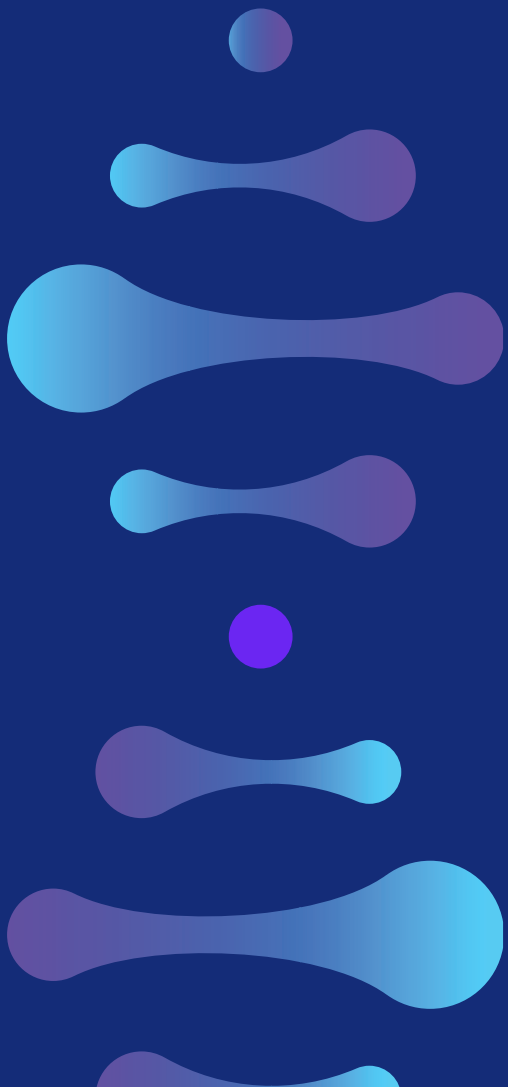
2020

# 15th ANNUAL MEETING OF KOREAN SOCIETY OF GENE AND CELL THERAPY

## 제15회 KSGCT 정기학술대회



**주최**

한국유전자세포치료학회(KSGCT) | 식품의약품안전처 식품의약품안전평가원
단국대학교 차세대오믹스연구소 | 충남대학교 유전자의약 이노베이션센터

**후원**

동아대학교 의과대학 | 한국연구재단 | (주)헬릭스미스 | 알지노믹스(주)
아이씨엠(주) | 안전성평가연구소 | (주)툴젠 | (주)젠셀메드 | (주)올릭스
(주)씨드모젠 | 부산대학교 혈관성질환 세포유전자치료센터 | 코아스템(주)
진원생명과학(주) | (주)지플러스생명과학 | (주)아바테라퓨틱스 | 써모피셔 사이언티픽
Cytiva | 찰스리버래보래트리즈 (주)다인토탈솔루션 | 원국제특허사무소 | (주)대일사이언스

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## 제15회 KSGCT 정기학술대회

**주최**

한국유전자세포치료학회(KSGCT) | 식품의약품안전처 식품의약품안전평가원
단국대학교 차세대오믹스연구소 | 충남대학교 유전자의약 이노베이션센터

**후원**

동아대학교 의과대학 | 한국연구재단 | (주)헬릭스미스 | 알지노믹스(주)
아이씨엠(주) | 안전성평가연구소 | (주)툴젠 | (주)젠셀메드 | (주)올릭스
(주)씨드모젠 | 부산대학교 혈관성질환 세포유전자치료센터 | 코아스템(주)
진원생명과학(주) | (주)지플러스생명과학 | (주)아바테라퓨틱스 | 써모피셔 사이언티픽
Cytiva | 찰스리버래보래트리즈 (주)다인토탈솔루션 | 원국제특허사무소 | (주)대일사이언스

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15th ANNUAL MEETING OF
**KOREAN SOCIETY OF GENE AND CELL THERAPY**

## Contents

# *ORGANIZATION CHART*

| | |
|---|---|
| **회장** | 이성욱 단국대학교 |
| **부회장, 운영위원장** | 권희충 원자력의학원 |
| **부회장** | 강형진 서울대학교 |
| **고문** | 김연수 충남대학교 / 김선영 서울대학교 / 이춘택 서울대학교 / 이제호 차병원<br>염영일 한국생명공학연구원 / 김주항 분당차병원 / 박기랑 충북보건과학대학교<br>황태호 부산대학교 |
| **사무국장** | 염선분 충남대학교 |
| **사무국** | 정동민, 유해나, 유용철 충남대학교 |
| **학술위원장** | 김대원 연세대학교 |
| **총무위원** | 최진우 경희대학교 / 김재호 부산대학교 |
| **재무위원** | 강주현 원자력의학원 |
| **학술1분과위원** | 정재균 ㈜헬릭스미스 / 김수정 코오롱생명과학 / 우동훈 넥셀<br>임광일 숙명여자대학교 / 김석중 툴젠 / 김종민 숙명여자대학교 / 장재형 연세대학교 |
| **학술2분과위원** | 이희란 울산대학교 / 박태관 순천향대학교 / 최경주 차의과대학교<br>권진아 에이치엘비 / 윤기태 부산대학교 / 정문섭 진원생명과학 |
| **국제협력위원** | 유승신 ㈜헬릭스미스 / 김대원 연세대학교 |
| **정보편집위원** | 박용석 연세대학교 |
| **산학협력위원** | 박현숙 세포바이오 / 김경숙 코아스템 |
| **기획위원** | 진현탁 SL BIGEN / 황동연 차의과학대학교 |

# *WELCOME ADDRESS*

2020년 한국유전자세포치료학회 (KSGCT) 정기학술대회에 많은 관심과 참여를 해주신 회원 여러분들께 감사와 환영 말씀을 전합니다. 우선 올해 전세계적으로 계속 피해를 입히고 있는 초유의 COVID19 감염 대유행 상황에서 여러분들의 건강을 진심으로 기원합니다. 이러한 COVID19 상황으로 인하여 학회 역사상 처음으로 온라인 학술대회를 개최하게 되었읍니다.

최근 이와 같은 전세계 감염 대유행의 불안정한 사태로 인하여 국내외 각 분야 연구개발 진척이 주춤한 상황에서도, 미국 및 유럽 등 선진국에선 유전자세포 치료제 분야 등 첨단 바이오 개발분야에 있어서는 괄목할 성장을 이루고 있습니다. 국내에서는 올해 8월 유전자세포 치료제와 같은 첨단바이오의약품에 대한 안전관리 강화와 신속한 제품화를 지원하는 첨단재생바이오법 및 하위법령이 시행됨에 따라 현재 운영을 위한 각 관련위원회가 구성 중이어서 곧 세부적인 운영체계가 구축될 것으로 알고 있읍니다. 따라서 유전자세포치료제 분야의 R&D 활성화, 연구개발진들의 네트워크 조성 활성화, 임상 및 사업화 지원 프로그램 활성화, 규제당국과의 적극적 소통창구로서의 기능을 통하여 국내 개발 유전자세포치료제의 글로벌 경쟁력 획득의 주요 지원기관으로서의 저희 학회의 역할이 어느 때보다도 중요하게 대두되고 있다 하겠읍니다,

올해 15번째 맞는 정기학술대회는 이틀에 걸쳐 진행될 예정이며, 국내외 우수 연구개발자를 연사로 초청하여 첫날엔 non-viral gene therapy 세션, new trends in Gene & cell therapy 및 cell therapy 세션으로, 그리고 둘째 날은 neurodegenerative disease 세션, education 세션으로 CMC for cell & gene therapy, cancer targeting approach 세션 및 young scientist colloquium 세션으로 구성함으로써 유전자세포치료제 분야의 가장 최신 연구 및 개발 동향을 공유하는 자리를 마련하였습니다.

바쁘신 일정에도 흔쾌히 강연을 수락해 주신 국내외 연자 분들께 감사드리며, 또한 귀중한 시간을 할애하셔서 학술대회 준비에 기꺼이 전념해 주시고 헌신해 주신 운영위원진 모든 분들께도 진심으로 감사드립니다. 이틀 간의 정기학술대회 기간동안 참여해 주신 회원 여러분들의 소중한 경험과 과학적 교류를 상호 나누고 최신 연구 개발 정보를 공유하시는 자리가 되길 바라며, 이를 통해 회원 여러분에게 실질적인 도움과 나아가 산학연병 협력관계가 구축될 수 있길 기대합니다. 앞으로도 학회는 국내 유전자세포치료제 연구개발 분야의 발전을 위한 주요 지원기관으로서 그 역할을 다하기 위해 노력하겠으며, 이에 학회 회원 여러분들의 적극적인 관심과 참여를 부탁드립니다.

**2020년 11월**
**한국유전자세포치료학회 학회장 이 성 욱**

# *PROGRAMME*

## DAY1 NOV 5(Thursday)

| Time | Session | Organizer/연사(존칭생략) |
|---|---|---|
| 08:30~09:00 | Registration | 총무위원장 최진우 |
| 09:00~09:10 | Welcome Note by the President of KSGCT | 회장 이성욱 |
| 09:10~10:30 | Session 1 Non-Viral Gene Therapy | 좌장 : 이성욱(단국대학교 생명융합학과/알지노믹스(주)) |
| 09:10~09:40 | Targeting Thrombosis with RNA Therapeutics | Bruce Sullenger (Duke University Medical Center) |
| 09:40~10:05 | Therapeutic Development Using Asymmetric siRNAs | 이동기(성균관대학교) |
| 10:05~10:30 | Polymer-based Gene and Cell Delivery for Immunocancer Therapy | 김원종(포항공과대학교) |
| 10:30~10:45 | Intermission | |
| 10:45~12:00 | Session 2 New Trends in Gene & Cell Therapy | 좌장 : 권희충(KIRAMS) |
| 10:45~11:10 | Regulating Regulatory T Cells in the Tumor Immune Microenvironment for Enhancing Efficacy of Cancer Immunotherapy | 하상준(연세대학교) |
| 11:10~11:35 | ASO Therapy for Rare Disease | 김진국(KAIST) |
| 11:35~12:00 | Functional Assessment of BRCA1 Variants using CRISPR-based Base Editors | 김용섭(울산대학교 의과대학) |
| 12:00~13:30 | Lunch | |
| 13:30~14:45 | Session 3 Cell Therapy | 좌장 : 강형진(서울대학교 의과대학) 문경식(안전성평가연구소) |
| 13:30~13:55 | CAR-NK 유전자치료제의 파이프라인 기술개발 | 김태돈(한국생명공학연구원) |
| 13:55~14:20 | 세포 및 유전자치료제의 안전성평가 측면에서의 접근 | 박상진(안전성평가연구소) |
| 14:20~14:45 | Endogenous and Engineered NK Cell Therapy against Solid Cancer | 이경미(고려대학교 의과대학) |
| 14:45~16:00 | Poster Session | 학술위원장 김대원 |
| 16:00~17:00 | 총회 | 운영위원장 권희충 |

# DAY2 NOV 6(Friday)

| Time | Session | Organizer/연사(존칭생략) |
|---|---|---|
| 08:30~09:00 | Registration | 총무위원장 최진우 |
| 09:00~10:20 | Session 4 Neurodegenerative Disease | 좌장 : 이정훈(㈜헬릭스미스) |
| 09:00~09:30 | Practical Considerations for Recombinant Adeno-associated Virus Scalable Production | Robert Kotin (University of Massachusetts Medical School) |
| 09:30~09:55 | Potential Immune Cell Therapy for Chronic Pain | 오석배(서울대학교) |
| 09:55~10:20 | Propagation of Synucleinopathy in Parkinson's Disease | 이승재(서울대학교) |
| 10:20~10:30 | Intermission | |
| 10:30~12:00 | Education Session CMC for Cell & Gene Therapy | 좌장 : 김연수(충남대학교) |
| 10:30~11:10 | 유전자치료제 임상연구를 위한 고려사항 | 이소영(MFDS 식품의약품안전평가원) |
| 11:10~11:35 | 유전자치료제의 생체분포 및 RCL 부정시험에서의 검출 민감도 | 김수진(유전자의약 이노베이션센터) |
| 11:35~12:00 | CAR-T 개발을 위한 CMC 고려사항 | 정남철(파로스백신) |
| 12:00~13:30 | Lunch | |
| 13:30~14:45 | Session 5 Cancer Targetting Approach | 좌장 : 송재진(연세대학교) |
| 13:30~13:55 | HSV Retargeting to Cancer | 백현정(젠셀메드) |
| 13:55~14:20 | Oncospreading Dual-RRV System for Cancer Gene Therapy | 강문경(알티큐어) |
| 14:20~14:45 | Myeloid Modulation in Combination with Replication -controllable Oncolytic Vaccinia Virus Therapy | 황태호(부산대학교) |
| 14:45~15:45 | Young Scientist Colloquium (15분*4인) | 학술위원장 김대원 |
| 15:45~16:00 | Poster Award / Closing Remark | 회장 이성욱 |

