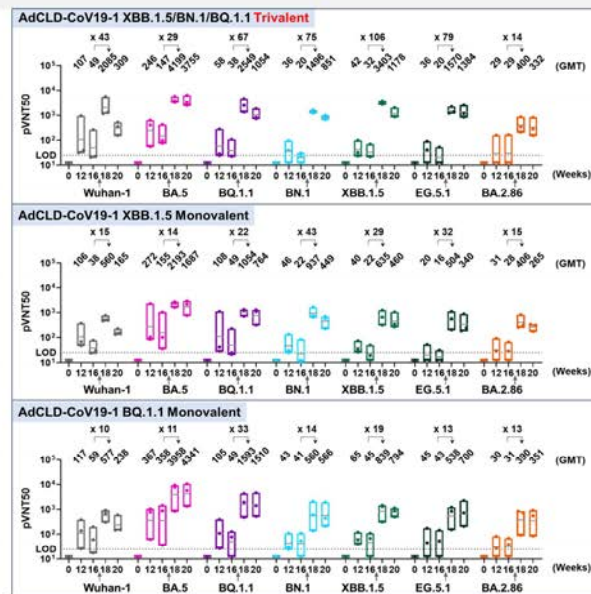
• By XBB/BN.1/BQ.1.1 trivalent vaccine, a **wide range of neutralizing antibodies** was produced, and **antigenic distance was reduced**.

Trivalent(XBB.1.5/BN.1/BQ.1.1) booster vaccine in non-human primates

• Immunogenicity of Omicron subvariant vaccines as a booster in *Cynomolgus macaque*

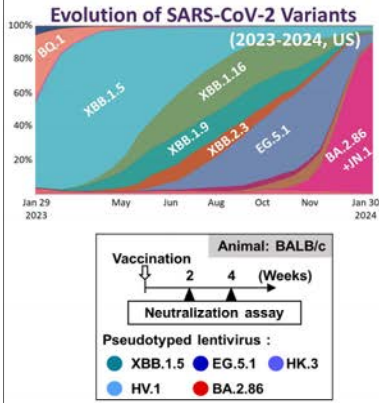


• By XBB.1.5/BN.1/BQ.1.1 trivalent vaccine as a booster, a **wide range of neutralizing antibodies** was produced.

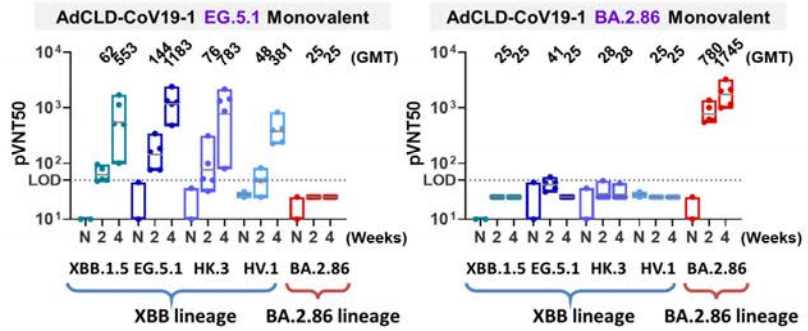


Chang et al., 2024, Proc Natl Acad Sci U S A. (in press)

Updated Vaccine to Response Emerging Variants



- Immunogenicity of Omicron subvariant vaccines after single administration

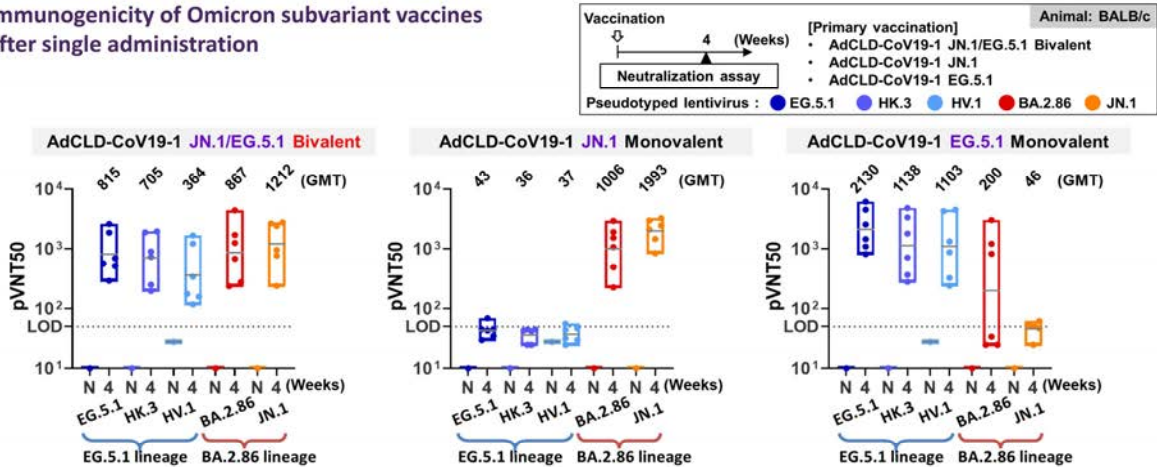


- EG.5.1 and BA.2.86 vaccines exhibit reduced cross-neutralization ability against each other.

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Updated Multivalent Vaccine - Bivalent(JN.1/EG.5.1) vaccine

- Immunogenicity of Omicron subvariant vaccines after single administration



- AdCLD-CoV19-1 JN.1/EG.5.1 bivalent vaccine enhanced cross-neutralizing activities.

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Summary

- The phase III clinical study of AdCLD-CoV19-1 OMI (BA.1) is currently ongoing.
- Ad5/35 platform can be easily modified to respond to variants by replacing the antigen with that of VOCs.
- We found that the trivalent vaccines could efficiently produce broadly neutralizing antibodies against most variants with a single administration and reduced antigenic distance compared to the monovalent vaccine.
- We found that EG.5.1 and JN.1 vaccines exhibit reduced cross-neutralization ability against each other. To enhance the cross-neutralizing activities to a wide range of variants, JN.1/EG.5.1 bivalent vaccines are needed.
- Ongoing efforts in vaccine development are crucial to address the challenges posed by currently circulating variants.

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CELLID

LEADER IN CELL-BASED THERAPEUTIC VACCINE

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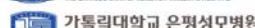
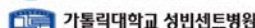
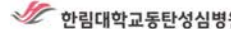
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