2020

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## Session 1
# Non-Viral Gene Therapy

**Session 1**
**Non-Viral Gene Therapy**

# *Moderator*

**이 성 욱**
단국대학교 생명융합학과
알지노믹스(주)

**Bruce Sullenger** | **Duke University Medical Center**
Targeting Thrombosis with RNA Therapeutics

**이 동 기** | **성균관대학교/(주)올릭스**
Therapeutic Development Using Asymmetric siRNAs

**김 원 종** | **포항공과대학교**
Polymer-based Gene and Cell Delivery for Immunocancer Therapy

## General Information

| | |
|---|---|
| **Name** | Bruce Sullenger |
| **Affiliation** | Duke University Medical Center |
| **Office** | 001-919-684-6375 |
| **Phone** | 001-919-451-8921 |
| **E-mail** | bruce.sullenger@duke.edu |

## Educational Background

| Year | Institute |
|---|---|
| 1986 | B.S. Indiana University |
| 1991 | Ph.D. Cornell University |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 1991-1994 | University of Colorado, Postdoctoral Fellow with Thomas Cech |
| 1994-2020 | Duke University Medical Center, Department of Surgery |

## List of Recent Publications

1. **Sullenger B.A.**, Nair S. (2016). From the RNA World to the Clinic. ***Science***. Jun17;352(6292):1417-20.
2. Gunaratne R, Kumar S, Frederiksen JW, Stayrook S, Lohrmann JL, Perry K, Bompiani KM, Chabata CV, Thalji NK, Ho MD, Arepally G, Camire, RM, Krishnaswamy S, **Sullenger, BA** (2018). Multimodal, antidote-controllable anticoagulation for cardiopulmonary bypass using aptamer-drug pairs. ***Nature Biotechnology*** 2018 Aug;36(7):606-613
3. Nimjee SM, Dornbos, III D, Pitoc GA, Wheeler DG, Layzer JM, Venetos N, Huttinger A, Talentino SE, Musgrave NJ, Moody H, Rempel RE, Jones C, Carlisle K, Wilson J, Bratton C, Joseph ME, Khan S, Hoffman MR, Sommerville L, Becker RC, Zweier JL, **Sullenger BA** (2019). Preclinical Development of a VWF Aptamer to Limit Thrombosis and Engender Arterial Recanalization of Occluded Vessels. ***Molecular Therapy***. 2019 July 3, 27(7): 1228-1241.
4. Gray BP, Requena MD, Nichols MD, **Sullenger BA** (2020). Aptamers as reversible ligands for preparation of cells in their native state. ***Cell Chemical Biology***, 2020 Feb 20; 27(2): 232-244
5. **Sullenger BA** (2020). RGEN editing of RNA and DNA: The long and winding road from catalytic RNAs to CRISPR to the clinic. ***Cell***, 2020 May 28;181(5):955-960

ABSTRACT

# *Targeting Thrombosis with RNA Therapeutics*

**Bruce Sullenger**
Duke University Medical Center

Thrombosis remains one of the major drivers of morbidity and mortality in theworld effecting cardiovascular disease, stroke, cancer and infectious disease patients including those with SARS-CoV-2. The main challenge with anti-thrombotic therapy continues to be striking the balance between effective anti-coagulation without increasing a patient's propensity to experience life threatening hemorrhage. Clinical evaluation of our factor IXa RNA aptamer in two thousand patients undergoing percutaneous coronary intervention has demonstrated that aptamers can rapidly and potently inhibit their target proteins in patients and that antidote molecules can rapidly and precisely control such activity in the minute time frame. These observations suggest that aptamers represent useful molecules to tightly control biochemical processes in humans in real time. To begin to explore this potential further, we have started to evaluate the utility of antidote mediated control of aptamers for a variety of other therapeutic and diagnostic applications. We will describe our recent progress developing a rapidly controllable factor Xa anticoagulant aptamer to effectively yet reversibly control blood coagulation during cardiopulmonary bypass surgeryand ECMO as well as a rapidly reversible VWF aptamer for improving the treatment of thrombotic stroke. We have observed that aptamers, which target exosites on coagulation factors, can complement active site inhibitors to yield potent anticoagulant regiments (Gunaratne et al., 2018) that can support circulation of blood through ECMO circuits. Moreover we have observed that an aptamer targeting the A1 domain of VWF can serveas a rapid onset and rapidly reversible antithrombotic agent. This aptamer prevents platelet recruitment and can induce recanalization of occluded arteries while a matched antidote oligonucleotide can rapidly reverse such anti-platelet activity and thereby limit bleeding following vascular injury (Nimjee et al., 2019). Collectively these clinical and preclinical studies leadus to believe that rapidly controllable aptamers represent valuable RNA therapeutics that will provide physicians the ability to monitorand precisely control blood coagulation in real time in response to individual patients' needs.

## General Information

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## Educational Background

| Year | Institute |
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| 1989-1993 | 한국과학기술원 화학과 (학사) |
| 1994-1999 | Cornell University, Biochemistry (Ph.D) |

## Professional Experience

| Year | Affiliation & Position |
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| 2004-2008 | 포항공과대학교 화학과 조교수 |
| 2008-현재 | 성균관대학교 화학과 교수 |
| 2010-현재 | 올릭스(주) Founder and CEO |

## List of Recent Publications

1. H.-s. Shin, V. Gedi, J.-k. Kim, and D.-k. Lee*, Detection of Gram-negative bacterial outer membrane vesicles using DNA aptamers. Sci Rep (2019)
2. H.-s. Shin, S. B. Jung, S. Park, P. Dua*, and D.-k. Lee*, ALPPL2 is a Potential Diagnostic Biomarker for Pancreatic Cancer Derived Extracellular Vesicles. Mol Ther Methods Clin Dev (2019)
3. Y. G. Kang, J. Y. Choe, S. Lee, J. Hwang, H. Lim, J. Lee, and D.-k. Lee*, Tripodal RNA with 3' Overhangs Prevents RIG-I mediated Innate Immune Response. Nucleic Acid Ther (2019)
4. Y. Kim, Y. G. Kang, J. Y. Choe, D. Lee, C. Shin, S. W. Hong*, and D.-k. Lee*, RNA interference-mediated gene silencing by branched tripodal RNAs does not require Dicer processing. Nucleic Acid Ther 28, 44-49(2018)
5. J. Hwang, C. Chang, J. H. Kim, C. T. Oh, H. N. Lee, C. Lee, D. Oh, C. Lee, B. Kim, S. W. Hong, and D.-k. Lee*, Development of Cell-Penetrating Asymmetric Interfering RNA Targeting Connective Tissue Growth Factor. J Invest Dermatol 136, 2305-2313(2016)

ABSTRACT

# *Therapeutic development using asymmetric siRNAs*

**이동기**
성균관대학교

Small interfering RNAs (siRNAs) are rapidly emerging as the third generation therapeutics development platform with the capability to target virtually any disease-causing genes present in human genome. We have developed asymmetric siRNA (asiRNA) structures, wherein the sense strands are shorter than conventional siRNAs, and demonstrated that the asiRNAs show comparable target gene silencing activity with reduced non-specific effects. To make asiRNA-based therapeutics, we have introduced various chemical modifications in sugar and backbone structure of RNA, along with conjugation of delivery moieties such as lipids and N-acetylglactosamine (GalNAc) to generate cp-asiRNA and GalNAc-asiRNA, respectively. In this presentation, I will summarize our asiRNA platform for therapeutics development and the pre-clinical and clinical data based on this highly efficient and versatile drug development platform.

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## Educational Background

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| 1991-1998 | 한양대학교 학사 |

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| 2018-현재 | 포항공대 무은재 석좌교수 |
| 2012-2017 | 기초과학연구원 복잡계자기조립연구단 그룹리더 |
| 2007-현재 | 포항공대 조교수, 부교수, 정교수 |
| 2004-2007 | 유타대학교 박사후 연구원 |

## List of Recent Publications

1. Sooseok Im, Donghyun Jang, Gurusamy Saravanakumar, Junseok Lee, Yeoul Kang, Yeong Mi Lee, Jaehyun Lee, Junsang Doh, Zung Yoon Yang, Myoung Ho Jang,and Won Jong Kim*, “Harnessing the Formation of Natural Killer-Tumor Cell Immunological Synapses for Enhanced Therapeutic Effect in Solid Tumors”, Advanced Materials, 2020, 2000020.
2. Sooseok Im, Junseok Lee, Dongsik Park, Areum Park, You-Me Kim, and Won Jong Kim, “Hypoxia-triggered Transforming Immunomodulator for Cancer Immunotherapy via Photodynamically Enhanced Antigen Presentation of Dendritic Cell”, ACS Nano, 2019, 13, 476-488.
3. Jiwon Yeo, Yeong Mi Lee, Junseok Lee, Dongsik Park, Kunho Kim, Jihoon Kim, Junghong Park, and Won Jong Kim*, “Nitric Oxide-Scavenging Nanogel for Treating Rheumatoid Arthritis”, Nano Letters, 2019, 19, 6716-6724.
4. Jinhwan Kim, Changshin Jo, Won-Gwang Lim, Sungjin Jung, Yeong Mi Lee, Jun Lim, Haeshin Lee, Jinwoo Lee*, and Won Jong Kim*, “Programmed nanoparticle loaded nanoparticle for deep penetrating 3D cancer therapy”, Advanced Materials, 2018, 30, 1707557.
5. Junghong Park, Swapan Pramanick, Dongsik Park, Jiwon Yeo, Jihyun Lee, Haeshin Lee, Won Jong Kim*, “Therapeutic Gas Responsive Hydrogel”, Advanced Materials, 2017, 29, 1702859

ABSTRACT

# *Polymer-based Gene and Cell Delivery for Immunocancer Therapy*

**김원종**
포항공과대학교

Gene and cell therapy have attracted a lot of attention because of their usability as a tool for the treatment of various disease such as cancer, cardiovascular disease, and rheumatoid arthritis. For maximizing the efficiency of gene and cell therapy, delivery vehicles which deliver therapeutic cargo into specific cells with high efficiency should be elaborately designed and formed. In this study, we designed polymeric gene carrier consisting of polymer and drug, and applied it to anti-cancer therapy. We prepared hypoxia-responsive mesoporous silica nanocarrier for an enhanced immunocancer therapy assisted by photodynamic therapy. Nanocarrier was designed as a hypoxia-responsive transforming carrier to improve the intracellular uptake of nanocarriers and the delivery of adjuvants to DCs. Furthermore, photodynamic therapy was exploited for the generation of immunogenic debris and recruitment of DCs in a tumor site, followed by enhanced antigen presentation. Finally, a significant inhibition of tumor growth was observed in vivo, signifying that the PDT would be a promising solution for DC-based immunotherapy.

As a cell therapy strategy, we used tumor-homing ability of natural killer (NK) cells for the delivery of drug-loaded polymeric micelle. NK cells are decorated with the immunologican synapse environment-responsive micellar system to ensure the release of payload when they attack cancer cells. Using this strategy, the immunological cytotoxic killing effect of NK cells against solid tumors is reinforced with the site-specific diffusion of chemotherapeutic agents. Harnessing the intrinsic mechanism for the recognition of abnormal cells and the tumor-homing effect of NK cells limit the adverse systemic effects of chemotherapeutic drugs. The overall design concept, physicochemical properties of polymeric micelles, in vitro behaviour and in vivo tumor-targeting ability will be presented in this presentation.

2020

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**KOREAN SOCIETY OF GENE AND CELL THERAPY**

## Session 2
# New Trends in Gene & Cell Therapy

**Session 2**
**New Trends in Gene & Cell Therapy**

# *Moderator*

**권 희 충**
한국원자력의학원
(주)젠셀메드

**하 상 준 | 연세대학교 생화학과**
Regulating regulatory T cells in the tumor immune microenvironment for enhancing efficacy of cancer immunotherapy

**김 진 국 | KAIST 의과학대학원**
ASO Therapy for Rare Disease:
Patient-customized Oligonucleotide Therapy for Rare Neurological Diseases

**김 용 섭 | 울산대학교 의과대학**
Functional Assessment of BRCA1 variants using CRISPR-based Base Editors

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## Educational Background

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| 1996-1998 | POSTECH 생명과학과, 석사 |
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## Professional Experience

| Year | Affiliation & Position |
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| 2001-2004 | POSTECH 생명과학부, 박사후연구원 |
| 2004-2009 | EMORY University, 박사후 연구원 |
| 2009-2014 | 연세대학교 생화학과, 조교수 |
| 2014-2019 | 연세대학교 생화학과, 부교수 |
| 2019-현재 | 연세대학교 생화학과, 교수 |

## List of Recent Publications

1. Lee B et al. Combination of PD-L1 and PVR determines sensitivity to PD-1 blockade. JCI Insight 2020 5(14):128633 (corresponding author)
2. Kim K et al. Single-cell transcriptome analysis revealed TOX as a transcription factor promoting CD8+ T cell exhaustion in cancer. ***Genome Medicine*** 2020 12(1):22 (corresponding author)
3. Kim HR et al. Tumor microenvironment dictates regulatory T cell phenotype: Upregulated immune checkpoints reinforce suppressive function. ***Journal for ImmunoTherapy of Cancer*** 2019 7(1):339 (corresponding author)
4. Kim TJ et al. CD160 serves as a negative regulator of NKT cells in acute hepatic injury. ***Nature Communications*** 2019 10(1):3258 (corresponding author)
5. Oh JH et al. Sustained type I interferon reinforces NK cell-mediated cancer immunosurveillance during chronic virus infection. ***Cancer Immunology Research*** 2019 7(4):584 (corresponding author)

ABSTRACT

# *Regulating regulatory T cells in the tumor immune microenvironment for enhancing efficacy of cancer immunotherapy*

**하상준**
연세대학교 생화학과

Regulatory T (Treg) cells have an immunosuppressive function in cancer, but the underlying mechanism of an preferential aqccumulation and a strong immunosuppression in the tumor microenvironment (TME) is unclear. To characterize tumor-infiltrating Tregs, we performed bulk RNA sequencing (RNA-seq) and found that proliferation-related genes were upregulated in tumor-infiltrating Tregs. Single-cell RNA sequencing and T-cell receptor sequencing also revealed active proliferation of tumor infiltrating Tregs by clonal expansion. One of the proliferation-associated genes, ST2, an interleukin-33 (IL33) receptor, was identified as a potential factor driving Treg accumulation in the TME. Indeed, IL33-directed ST2 signaling induced the preferential proliferation of tumor infiltrating Tregs and enhanced tumor progression, whereas genetic deletion of ST2 in Tregs limited their TME accumulation and delayed tumor growth. These data demonstrated the IL33/ST2 axis in Tregs as one of the critical pathways for the preferential accumulation of Tregs in the TME and suggests that the IL33/ST2 axis may be a potential therapeutic target for cancer immunotherapy.

## General Information

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## Educational Background

| Year | Institute |
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| 2004–2011 | MIT / Ph.D. in Bioinformatics and Integrative Genomics |
| 1996–1998 | KAIST / B.S. in Computer Science |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 2020–present | Graduate School of Medical Science and Engineering, KAIST, Assistant Professor |
| 2017–2020 | Harvard Medical School / Boston Children's Hospital, Research Fellow |
| 2016–2017 | Deep Genomics, Inc., Senior Bioinformatics Analyst |
| 2011–2015 | Samsung Medical Center, Senior Engineer |

## List of Recent Publications

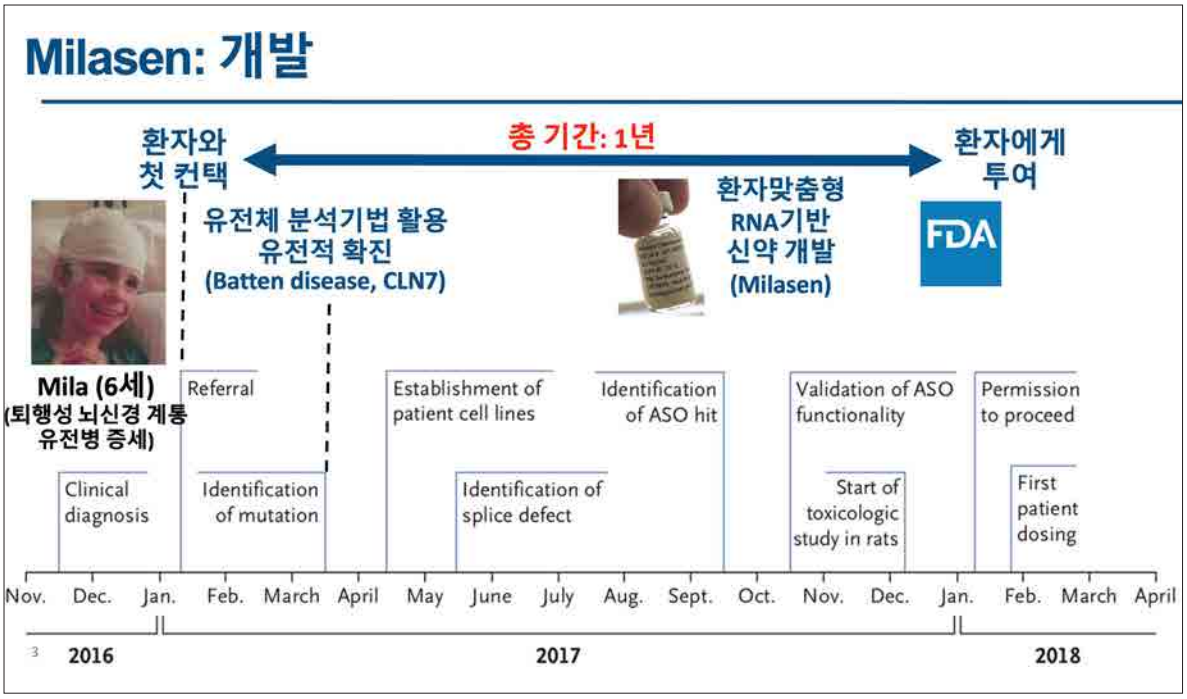
1. **Jinkuk Kim***, Chunguang April Hu*, ..., Timothy W. Yu, Patient-customized oligonucleotide therapy for a rare genetic disease, ***New England Journal of Medicine*** 2019, 381(17):1644-1652
2. **Jinkuk Kim***, In-Hee Lee*, Hee Jin Cho*, Chul-Kee Park*, ..., Peter J. Park†, and Do-Hyun Nam†, Spatiotemporal evolution of the primary glioblastoma genome, ***Cancer Cell*** 2015, 28:318–328
3. **Jinkuk Kim***, Yeri Lee*, ..., Do-Hyun Nam, NTRK1 fusion in glioblastoma multiforme, ***PLOS ONE*** 2014, 9(3):e91940
4. Kyeung Min Joo*, **Jinkuk Kim***, Juyoun Jin*, Misuk Kim*, Ho Jun Seol*, ..., Do-Hyun Nam, Patientspecific orthotopic glioblastoma xenograft models recapitulate the histopathology and biology of human glioblastomas in situ, ***Cell Reports*** 2013, 3(1):260–273
5. **Jinkuk Kim**, David P. Bartel, Allelic imbalance sequencing reveals that single-nucleotide polymorphisms frequently alter microRNA-directed repression, ***Nature Biotechnology*** 2009, 27(5):472–477

ABSTRACT

# *ASO Therapy for Rare Disease: Patient-customized Oligonucleotide Therapy for Rare Neurological Diseases*

**김진국**
KAIST 의과학대학원

Genome sequencing has been revolutionizing the diagnosis of rare diseases, but many of these conditions lack specific treatments. We recently demonstrated how molecular diagnosis of a child with an ultra-rare, fatal neurodegenerative condition led to rational design, testing, and manufacture of milasen, a splice-modulating antisense oligonucleotide drug, tailored to the patient. Proof-of-concept experiments in patient cell lines served as the basis for launching an n-of-1 trial of milasen within one year of patient contact. There were no serious adverse events and treatment was associated with seizure improvement. This study offers a template for the rapid development of patient-customized treatments for rare neurological disorders in a timely fashion. It is an example of individualized genomic medicine.



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## Educational Background

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| 2008 – 2014 | 서울대학교 자연과학대학 화학부 박사 |

## Professional Experience

| Year | Affiliation & Position |
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| 2014 – 2016 | 삼성전자 종합기술원 |
| 2016 – 현재 | 울산대학교 의과대학 의생명과학교실 조교수 |

## List of Recent Publications

1. Kweon J. et al. (2020) A CRISPR-based base-editing screen for the functional assessment of BRCA1 variants. Oncogene 39(1): 30-35
2. Koo B. et al. (2018) CRISPR/dCas9-mediated biosensor for detection of tick-borne diseases. Sensors and Actuators B: Chemical 273:316-321
3. Park D. et al. (2017) Targeted base editing via RNA-guided cytidine deaminases in Xenopus laevis embryos. Molecules and Cells 40(11):823-827
4. Kweon J. et al. (2017) Fusion guide RNAs for orthogonal gene manipulation with Cas9 and Cpf1. Nature Communications 8:1723
5. Kim Y. et al. (2016) Generation of knockout mice by Cpf1-mediated gene targeting. Nature Biotechnology 34(8):808-810

ABSTRACT

# *Functional Assessment of BRCA1 variants using CRISPR-based Base Editors*

**김용섭**
울산대학교 의과대학

The bacteria-derived clustered regularly interspaced short palindromic repeat (CRISPR)–Cas system (such as Cas9 and Cpf1) is a powerful tool for genome engineering, and its programmability and simplicity have enabled various types of gene manipulation such as gene disruption, transcriptional and epigenetic perturbation, and targeted base editing. We focus on the development and clinical application of genome editing technology. Recently, we have applied CRISPR-Cas9 system for functional analysis of BRCA1 variants. Genetic mutations in BRCA1, crucial for the process of DNA repair and maintaining genomic integrity, are known to confer highly elevated risk of breast and ovarian cancers. Clinical genetic testing identified new BRCA1 variants, however, their functional assessment and identification of pathogenicity are challenges for clinical management. Using CRISPR-Cas9 based Base Editor, we identified several loss-of-function variants in BRCA1 which are classified as variants of uncertain significance (VUSs).

2020

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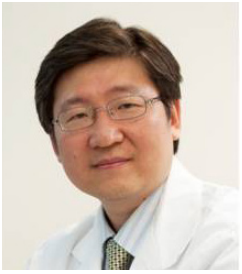
## Session 3
# Cell Therapy

**Session 3**
**Cell Therapy**

# *Moderator*



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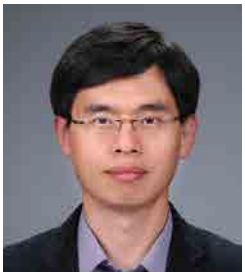

**문 경 식**
안전성평가연구소

**김 태 돈 | 한국생명공학연구원**
CAR-NK 유전자치료제의 파이프라인 기술개발

**박 상 진 | 한국화학연구원 부속 안전성평가연구소**
Approach to Safety Evaluation of Cell and Gene Therapy Products

**이 경 미 | 고려대학교 의과대학**
Endogenous and Engineered NK Cell Therapy against Solid Cancer

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| 1992~1996 | 성균관대학교 유전공학과 학사 |

## Professional Experience

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| 2009~2011 | Univ. of Washington, 방문과학자 |
| 2008~2014 | 한국생명공학연구원, 선임연구원 |
| 2005~2008 | POSTECH, 박사 후 연구원 |

## List of Recent Publications

1. A three-dimensional hyaluronic acid-based niche enhances the therapeutic efficacy of human natural killer cell-based cancer immunotherapy. Biomaterials (2020)
2. MicroRNA-150 controls differentiation of intraepithelial lymphocytes through TGFb receptorII regulation. J Allergy Clin Immunol. (2018)
3. MicroRNA-150 modulates intracellular Ca 2+ levels in naive CD8+ T cells by targeting TMEM20. Scientific Reports (2017)
4. miR-150-mediated Foxo1 regulation programs CD8+ T cell differentiation. Cell Reports (2017)

ABSTRACT

# *CAR-NK gene therapy and its 3D applications*

**김태돈**
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Adoptive transfer of natural killer (NK) cells is becoming one of the most important parts of cancer immunotherapy. However, recent accomplishments have focused on the improvement of the targeting effects based on the engineering of chimeric antigen receptors (CARs) on cell surfaces. Despite the large quantity of therapeutic cells required for clinical applications, the technology for ex vivo expansion is not well developed. Herein, a three-dimensional (3D) engineered hyaluronic acid-based niche for cell expansion (3D-ENHANCE) is introduced. Compared with the conventional two-dimensional (2D) method, NK-92 cell lines and human EGFR-specific (CAR)–NK cells cultured in 3D-ENHANCE yield favorable mRNA expressions, elevated cytokine release, upregulated proliferative and tumor-lytic abilities, and result in enhanced antitumor efficacy. Furthermore, controllable degradation rates can be realized by tuning the formulation of 3D-ENHANCE so that it can be applied as an implantable cell reservoir at surgical sites. In vivo results with the incompletely resected MDA-MB-231 model confirm that the peri-operative implantation of 3D-ENHANCE prevents the relapse and metastases after surgery. Overall, 3D-ENHANCE presents an effective cytokine-free niche for ex vivo expansion and postsurgical treatment that enhances the low-therapeutic efficacy of human NK cells.

## General Information

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## Educational Background

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## Professional Experience

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| 2015- | 안전성평가연구소 선임연구원 |

## List of Recent Publications

1. Park, S. J., Yoo, G., Kim, Y. M., Jung, J. S., Kim J. Y., Lee, A. R., Yoo, M. H. Kim, D. O., Lee, S. Y., Na, S., Kim, H. J., & Moon, K. S. (2019). A General Toxicity and Biodistribution Study of Human Natural Killer Cells by Single or Repeated Intravenous Dose in SCID Mice. 14th KSGCT.
2. Han, S.,,Lee, S., Park, S. J., Kim, J. Y., Na, S., Yoo, G, Lee, A. R., Yoo, M. H., Kim, D. O., & Moon, K. S. (2018). Biodistribution and Shedding Studies of Adeno-associated Virus 5 in C57BL/6 Mice by quantitative PCR. Molecular Therapy
3. Lim, S. R., Hyun, S. H., Lee, S. G., Kim, J. Y., Kim, S. H., Park, S. J., ... & Choi, H. K. (2017). Potential urinary biomarkers of nephrotoxicity in cyclophosphamide-treated rats investigated by NMR-based metabolic profiling. Journal of biochemical and molecular toxicology, 31(3), e21871.
4. Lee, B. S., Park, S. J., Kim, Y. B., Han, J. S., Jeong, E. J., Son, H. Y., & Moon, K. S. (2017). Twenty-six-week oral carcinogenicity study of 3-monochloropropane-1, 2-diol in CB6F1-rasH2 transgenic mice. Archives of toxicology, 91(1), 453-464.
5. Lee, B. S., Park, S. J., Kim, Y. B., Han, J. S., Jeong, E. J., Moon, K. S., & Son, H. Y. (2015). A 28-day oral gavage toxicity study of 3-monochloropropane-1, 2-diol (3-MCPD) in CB6F1-non-Tg rasH2 mice. Food and Chemical Toxicology, 86, 95-103.

ABSTRACT

# *Approach to Safety Evaluation of Cell and Gene Therapy Products*

**박상진**
한국화학연구원 부속 안전성평가연구소

Cell and gene therapies hold the promise of bringing significant clinical benefits by directly targeting the underlying cause of disease. The global cell and gene therapy market is one of the fastest-growing segments in the regenerative medicine market and expected to grow at a faster pace during the forecast period. Cell and gene therapies are providing patients with treatments for many traditionally incurable diseases. The design and conduct of preclinical toxicity studies are thus important to inform regulatory decisions that help define the safe administration of an investigational cell and gene therapy product in humans.

The intrinsic material composition and putative MOA of cell and gene therapy products differ from small molecular drugs and macromolecular biologic drugs. Therefore, the traditional, standardized approaches for preclinical toxicity testing, which were developed for drug development, are often not appropriate for evaluating the safety of cell and gene therapy products. Preclinical assessment of the safety of an investigational cell and gene therapyproduct contributes to the definition of an acceptable risk-benefit ratio for a proposed clinical trial. The safety assessment should be sufficiently comprehensive to permit identification, characterization, and quantification of potential local and systemic toxicities, their onset, the possibility for resolution of any toxicities, and the effect of product dose level on toxicity findings. Therefore, preclinical safety considerations for cell and gene therapy products include systemic toxicity, biodistribution, persistence and immunotoxicity in relevant animal species, and are the critical elements need to be addressed prior to intended clinical trials. In this review, we summarize cell and gene therapy products, discuss their preclinical experiences and safety concerns, and also describes regulatory frameworks for developers to support product development and IND application.

## General Information

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## Educational Background

| Year | Institute |
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| 1983.03-1987.02 | 서울대학교 학사 |
| 1987.03-1989.08 | 서울대학교 석사 |
| 1989.09-1995.08 | University of Chicago 박사 |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 2006.09-2009.08 | 고려대학교 의과대학 생화학교실 부교수 |
| 2009.09-현재 | 고려대학교 의과대학 생화학교실 교수 |
| 2013.03-현재 | MD Anderson cancer center 겸임교수 |
| 2019.03-현재 | Northwestern university 겸임교수 |

## List of Recent Publications

1. Kim T-J, Park G-Y, Kim J-M, Lim S-A, Kim J-Y, IM K-T, Shin M-H, Yang-Xin Fu, Maria-Luisa Del Rio, Jose-Ignacio Rodriguez-Barbosa, Cassian Yee, Suh K-S, Kim S-J, Ha S-J*and **Lee K-M***. 2019. CD160 serves as a negative regulator of NKT cells in acute hepatic injury. Nature Communications. 22;10(1):3258.
2. Lim S-A, Kim J-W, Jeon S-H, Shin M-H, Kwon J-H, Kim T-J, Im K-T, Han Y-M, Kwon W-I, Kim S-W, Cassian Yee, Kim S-J*, Jang J-Y* and **Lee K-M***. 2019. Defective localization with impaired tumor cytotoxicity contributes to the immune escape of NK cells in pancreatic cancer patients. Frontiers in Immunology. 9;10:496.
3. OH J-H, Kim M-J, Choi S-J, Ban Y-H, Lee H-K, Shin E-C, **Lee K-M***, Ha S-J. 2019. Sustained Type I interferon Reinforces NK Cell-mediated Cancer Immunosurveillance During Chronic Virus Infection. Cancer immunology Res. 7(4):584-599.
4. DAVIES ALEXANDERJ, Kim H-W, Gonzalez-Cano R, Choi J, Back S-K, Roh S-E, JOHNSON E, Gabriac M, Kim M-S, Lee J, Lee J-E, Kim Y-S, Bae Y-C, **Lee K-M**, Kim S-J, Na H-S, Riva P, Latremoliere A, RINALDI SIMON, Ugolini S, Costigan M., Oh S-B. 2019. Natural Killer Cells Degenerate Intact Sensory Afferents Following Nerve Injury. Cell. 176(4):716-728.
5. Chen X, Park Y-J, Kang M, Kang S-K, Koo J, Shinde SM, Shin J, Jeon S, Park G, Yan Y, MacEwan MR, Ray WZ, **Lee K-M***, Rogers J.A, Ahn J-H. 2018. CVD-grown monolayer MoS2 in bioabsorbable electronics and biosensors. Nat Commun. 27;9(1):1690.

ABSTRACT

# *Endogenous and Engineered NK cell therapy against Solid Cancer*

**이경미**
고려대학교 의과대학

With the development of technologies that can transform immune cells into therapeutic modalities, immunotherapy has remarkably changed the current paradigm of cancer treatment in recent years. Natural killer (NK) cells are components of the innate immune system that act as key regulators and exhibit a potent tumor cytolytic function. Unlike T cells, NK cells exhibit tumor cytotoxicity by recognizing non-self, without deliberate immunization or activation. Currently, researchers have developed various approaches to improve the number and anti-tumor function of NK cells. These approaches include the use of cytokines and antibodies to stimulate the efficacy of NK cell function, adoptive transfer of autologous or allogeneic ex-vivo expanded NK cells, establishment of homogeneous NK cell lines using the NK cells of patients with cancer or healthy donors, derivation of NK cells from induced pluripotent stem cells (iPSCs), and modification of NK cells with cutting-edge genetic engineering technologies to generate chimeric antigen receptor (CAR)-NK cells. Such NK cell-based immunotherapies are currently reported as being promising anti-tumor strategies that have shown enhanced functional specificity in several clinical trials investigating malignant tumors.Here, we discuss the recent advances in NK cell-based cancer immunotherapies that have focused on providing improved function through the use of the latest genetic engineering technologies.

2020

15th ANNUAL MEETING OF
**KOREAN SOCIETY OF GENE AND CELL THERAPY**

## Session 4
# Neurodegenerative Disease

**Session 4**
**Neurodegenerative Disease**

# *Moderator*

**이 정 훈**
㈜헬릭스미스

**Robert Kotin | University of Massachusetts Medical School**
Practical Considerations for Recombinant Adeno-associated Virus Scalable Production

**오 석 배 | 서울대학교 치의과대학원**
Potential Immune Cell Therapy for Chronic Pain

**이 승 재 | 서울대학교**
Propagation of Synucleinopathy in Parkinson's Disease

## General Information

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## Educational Background

| Year | Institute |
|---|---|
| 1976~1979 | University of California Santa Cruz |
| 1979~1986 | Rutgers University |
| 1986~1990 | Cornell University Medical School (post-doctoral positions) |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 1994~2014 | National Heart, Lung, and Blood Institute / NIH |
| 2014~present | University of Massachusetts Medical School |
| 2014~2016 | Voyager Therapeutics |
| 2017~2019 | Generation Bio |

## List of Recent Publications

1. Hildebrandt, E., Penzes, J.J., Gifford, R.J., Agbandje-McKenna, M., and Kotin, R.M.: Evolution of dependoparvoviruses across geological timescales – implications for design of AAV-based gene therapy vectors. *Virus Evolution* 2020; https://doi.org/10.1093/ve/veaa043
2. Smith, R.H., Hallwirth, C.V., Westerman, M., Hetherington, N.A., Tseng, Y.-S., Cecchini, S., Virag, T., Ziegler, M.-L., Rogozin, I.B., Koonin, E.V., Agbandje-McKenna, M., Kotin, R.M., and Alexander, I.E.: Germline viral "fossils" guide in silico reconstruction of a mid-Cenozoic era marsupial adeno-associated virus. *Scientific Reports*, 6, Article number: 28965, 2016 doi:10.1038/srep28965.
3. Kotin, R.M. and Snyder, R.O.: Manufacturing clinical grade recombinant adeno-associated virus using invertebrate cell lines. *Human Gene Therapy* 28 (4), 350-360.
4. Kotin, R.M. and Wright, J.F.: Recombinant Adeno-Associated Virus Quality Control for Non-Clinical and Clinical Vectors: How an Unregulated Commercial Sector Can Compromise Development of New Gene Therapies. *Human Gene Therapy* 2019; 30 (12) https://doi.org/10.1089/hum.2019.29099.rmk
5. Li, L., Dimitriadis, E.K., Yang, Y., Li, J., Yuan, Z., Qiao, C., Beley, C., Smith, R.H., Garcia, L., Kotin, R.M.: Production and characterization of novel recombinant adeno-associated virus replicative-form genomes: a eukaryotic source of DNA for gene transfer. 2013 PLoS One https://doi.org/10.1371/journal.pone.0069879

ABSTRACT

# *Practical considerations for adeno-associated virus scalable production*

**Robert M. Kotin**
University of Massachusetts Medical School

The supply of recombinant adeno-associated virus (rAAV) is not keeping up with the demand due to increased academic research activity and more significantly, the large investment in rAAV gene therapy by biopharma. Clinical gene therapy development consumes large quantities of rAAV for research, rodent and large animal dose escalation and toxicological studies. Non-clinical rAAV used for research and development or for academic research may be produced and sold without regulatory agency oversight. Therefore, vector quality may vary widely between different suppliers or even between different lots from the same supplier. The end-user expects that the certificate of analysis (CoA) provided with the vector is accurate and reliable, however, it is not uncommon that independent analytical assays do not support the CoA data. The vector quality affects the experimental results which may not be attributable to the vector per se. In addition, to produce clinical grade vector requires establishing and stringently adhering to an appropriate Chemistry, Manufacturing, and Control (CMC) documents that are reviewed by regulatory agencies, e.g., the Federal Drug Agency (FDA) in the US. Thus, rAAV production using current Good Manufacturing Practices (cGMP) is thoroughly documented and the vector extensively characterized. In order to meet vector demands for large dosage, large animal studies, we developed an Sf9/baculovirus-based system that allows high manufacturing capacity. This technology has been adopted by different biopharmaceutical companies and demonstrated to produce safe vectors from different serotypes, now used in advanced clinical trials and the first rAAV approved product.

## General Information

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## Educational Background

| Year | Institute |
|---|---|
| 1984 – 1990 | 서울대학교 치과대학 학사 |
| 1990 – 1997 | 서울대학교 대학원 치의학석사 (1992), 치의학박사 (1997) |
| 1998 – 2000 | Postdoctoral fellow in Dept. Neurobiology, Pharm. & Physiol. Sci. University of Chicago, USA |
| 2000 – 2002 | Research Associate in Dept. Mol. Pharm. & Biol. Chem. Northwestern University Medical School, USA |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 2007 – 2010 | Honorary Visiting professor, University of Manchester, UK |
| 2008 – 2009 | Visiting professor, Dept. of Neurobiology Harvard Medical School, USA |
| 2013 – 2020 | Professor in Dept. of Brain and Cognitive Sciences College of Natural Sciences, Seoul National University |
| 2002 – Present | Professor in Dept. of Neurobiology and Physiology, School of Dentistry Seoul National University, Assistant professor (2002), Tenured Associate Professor (2006) and Professor (2011) |

## List of Recent Publications

1. Hedonic drinking engages a supra-spinal inhibition of thermal nociception in adult rats. Davies AJ, Kim D, Park J, Lee JY, Vang H, Pickering AE, **Oh SB**. Pain 2019 160(5):1059-1069
2. Natural Killer Cells Degenerate Intact Sensory Afferents following Nerve Injury. Davies AJ, Kim HW, Gonzalez-Cano R, Choi J, Back SK, Roh SE, Johnson E, Gabriac M, Kim MS, Lee J, Lee JE, Kim YS, Bae YC, Kim SJ, Lee KM, Na HS, Riva P, Latremoliere A, Rinaldi S, Ugolini S, Costigan M, **Oh SB**. Cell 2019 176(4):716-728
3. The analgesic effect of refeeding on acute and chronic inflammatory pain. Lee JY, Lee GJ, Lee PR, Won CH, Kim DY, Kang Y, **Oh SB** Scientific Reports 2019 Nov 14;9(1):16873.
4. TRPM8 Mediates Hyperosmotic Stimuli-Induced Nociception in Dental Afferents. Lee PR, Lee JY, Kim HB, Lee JH, **Oh SB**. J Dent Res. 2020 Jan;99(1):107-114
5. Cytotoxic Immunity in Peripheral Nerve Injury and Pain. Davies AJ, Rinaldi S, Costigan M, **Oh SB**. Front Neurosci. 2020 Feb 21;14:142. doi: 10.3389/fnins.2020.00142. 2020.

ABSTRACT

# *Potential Immune Cell Therapy for Chronic Pain*

**오석배**
서울대학교 치의학대학원

Chronic pain is often induced by peripheral nerve damage which results from traumatic injury, diabetes or chemotherapies for cancer treatment. In these peripheral neuropathic conditions, nerve damage amplifies pain signals not only by sensitized neurons that respond to non-painful stimulus but also by spontaneous ectopic firings from injured neurons. As these conditions continue, acute pain from initial nerve damage transits into chronic pain, which becomes frequently uncontrollable even with strong analgesic drugs currently available in the clinic. Diversity and complexity of underlying cellular and molecular mechanisms behind the amplification of pain signals in neuropathic pain and chronic painconditions make the development of new analgesics and therapeutic interventions very difficult.
We investigated the response and functional consequences of Natural Killer (NK) cells, a cytotoxic peripheral immune cells, in the context of peripheral nerve injury from the adult mouse. Our study revealed cytotoxic NK cells as a novel cellular trigger for the specific degeneration of damaged primary afferent axons. This discovery further provides new insight into non-neuronal mechanisms of damaged axon clearance. We propose that NK cells can be a therapeutic target for the treatment of peripheral neuropathies and chronic pain.

## General Information

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## Educational Background

| Year | Institute |
|---|---|
| 1985-1989 | 서울대학교 (학사) |
| 1990-1992 | 포항공대 (석사) |
| 1992-1995 | 포항공대 (박사) |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 1995-1996 | NIH (postdoc) |
| 1996-2000 | Harvard Medical School (postdoc, Instructor) |
| 2000-2006 | The Parkinson's Institute (조교수) |
| 2006-2015 | 건국대학교 (부교수, 교수) |
| 2015- 현재 | 서울대학교 (교수) |

## List of Recent Publications

1. Strohäker T, Jung BC, Liou S-H, Fernandez CO, Riedel D, Becker S, Halliday GM, Bennati M, Kim WS*, **Lee S-J*** & Zweckstetter M* (2019) Structural heterogeneity of α-synuclein fibrils amplified from patient brain extracts. Nature Communications, 10:5535 (*co-corresponding authors)
2. Lee JS, Kanai K, Suzuki M, Kim WS, Yoo HS, Fu YH, Kim D-K, Jung BC, Choi M, Oh KW, Li Y, Nakatani M, Nakazato T, Sekimoto S, Funayama M, Yoshino H, Kubo S, Nishioka K, Sakai R, Ueyama M, Mochizuki H, **Lee H-J**, Sardi SP, Halliday GM, Nagai Y, Lee PH, Hattori N, Lee S-J (2019) Arylsulfatase A, a genetic modifier of Parkinson's disease, is an α-synuclein chaperone. Brain doi: 10.1093/brain/awz205
3. Bae E-J, Kim D-K, Kim C, Mante M, Adame A, Rockenstein E, Ulusoy A, Klinkenberg M, Jeong GR, Bae JR, Lee C, **Lee H-J**, Lee B-D, Di Monte DA, Masliah E, Lee S-J (2018) LRRK2 kinase regulates a-synuclein propagation via RAB35 phosphorylation. Nat Commun. 9(1):3465.
4. Lim S, Kim H-J, Kim D-K, **Lee S-J** (2018) Non-cell-autonomous actions of alpha-synuclein: implications in glial synucleinopathies. Prog Neurobiol, 169, 158-171
5. Kim DK, Lim HS, Kawasaki I, Shim YH, Vaikath NN, El-Agnaf, OMA, Lee HJ, **Lee S-J** (2016) Anti-aging treatments slow propagation of synucleinopathy by restoring lysosomal function. Autophagy, 12, 1849-1863

ABSTRACT

# *Propagation of synucleinpathy in Parkinson's disease*

**이승재**
서울대학교

Parkinson disease (PD) is characterized by deposition of alpha-synuclein aggregates in neuronal inclusion bodies, known as Lewy bodies and Lewy neurites. Several inherited forms of PD have been linked to mutations in SNCA, the gene encoding alpha-synuclein. Furthermore, common genetic variants of SNCA have been associated with sporadic forms of PD. Alpha-synuclein aggregates appear at a few discrete regions of the brain and spread throughout the brain in PD patients. This aggregate spreading is thought to be driven by cell-to-cell propagation of alpha-synuclein. Intercellular propagation of alpha-synuclein aggregates is considered a promising therapeutic target for slowing the disease progression. Collectively, these findings suggest that alpha-synuclein is critically involved in the pathogenesis of PD and is a leading therapeutic target. Recently, several trials for developing immune-based therapies are underway at different stages, some in clinical trials and others in preclinical stages. In this talk, I will review the ongoing efforts towards immunotherapies targeting alpha-synuclein. I will also discuss the results from animal and cell studies, which provides insights into the mechanism of action for the alpha-synuclein-targeted immunotherapies. Finally, Potential targets for PD immunotherapies other than alpha-synuclein will be discussed.

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**KOREAN SOCIETY OF GENE AND CELL THERAPY**

## Education Session

# CMC for Cell & Gene Therapy

**Education Session**
**CMC for Cell & Gene Therapy**

# *Moderator*

**김 연 수**
충남대학교 신약전문대학원

**이 소 영 | 식품의약품안전처**
Considerations for investigational advanced biopharmaceutical products

**김 수 진 | 유전자의약 이노베이션센터 / (주)알티큐어**
Detection sensitivity of gene therapy in biodistribution and RCL assay.

**정 남 철 | ㈜파로스백신**
CAR-T 개발을 위한 CMC 고려사항

## General Information

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| **Name** | 이소영 |
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## Educational Background

| Year | Institute |
|---|---|
| 2001-2005 | 포항공과대학교 신경생리학 전공 |
| 1999-2000 | 포항공과대학교 심장세포생리학 전공 |
| 1995-1998 | 한양대학교 생화학 |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 2012-현재 | 식품의약품안전처 의약품 심사 |
| 2011-2012 | KAIST, 연구교수 |
| 2008-2011 | Tufts Univ. 박사후 연구원 |
| 2006-2008 | Univ. of Pennsylvania 박사후 연구원 |

## List of Recent Publications

1. 세포치료제 품질관리 시험항목 설정 가이드라인(식품의약품안전평가원, 2019)
2. 첨단바이오의약품 규제과학 상담 사례집(식품의약품안전평가원, 2018)
3. 유전자편집기술을 이용한 첨단바이오의약품 품질평가 가이드라인(식품의약품안전평가원, 2018)
4. 유전자치료제 비임상시험 평가 가이드라인(식품의약품안전평가원, 2017)

ABSTRACT

# *Considerations for investigational advanced biopharmaceutical products*

**이소영**
식품의약품안전처

Advanced biopharmaceutical products are getting growing attention as they have shown to have the potential to treat and to cure serious disease rather than just treating the symptoms. However, it has been challenges for regulatory agencies and drug developers due to lack of detailed regulatory guidelines and rapidly evolving technologies in this field. Here, the current regulatory framework will be summarized and considerations on quality, non-clinical and clinical requirements for investigational advanced biopharmaceutical products, especially gene therapy products.

## General Information


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## Educational Background

| Year | Institute |
|---|---|
| 2005 – 2010 | 성신여자대학교 생명과학과 이학사 |
| 2012 – 2019 | 인제대학교 식의약생명공학과 이학박사 |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 2011 – 2015 | 인제대 인당분자생물학 연구실 연구원 |
| 2015 – 2019 | 충남대 신약전문대학원 유전자의약 연구실 연구원 |
| 2019 – 현재 | 충남대 신약전문대학원 유전자의약 연구실 박사 후 연구원 |
| 2019 – 현재 | (주)알티큐어 고객지원 및 QC 팀장 |

## List of Recent Publications

1. Hepatitis B Virus-X Downregulates Expression of Selenium Binding Protein 1. Viruses 2020, 12, 565.
2. Chlorella virus-mediated disruption of microalgal cell wall for biodiesel production, Korean J. Microbiol 2018;54(2):140-145.

ABSTRACT

# *Detection Sensitivity in Biodistribution and RCL Assay of Gene Therapy Products*

**김수진**
충남대 신약전문대학원 유전자의약 이노베이션센터 / (주)알티큐어

장태경, 이선화, 박경록, 정채홍, 최현지, 김연수
충남대 신약전문대학원 유전자의약 이노베이션센터

Gene therapy is being marketed beyond the R&D stage. For applying gene therapy as new drugs to patients, safety issues should be cleared. Unlike other pharmaceuticals, there are additional safety items for gene therapy, such as biodistribution and replication-competent virus assay. In such validation issues, the sensitivity of quantitative PCR and sample size are crucial. In this presentation, I will introduce practical information to achieve the sensitivity and proper sample size for safety validation that meets criteria in quantitative PCR guideline.

## General Information

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## Educational Background

| Year | Institute |
|---|---|
| 2011~2016 | 차의과학대학교 의생명과학, 박사 |
| 1999~2001 | 한남대학교 미생물학, 석사 |
| 1992~1999 | 한남대학교 미생물학, 학사 |

## Professional Experience

| Year | Affiliation & Position |
|---|---|
| 2013~현재 | ㈜파로스백신 부설연구소 이사 |
| 2017~현재 | 차의과학대학교 겸임교수 |
| 2018~현재 | 중국 IAS 기술자문위원 |
| 1999~2013 | JW크레아젠(주) 부설연구소 책임연구원, GMP 팀장 |

## List of Recent Publications

1. Lee JH, Choi SY, Jung NC, Song JY, Seo HG, Lee HS, Lim DS. The Effect of the Tumor Microenvironment and Tumor-Derived Metabolites on Dendritic Cell Function. J. Cancer. 2020; 11(4): 769-775.
2. Chen R, Wang M, Liu Q, Wu J, Huang W, Li X, Du B, Xu Q, Duan J, Jiao S, Lee HS, Jung NC, Lee JH, Wang Y, Wang Y. Sequential treatment with aT19 cells generates memory CAR-T cells and prolongs the lifespan of Raji-B-NDG mice. Cancer Letters. Cancer Lett. 2020 Jan 28;469: 162-172.
3. Yoo JY, Jung NC, Lee JH, Choi SY, Choi HJ, Park SY, Jang JS, Byun SH, Hwang SU, Noh KE, Park Y, Lee J, Song JY, Seo HG, Lee HS, Lim DS. Pdlim4 is essential for CCR7-JNK-mediated dendritic cell migration and F-actin-related dendrite formation. FASEB J. 2019 Oct;33(10):11035-11044.
4. Jang JS, Lee JH, Jung NC, Choi SY, Park SY, Yoo JY, Song JY, Seo HG, Lee HS, Lim DS. Rsad2 is necessary for mouse dendritic cell maturation via the IRF7-mediated signaling pathway. Cell Death Dis. 2018 Aug 1;9(8): 823.
5. Jung NC, Lee JH, Chung KH, Kwak YS, Lim DS. Dendritic Cell-Based Immunotherapy for Solid Tumors. Transl Oncol. 2018 Apr 5;11(3): 686-690.

ABSTRACT

# *CAR-T 개발을 위한 CMC 고려사항*

**정남철**
㈜파로스백신

키메릭 항원 수용체(chimeric antigen receptor, CAR)-T 세포치료제(CAR-T)는, T 세포에 암항원을 인지하는 CAR 유전자를 탑재하여 원하는 표적을 공격하는 세포로 전환시켜 환자에게 주입하는 유전자이입 T 세포치료제로서, 기존의 암을 표적하는 항체나 면역세포치료제와 비교하여 획기적으로 강화된 항암 효과를 나타내고 있다. 이들 CAR-T 세포의 개발 및 임상시험 진입을 위해서는 의약품 품질평가 자료 작성 시 관련 규정에 근거한 구체적 범위와 요건을 갖추어야 한다. 이를 위해 본 발표에서는 B 세포 특이 항원 CD19를 표적으로 하는 CAR-T 세포의 개발사례로서 해외 기술이전, 그리고 이를 이용한 임상시험 결과를 소개하고, 개발기업에서 경험한 비임상시험 및 CMC 개발 시 고려사항에 대한 내용을 소개하고자 한다.

2020

15th ANNUAL MEETING OF
**KOREAN SOCIETY OF GENE AND CELL THERAPY**

## Session 5
# Cancer Targetting Approach

**Session 5**
**Cancer Targetting Approach**

# *Moderator*

**송 재 진**
연세대 의대 의생명과학부

**백 현 정** | **㈜젠셀메드**
HSV Retargeting to Cancer

**강 문 경** | **㈜알티큐어**
Oncospreading Dual-RRV System for Cancer Gene Therapy

**황 태 호** | **부산대학교**
Myeloid Modulation in Combination with Replication
-controllable Oncolytic Vaccinia Virus Therapy

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| 2006-2011 | 고려대학교, 박사, 유전자치료 |

## Professional Experience

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| 2003-2013 | 한국원자력의학원, 박사후연구원 |
| 2013-2019 | 경희대학교 한의과대학, 학술연구교수 |
| 2019-현재 | ㈜젠셀메드, R&D센터 수석연구원 |

## List of Recent Publications

1. Baek. et al., Bee venom phospholipase A2 induces regulatory T cell populations by suppressing apoptotic signaling pathway. *Toxins* (2020) 12:198
2. Baek. et al., Bee venom phospholipase A2 ameliorates Alzheimer's disease pathology in Aβ vaccination treatment without inducing neuro-infalmmation in a 3xTg-AD mouse model. *Sci Rep*. (2018) 8:17369
3. Baek. et al., Comparison of administration routes on the protective effects of bee venom phospholipase A2 in a mouse model of parkinson's disease. *Front Aging Neurosci*. (2018) 10:179
4. Baek. et al., Bee venom phospholipase A2 ameliorates house dust mite extract induced atopic dermatitis like skin lesions in mice. *Toxins* (2017) 9:E68
5. Baek. et al., The therapeutic effects of tuberostemonine against cigarette smoke-induced acute lung inflammation in mice *Eur J Pharmacol* (2016) 774:80

ABSTRACT

# *HSV Retargeting to Cancer*

**백현정**
㈜젠셀메드

Oncolytic viruses (OVs) are powerful novel immunotherapeutic agents in cancer therapy. OVs are spontaneously occurring or genetically modified viruses that selectively infect and lyse tumor cells, not harming normal cells. The viral infection will activate virus-directed immune responses, and may trigger immune responses directed against tumor cells and tumor antigens. The effectiveness of OVs has been demonstrated in many preclinical and clinical trials. Oncolytic herpes simplex viruses (oHSVs) are the most widely studied OVs for the treatment of solid tumors and accounts for nearly a quarter of all ongoing clinical trials using OVs. Amgen's herpesvirus talimogene laherparepvec (T-VEC) is the first and only FDA-approved OVs for the treatment of metastatic melanoma. T-VEC was designed to kill tumor cells and stimulate the tumor-antigen-specific adaptive immune response. Deletions in the ICP34.5 gene confers tumor-selective replication and markedly reduces neurovirulence. Insertion of the granulocyte-macrophage colony-stimulation factor (GM-CSF) promotes the activation of dendritic cells (DCs) at sites of inflammation and enhances antigen presenting cell function. After the success of T-VEC, oncolytic virotherapy is a strategically attractive class of immunotherapeutics that is sure to rapidly expand in clinical trials treating a broad array of malignancies as both monotherapy and in combinations with checkpoint inhibitors.

HSV-1 is an enveloped, double-stranded linear DNA virus that has been investigated as an oncolytic virus. The viral particle is an icosahedral capsid containing the viral DNA with a genome of 152 kb encoding at least 84 genes products. HSV possesses the following advantages as an oncolytic virus: i) HSV replicate quickly in cells and has capability to infiltrate multiple types of cancer cells; ii) HSV contains many non-essential genes that can be easily engineered and be inserted with multiple transgenes; iii) HSV retain sensitivity to anti-herpes drugs, such as acyclovir and ganciclovir, providing an additional safety feature; iv) Modifying the glycoprotein of HSV can improve the targeting of tumor cells. In addition, HSV has proven ideal for targeting cancers of neural origin, such as glioma, due to its intrinsic neurotropism. To enhance antitumor responses of oHSVs, modification of several viral envelope glycoproteins to allow only tumor-specific virus infection. Another strategy is to generate insert immunomodulatory genes, including IL-2, IL-12, IL-15, IL-18, tumor necrosis factor alpha (TNF-α), CD80, and GM-CSF like T-VEC, into oHSVs. These immunomodulatory genes have many functions to activate, proliferate, differentiate, and maturate innate and acquired immune cells important for antitumor responses.

In this talk, I will discuss important biological features of HSV that make it an attractive OV and potential strategies to increase applicability to cancer treatment. In the last section, I will briefly introduce GenCellMed's double-targeted oncolytic virus.

## General Information

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| 2016-현재 | 충남대학교 신약전문대학원 / ㈜알티큐어 |

## List of Recent Publications

1. Novel Semi-Replicative Retroviral Vector mediated Double suicide gene transfer enhances antitumor effects in Patient-derived Glioblastoma models **Cancers** 2019 : 11(8) : 1090
2. 특허등록 : Gene Therapy Vector System and Prodrug genes (2018) 미국/10039841
3. 특허등록 : Replication competent pseudo-type retrovirus vector system (2012) 미국/9657312
4. Intrahippocampal injection of a lentiviral vector expressing neurogranin enhances cognitive function in 5XFAD mice **Experimental & Molecular Medicine** 2018 : 50, e461
5. Targeting mutant KRAS with CRISPR-Cas9 controls tumor growth **Genome Res** 2018 : 28(3) : 374-382

ABSTRACT

# *Oncospreading Dual-RRV System for Cancer Gene Therapy*

**강문경**
㈜알티큐어

Replicating Retroviral vectors (RRVs) has become a good choice for gene transfer due to their tumor-selective gene delivery and self-replication. The increase of clinical trials on viral vector-mediated gene therapy is stimulating development for RRVs in gene transfer. Therefore, to enhance the therapeutic effect higher than single RRVs vectors in solid tumors, we developed dual-RRV vectors expressing two therapeutic genes.(sRRVgp-yCD and spRRVe-TK) Also, we developed the human-codon optimized opt-yCD that shows more enhanced prodrug sensitive and genome stability than the original yCD, introduced into spRRV vectors. The established dual-RRV vectors showed superior genome stability during replication and efficient cell death after prodrug administration in vitro and in vivo glioblastoma model. Next, we were willing to establish the virus producer cells (VPC) that can produce high titers of the dual RRVs and to manufacture master cell banks (MCBs) for clinical use. Each of the dual RRVs (sRRVgp-yCD & spRRVe-TK) was separately transduced into retrovirus packaging cell line PG13. And then, PG13/env-HSV1-TK and PG13/gagpol-yCD VPCs were selected clonally and amplified for the screening of VPCs producing high titer retroviral vector particles. Currently, MCBs of the validated PG13/env-HSV1-TK and PG13/gagpol-yCD VPCs are under manufacturing in the GMP facility.

## General Information

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| 2015 – 현재 | 양산부산대학교병원 임상약리학과 과장 |
| 2016 – 2018 | 한국유전자세포치료학회 (KSGCT) 회장 |

## List of Recent Publications

1. Neutrophil-lymphocyte ratio predicts the therapeutic benefit of neoadjuvant transarterial chemoembolization in patients with resectable hepatocellular carcinoma Eur J Gastroenterol Hepatol. 2020 Sep;32(9):1186-1191. doi: 10.1097/MEG.0000000000001629.
2. Engineering and Characterization of Oncolytic Vaccinia Virus Expressing Truncated Herpes Simplex Virus Thymidine Kinase Cancers (Basel). 2020 Jan 17;12(1):228. doi: 10.3390/cancers12010228.
3. Characterization of Oncolytic Vaccinia Virus Harboring the Human IFNB1 and CES2 Transgenes Cancer Res Treat. 2020 Jan;52(1):309-319. doi: 10.4143/crt.2019.161. Epub 2019 Aug 6.
4. Changes in the neutrophil-to-lymphocyte ratio predict the prognosis of patients with advanced hepatocellular carcinoma treated with sorafenib Eur J Gastroenterol Hepatol. 2019 Oct;31(10):1250-1255. doi: 10.1097/MEG.0000000000001405.
5. Preclinical safety evaluation of hepatic arterial infusion of oncolytic poxvirus Drug Des Devel Ther. 2018 Aug 8;12:2467-2474. doi: 10.2147/DDDT.S171269. eCollection 2018.

ABSTRACT

# *Myeloid modulation in replication controllable oncolytic vaccinia virus therapy*

**황태호**
부산대학교

Viral replication of thymidine kinase deleted (tk-) vaccinia virus (VV) is attenuated in resting normal cells, enabling cancer selectivity, however, replication potency of VV-tk- appears to be diminished in cancer cells. Previously, we found that wild-type herpes simplex virus (HSV)-tk (HSV-tk) disappeared in most of the recombinant VV after multiple screenings, and only a few recombinant VV containing naturally mutated HSV--tk remained stable. In this study, VV-tk of western reserve (WR) VV was replaced by A167Y mutated HSV-tk (HSV-tk418m), to alter nucleoside selectivity from broad spectrum to purine exclusive selectivity. WOTS-418 remained stable after numerous passages. WOTS-418 replication was significantly attenuated in normal cells, but cytotoxicity was almost similar to that of wild type WR VV in cancer cells. WOTS-418 showed no lethality following a 5 × 108 PFU intranasal injection, contrasting WR VV, which showed 100% lethality at 1 × 105 PFU. Additionally, ganciclovir (GCV) but not BvdU inhibited WOTS-418 replication, confirming specificity to purine nucleoside analogs. The potency of WOTS-418 replication inhibition by GCV was > 10-fold higher than that of our previous truncated HSV-tk recombinant OTS-412. Overall, WOTS-418 demonstrated robust oncolytic efficacy and pharmacological safety which may delegate it as a candidate for future clinical use in OV therapy.

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# Young Scientist Colloquium

**Young Scientist Colloquium**

# *Moderator*

**김 대 원**
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아이씨엠(주)

**이 지 현** | **Viral Disease Research Division, Animal and Plant Quarantine Agency**
Anti-tumor effects of canine immune cell-derived exosomes in a mouse mammary tumor model

**이 창 호** | **Department of Life Convergence, Dankook University**
Cancer control through CRISPRi mediated epigenetic editing of mutant TERT promoter

**Steven Hyun Seung Lee** | **CuroGene Life Sciences Co.,**
Wide-ranging effects of a novel mTOR-inhibiting gene therapeutic for diabetic retinopathy in a STZ-induced mouse model

**송재원** | **Laboratory of Pharmacogenetics, Department of Biomedical and Pharmaceutical Sciences, Graduate School of Kyung Hee University**
Viral vector-based diagnosis of circulating tumor cells

P-07

# *Anti-tumor effects of canine immune cell-derived exosomes in a mouse mammary tumor model*

**Jienny Lee, Se-A Lee, Na-Yeon Gu, So Yeon Jeong, Yoon-Hee Lee, Bang-Hun Hyun**

*Viral Disease Research Division, Animal and Plant Quarantine Agency, 177, Hyeoksin 8-ro, Gimcheon-si, Gyeongsangbuk-do, 39660 Republic of Korea*

Natural killer (NK) cells are key immune cells against infection and malignant transformation. Exosomes have been the focus of extensive interest, as they appear to be involved in numerous crucial cellular processes. Canine mammary tumors are most common neoplastic diseases of female dogs, and more than 50% are malignant. In this study, we examined the anti-tumor effects of the canine NK cell-derived exosomes (NK-exosomes) in an experimental murine mammary tumor model using the canine mammary carcinoma cells, REM134. The NK-exosomes were injected at the tumor site and tail vein of the REM134 xenografted mice group. We found that the tumor size of the NK-exosomes-treated tumor group decreased compared to those of the only tumor group in the REM134-driven tumorigenic model. Also, the NK-exosomes-treated tumor group showed meaningfully reduced expression levels of the Bmi-1, MMP-3, IL-6, TNF-α, Bax, and Bcl-xL compared to those in the tumor group. We also confirmed that the expression level of the CD133, potent cancer stem cell (CSC) markers, decreased in the NK-exosomes-treated tumor group compared to the tumor group. This study suggests that the NK-exosomes exhibited anti-tumor effects through the downregulating CSC-related markers in the canine mammary tumor murine model. Further study is needed in the future, and we are conducting research on the detailed anti-tumor mechanism of the NK-exosomes.

P-13

# *Cancer control through CRISPRi mediated epigenetic editing of mutant TERT promoter*

**Chang Ho Lee[1], Seung Ryul Han[2], Ji Hyun Kim[2], Seong-Wook Lee[1,2]**

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In this study, we will introduce our efforts to develop novel specific and effective gene therapy for human malignant diseases, which is based on the system capable of inhibiting cancer growth through cancer-specific suppression of TERT expression. To this end, we developed CRISPRi system that can specifically and efficiently suppress TERT expression in cancer cells only, through genomic targeting and epigenetic editing of highly activated TERT promoter somatic mutation that is one of the most frequent genetic alterations in malignant diseases including hepatocellular carcinoma, melanoma, glioblastoma, and etc. We constructed an adenoviral vector encoding the CRISPRi system, observed anticancer efficacy, specificity, hepatotoxicity, and safety of the vector, and studied the anticancer mechanism of the vector. These proof-of-concept studies established the feasibility of CRISPRi mediated epigenetic control as a therapeutic tool for highly activated TERT promoter somatic mutation as a cancer-specific therapeutic target.

P-20

# *Wide-ranging effects of a novel mTOR-inhibiting gene therapeutic for diabetic retinopathy in a STZ-induced mouse model*

**Steven Hyun Seung Lee[1,2,3*], Joo Yong Lee[4,5*], Jun-Sub Choi[1], Hee Jong Kim[1], Jin Kim[1], Seho Cha[1], Kyoung Jin Lee[2,4], Ha-Na Woo[2,4], Keerang Park[6**], Heuiran Lee[2,4**]**

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Despite being a multifactorial condition, therapeutic interventions for diabetic retinopathy (DR) consist of laser photocoagulation or anti-VEGF drugs, treatment strategies that may not fully address the condition's complex pathophysiology, among other limitations inherent to the treatments themselves. However, a gene therapy focusing on a therapeutic target with broader effects, such as the mechanistic target of rapamycin (mTOR), may be a potential solution to overcome these concerns. Having previously demonstrated the suitability of a mTOR-inhibiting shRNA packaged in a recombinant adeno-associated virus to treat angiogenic retinal disorders, here we explore the effects of rAAV2-shmTOR-SD in a streptozotocin-induced diabetic mouse model. Delivered via intravitreal injection, the therapeutic virus vector was shown to effectively transduce mouse retinas and therein downregulate mTOR expression, which was elevated in sham-treated and control shRNA-injected (rAAV2-shCon-SD) control groups. mTOR inhibition lead to marked reductions in pericyte loss, vascular permeability, and cell layer thinning in the retina, three processes involved in DR progression. Immunohistochemistry showed that rAAV2-shmTOR-SD limited retinal angiogenesis and reduced pathogenic Müller cell activation and proliferation, thereby addressing DR-related activities linked to vision loss, while also having anti-apoptotic effects. Taken together, these results demonstrate the promise of rAAV2-shmTOR-SD as a potential gene therapeutic for DR.

**Co-first authors:** Steven Hyun Seung Lee, Joo Yong Lee
**Co-corresponding authors:** Keerang Park, Heuiran Lee

P-23

# *Viral vector-based diagnosis of circulating tumor cells*

**Jae Won Song[1,2], Sun Kyung Kim[1,2], Bada Lee[1,2], Peter Goughnour[1] Jong Man Park[3] and Jin Woo Choi[1,3] ***

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Cancer metastasis is the spread of cancer cells to distal organs or tissue, and is actively researched to understand and treat more advanced stages of cancer. Circulating tumor cells (CTCs) is a main factor that mediates cancer metastasis. They circulate in the blood making it suitable for liquid biopsy unlike tissue biopsy that is invasive and highly demanding for patients. In addition, it is more efficient to detect the comprehensive gene expression of tumor.
Epithelial cell adhesion molecule (EpCAM), which is well known to be highly expressed in epithelial cancer cells, is the current biomarker to detect CTCs, However, EpCAM expression is reduced in some CTCs that undergo epithelial-mesenchymal transition (EMT) before disseminating from primary tumor cells leading to false negative results. This is the main cause of false negative diagnosis in the previous CTC detection trials. Here, we present a novel method using adenovirus for detecting all types of CTCs. This technology uses a chimeric adenovirus 3/5 that has a cancer specific hTERT promoter with a green fluorescence protein (GFP) for easy detection in blood samples.
In this report, we verified the adenovirus 3/5 virus infection efficacy and cancer specificity. Since chimeric adenovirus 3/5 binds specifically to desmoglein-2 (DSG2) and CD46, it was shown that the expression of these receptors in each cell line were highly correlated with the infection rate of virus. The correlation between infection rate and mRNA/protein expression level was highest in DSG2 . The same method was also applied to detection of CTCs in patient's blood of prostate cancer and renal cell carcinoma. The number of CTCs was significantly decreased after prostatectomy and the number is correlated with the tumor stage of renal cell carcinoma.
Taken together, our novel method can be used for the prognosis and point of care for cancer patients.

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# Poster Abstract

P-01

# *Alteration of gammaretroviral vector integration patterns by insertion of histone and leucine zipper into integrase*

**Yeji Yang[1,2], Ji-eun Lee[1,3], Hye-young Jeong[1], Ji-yeon Shim[1], Min-jeong Baek[4], Min-jeong Son[1], Yeon-ju Kim[1], Hohsuk Noh[5], Kwang-il Lim[1,6]**

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Retroviral vectors show long-term gene expression in gene therapy through the integration of transgenes into the human cell genome. Murine leukemia virus (MLV), a well-studied gammaretrovirus, has been often used as a representative retroviral vector. However, frequent integrations of MLV-based vectors into transcriptional start sites (TSSs) could lead to the activation of oncogenes by enhancer effects of the genetic components within the vectors. Therefore, the MLV integration preference for TSSs limits its wider use in clinical applications. To reduce the integration preference of MLVbased vectors, we attempted to perturb the structure of the viral integrase that plays a key role in determining integration sites. For this goal, we inserted histones and leucine zippers, having DNA-binding property, into internal sites of MLV integrase. This integrase engineering yielded multiple mutant vectors that showed significantly different integration patterns compared with that of wildtype vector. Some mutant vectors did not prefer the key regulatory genomic domains of human cells, TSSs. Moreover, a couple of engineered vectors did not integrate into the genomic sites near the TSSs of oncogenes. Overall, this study suggests that structural perturbation of integrase is a simple way to develop safer MLV-based retroviral vectors for use in clinical applications.

P-02

# *Development of RNase-resistant RNA Aptamer that Inhibits Methyltransferase Activity of Zika virus*

**Su-Byeong Lim, Ju-Won Cha and Seong-Wook Lee***

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Zika virus (ZIKV) infection is associated with microcephaly in newborn during pregnancy and Guillain-Barre syndrome in adults. However, the anti-ZIKV therapeutic agent has not been developed. ZIKV is a member of the *Flavivirus* genus and *Flaviviridae* family. The RNA genome of ZIKV contains a 5' Cap 1 structure. This is formed by a methyltransferase (MTase) located at the N-terminal of nonstructural protein 5 (NS5) that methylates 5' end of 5'-untranslated region (UTR) of the viral RNA. The capping of the viral RNA 5'-UTR is essential for replication and escaping the host innate immune response. The ZIKV methylation occurs in cytoplasm, but human methylation in nucleus. Due to the different intracellular localization for viral RNA methylation process from host mRNA methylation process, ZKIV needs its own MTase. Therefore, targeting the MTase for therapy of disease caused ZIKV might be a proper therapeutic strategy. We identified the 2'-fluoro-modified RNA aptamer capable of specifically binding to the MTase of ZIKV using systematic evolution of ligands by exponential enrichment (SELEX). We verified that this RNA aptamer specifically binds to MTase with $K_d$ ~ 9 nM but not to other proteins, and inhibits its N-7 methylation activity of the viral MTase. In addition, we confirmed that aptamer efficiently interfered the binding of 5'-UTR viral RNA and MTase. We anticipate that the ZIKV MTase-specific RNA aptamer can block viral replication and induce the host innate immune response, and it could be useful for anti-ZIKV agents.

P-03

# *Sequence-specific prediction of the efficiencies of adenine and cytosine base editors*

**Myungjae Song[1,2], Hui Kwon Kim[1,2], Sungtae Lee[1], and Hyongbum Henry Kim[1,2]**

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Base editors, including adenine base editors (ABEs)$_1$ and cytosine base editors (CBEs)$_{2,3}$, are widely used to induce point mutations. However, determining whether a specific nucleotide in its genomic context can be edited requires time-consuming experiments. Furthermore, when the editable window contains multiple target nucleotides, various genotypic products can be generated. To develop computational tools to predict base-editing efficiency and outcome product frequencies, we first evaluated the efficiencies of an ABE and a CBE and the outcome product frequencies at 13,504 and 14,157 target sequences, respectively, in human cells. We found that there were only modest asymmetric correlations between the activities of the base editors and Cas9 at the same targets. Using deep-learning-based computational modeling, we built tools to predict the efficiencies and outcome frequencies of ABE- and CBE-directed editing at any target sequence, with Pearson correlations ranging from 0.50 to 0.95. These tools and results will facilitate modeling and
therapeutic correction of genetic diseases by base editing.

Reference : Nat Biotechnol, 2020 Sep;38(9):1037-1043

P-04

# *Inhibition of maturation of primary microRNA by Adenovirus VA RNA*

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Recombinant adenovirus has been used as the gene delivery tool over the past several decades. We also used adenoviral vector to express tumor suppressive primary miRNA (pri-miRNA) in cells for cancer gene therapy. However, here we found that adenovirus-mediated pri-miRNA expression impaired miRNA maturation. Previous studies demonstrated that adenoviruses express two non-coding virus-associated (VA) RNA, VA I and VA II RNA. Besides, VA I and VA II RNA are processed into viral small RNAs, called the mivaRNA I and mivaRNA II, respectively. These mivaRNAs can be incorporated into RISC and thus act similarly to miRNAs. In this study, we observed adenovirus VA RNAs are the main factors to influence the processing of pri-miRNA when delivered using adenovirus. Then, pri-miRNA processing was specifically blocked by VA expression and recovered by anti-3'VA expression. In addition, VA RNAs were transcribed into VAI-II full length RNA, which binds to Drosha protein. These results indicated that expression of adenovirus VA RNAs should be suppressed when using adenovirus to successfully deliver and express pri-miRNA or shRNA.

P-05

# *Long-term storage and stemness of animal mesenchymal stem cells*

**Jienny Lee, So Yeon Jeong, Na-Yeon Gu, Se-A Lee, Yoon-Hee Lee, Bang-Hun Hyun**

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Mesenchymal stem cells (MSCs) exhibit long-lasting self-renewing capacity and a multi-lineage differentiation potential. They contribute to the replacement of lost, damaged, or dysfunctional cells in mesenchymal tissues and therefore play a central role in cellular homeostasis and regeneration. Cells might be damaged by environmental changes during the freezing process. There are various factors that influence the function of cells cultured after cryopreservation and thawing. In this study, we investigated the effects of long-term storage (7 years in liquid nitrogen phase) on the characteristics of equine adipose tissues-derived MSCs (eAD-MSCs). We examined the cell viability of cryopreserved eAD-MSCs (10% DMSO, 40% FBS, 50% culture medium) in liquid nitrogen phase for 7 years. We also investigated the cellular morphology, proliferating capacities, expression of cell surface markers such as CD13, CD34, CD44, CD45, CD90, and CD105, mesodermal differentiation potentials, and expression of senescence-related markers of p53, p21, and telomerase reverse transcriptase in eAD-MSCs after cryopreservation. The eAD-MSCs were analyzed immediately and after being frozen in liquid nitrogen for 1 year (< 1 year, A) and more than 7 years (> 7 years, B), respectively. After cryopreservation for 7 years, B eAD-MSCs were similar their cellular morphology, proliferating capacities, and expression of cell surface markers compared with A eAD-MSCs. Also, cryopreservation did not affect the adipogenic, chondrogenic, or osteogenic differentiation potentials of A and B eAD-MSCs. In this study, cryopreservation for (or over) 7 years maintain the stem cell phenotype and differentiation potentials of eAD-MSCs. These results will be an advantage that can be effectively used for future development of cell-based therapies.

P-06

# *Differentiation potential of CD271 positive mesenchymal stem cells through electrical stimulation*

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Mesenchymal stem cells (MSCs) are a heterogeneous population of cells with varying magnitudes of differentiation potential among single clone of MSCs. CD271 has been identified as a marker of the most homogeneous MSCs subset. In this study, we separated CD271 positive (CD271-P) or negative cells (CD271-N) from canine adipose tissue-derived MSCs (cAD-MSCs) using immunomagnetic selection method. CD271-P and CD271-N cells from cAD-MSCs exhibited abilities to attach to culture plate and expand *in vitro*. CD271-P cells had spindle-shaped morphology, but CD271-N cells had spindle and round shape morphology. CD271-P and CD271-N cells displayed similar immunophenotypic markers (CD34, CD44, CD45, and CD90). However, CD271-P and CD271-N cells exhibited difference in differentiation potential. Two types of cells exhibited chondrogenic differentiation potential. Specifically, CD271-P cells have a greater capacity for chondrogenic differentiation potential compared to CD271-N cells at 5 passage. Many studies have been reported that stem cells can differentiate into various cells by electrical stimulation (ES). ES was applied to CD271-P cells and gene expression of chondrogenic markers such as type II collagen (COL2A1), Aggrecan, and HSP70 was analyzed at 3 days. As a result, electrical stimulated CD271-P cells have a greater capacity for chondrogenic differentiation potential compared to those of control in absence of exogenous differentiation condition. This study might contribute to the differentiation of MSCs into cartilage cells by inducing pre-chondrogenic condition under specific ES.

P-07

# *Anti-tumor effects of canine immune cell-derived exosomes in a mouse mammary tumor model*

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Natural killer (NK) cells are key immune cells against infection and malignant transformation. Exosomes have been the focus of extensive interest, as they appear to be involved in numerous crucial cellular processes. Canine mammary tumors are most common neoplastic diseases of female dogs, and more than 50% are malignant. In this study, we examined the anti-tumor effects of the canine NK cell-derived exosomes (NK-exosomes) in an experimental murine mammary tumor model using the canine mammary carcinoma cells, REM134. The NK-exosomes were injected at the tumor site and tail vein of the REM134 xenografted mice group. We found that the tumor size of the NK-exosomes-treated tumor group decreased compared to those of the only tumor group in the REM134-driven tumorigenic model. Also, the NK-exosomes-treated tumor group showed meaningfully reduced expression levels of the Bmi-1, MMP-3, IL-6, TNF-α, Bax, and Bcl-xL compared to those in the tumor group. We also confirmed that the expression level of the CD133, potent cancer stem cell (CSC) markers, decreased in the NK-exosomes-treated tumor group compared to the tumor group. This study suggests that the NK-exosomes exhibited anti-tumor effects through the downregulating CSC-related markers in the canine mammary tumor murine model. Further study is needed in the future, and we are conducting research on the detailed anti-tumor mechanism of the NK-exosomes.

P-08

# *Characterization and safety evaluation of canine cell-derived exosomes*

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Exosomes are membrane-bound extracellular vesicles (EVs) that are produced in the endosomal compartment of most eukaryotic cells. Exosome production and content may be influenced by molecular signals received by the cell of origin. Recently, accumulating evidence suggests that cell-secreted exosomes as a novel cell-free therapy might constitute a compelling alternative because of their advantages over the corresponding cells. In this study, we tried to isolate, characterize and test for safety of exosomes from canine mesenchymal stem cells (MSCs) and natural killer (NK) cells. Firstly, isolation of exosomes was done in accordance to ultracentrifugation (UC) method. Also, electron microscopy confirmed that particles from UC possess a circular morphology with an intact membrane based on negative staining and are consistent in size using nanoparticle tracking analysis. Two type of cell-derived exosomes are a fraction that are less than 200 nm in size, express exosome markers (CD63, CD81, Alix, HSP70, and TSG101). Specifically, NK cell-derived exosomes expressed activated NK cell markers such as perforin and granzyme B. Next, we conducted to test for safety on MSCs and NK cell-derived exosomes. As results, we observed that positive controls were detected in blood agar plates and Luria-Bertani broth confirming microbial contamination, but not in MSCs and NK cell-derived exosomes. In addition, we confirmed that limulus amebocyte lysate test as an endotoxin test and mycoplasma test were not detected in the both exosomes. Collectively, microbial contaminations were not detected in MSCs and NK cell-derived exosomes, and is thought to be useful for basic and therapeutic research applications.

P-09

# *Development of in vitro neutralization assay based on the SARS-CoV-2-spike pseudotyped virus*

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, at the end of 2019, and its rapid national and international spread pose a global health emergency. With the development of the COVID-19 epidemic, there is an urgent need to establish a system for determining the effectiveness of vaccine and therapeutics in biosafety level 2 (BSL-2) facilities. Here, we developed a pseudotyped virus-based neutralization assay against SARS-CoV-2 in biosafety level 2 facilities. We generated a Nanoluciferase-CopGFP dual-expressing pseudovirus containing the wild-type or mutant Spike protein (D614G) of SARS-CoV-2 in the envelope-defective HIV-1 backbone. To increase susceptibility to our pseudotyped virus model, we established a cell line, HEK293T-ACE2, that stably expressed SARS-CoV-2 receptor, ACE-2. Both wild-type and mutant Spike protein (D614G) of SARS-CoV-2 pseudovirus was effectively transduced in HEK293T-ACE2 cells compared to ΔENV virus. Furthermore, the SARS-CoV-2 spike pseudotyped virus was neutralized by commercially available ACE-2 antibody or SARS-CoV-2 spike RBD monoclonal antibody. Thus, we developed a pseudovirus-based neutralization assay for SARS-CoV-2, which will be valuable for evaluating viral entry inhibitors and neutralizing antibodies against SARS-CoV-2.

Keyword: SARS-Cov-2, pseudovirus, HEK293T-ACE2, Neutralizing assay

P-10

# *Inhibitory Effects of Human Adipose Stem Cell derived Extracellular Vesicles in Melanogenesis of Mouse Melanoma.*

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Human adipose derived stem cells (hASC) and their secretory factors are known to hold broad therapeutic promise. Recent advances in biotechnology has brought expansion of research field such as secretory machinery of extracellular vesicles (EVs). EVs are facilitators of cell to cell communications released by virtually all kinds of cells. They are known to execute their functions through diverse array of cargos such as protein polymers, nucleic acids and lipids. Here, we evaluated highly defined EVs originated from hASC for their potential application in skin lightening. In order to assess lightening of cellular pigmentations by EVs, we quantified melanin levels within mouse melanoma (B16-F10) cells ("intracellular melanins") and melanin levels outside mouse melanoma cells ("extracellular melanins") , three days after the treatment using ELISA reader. For the negative control and positive control of experimental set, equivalent volumes of PBS or 500 μM Arbutin were used, respectively. Among three concentrations of the EVs tested, 30 and 50 μg/mL treatment significantly lowered the intracellular melanin levels, while all three concentrations (10, 30, and 50 μg/mL) resulted in significant decline in extracellular melanin levels. All of the results indicated dose-dependent action of hASC derived EVs. Two batches of EVs with different manufactured dates resulted in similar outcome. Further work may be necessary to identify crucial cargo within hASC derived EVs that undertake this skin whitening phenomenon.

Keyword: extracellular vesicle, adipose derived stem cell, melanin, melanogenesis, efficacy

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P-11

# *Screening of APOBEC3G inhibitors for retroviral replicating vector-mediated gene therapy.*

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Gene therapy mediated by retroviral replicating vectors(RRVs) has been proven to be a highly promising strategy to treat a variety of cancer models through its tumor-selective transduction and non-cytolytic property. However, host innate immunity against retrovirus is an obstacle to successful RRV-based gene therapy. APOBEC3G(apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G; A3G) is an anti-retroviral host factor, which provides the innate immune response to retroviral infection through cytidine deaminase activity. APOBEC3G can bind single-stranded RNA and induce C to U deamination, results in antiviral effect through G-to-A hypermutation at proviral DNA. Unlike lentivirus, which has evolved the vif gene to prevent A3G activity, the retrovirus is susceptible to A3G-mediated immunity.

In this study, we tested several derivatives of A3G inhibitor derived from ChEMBL database. Stable A3G expressing cell line was previously established by transducing U-87 MG cells with a lentiviral vector encoding A3G gene. U-87 MG-A3G cells were infected by dual-RRV vectors (spRRVeGFP/sRRVgpDsRed) in the absence or presence of A3G inhibitor compounds. GFP expression was monitored by fluorescence microscopy and flow cytometry after transduction with spRRVeGFP/sRRVgpDsRed retroviral particles at 0.2 MOI.

The GFP expression levels of U-87 MG-A3G cells were significantly low as compared with the U-87 MG control cells. Flow cytometry data showed that several A3G inhibitor compounds increased the spreading of spRRVeGFP/sRRVgpDsRed retroviral vectors. These results suggest that APOBEC3G inhibition can provide an improvement in the therapeutic efficacy of RRV-based gene therapy.

P-12

# *Rationally designed redirection of natural killer cells anchoring a cytotoxic ligand for pancreatic cancer treatment*

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The emergence of T-cell engineering with chimeric antigen receptors (CARs) has led to attractive therapeutics; however, autologous CAR-T cells are associated with poor clinical outcomes in solid tumors because of low safety and efficacy. Therefore, the aim of our study was to develop a CAR therapy with enhanced cytotoxicity against solid cancer using allogeneic NK cells. In this study, we engineered “off-the-shelf” NK cells to redirect them towards pancreatic ductal adenocarcinoma (PDAC) by improving their target-specific cytotoxic potential. By integrated bioinformatic and clinicopathological analyses, folate receptor alpha (FRα) and death receptor 4 (DR4) were significantly highly expressed in patient-derived tumor cells. The combined expression of FRα and DR4/5 was associated with inferior clinical outcomes, therefore indicating their use as potential targets for biomolecular treatment. Thus, FRα and DR4 expression pattern can be a strong prognostic factor as promising therapeutic targets for the treatment of PDAC. For effective PDAC treatment, allogeneic CAR-NK cells were reprogrammed to carry an apoptosis-inducing ligand and to redirect them towards FRα and initiate DR4/5-mediated cancer-selective cell death in FRα- and DR4/5-positive tumors. As a result, the redirected cytotoxic ligand-loaded NK cells led to a significantly enhanced tumor-selective apoptosis. Accordingly, use of allogeneic CAR-NK cells that respond to FRα and DR4/5 double-positive cancers might improve clinical outcomes based on personal genome profiles. Thus, therapeutic modalities based on allogeneic NK cells can potentially be used to treat large numbers of patients with optimally selective cytotoxicity.

Keyword : CAR-NK, Cancer immunotherapy, Pancreatic cancer, Allogeneic therapy, TRAIL

P-13

# *Cancer control through CRISPRi mediated epigenetic editing of mutant TERT promoter*

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In this study, we will introduce our efforts to develop novel specific and effective gene therapy for human malignant diseases, which is based on the system capable of inhibiting cancer growth through cancer-specific suppression of TERT expression. To this end, we developed CRISPRi system that can specifically and efficiently suppress TERT expression in cancer cells only, through genomic targeting and epigenetic editing of highly activated TERT promoter somatic mutation that is one of the most frequent genetic alterations in malignant diseases including hepatocellular carcinoma, melanoma, glioblastoma, and etc. We constructed an adenoviral vector encoding the CRISPRi system, observed anticancer efficacy, specificity, hepatotoxicity, and safety of the vector, and studied the anticancer mechanism of the vector. These proof-of-concept studies established the feasibility of CRISPRi mediated epigenetic control as a therapeutic tool for highly activated TERT promoter somatic mutation as a cancer-specific therapeutic target.

P-14

# *RNA reprogramming based on trans-splicing ribozyme for liver cancer gene therapy.*

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Group I intron-based trans-splicing ribozyme enables to sense and reprogram target RNA into gene of interest through RNA replacement. Previously, we proposed hTERT-targeting trans-splicing ribozyme downstream therapeutic suicide gene for cancer therapy. Here, we optimized the specific ribozyme for highly efficient antitumor activity with less off-target effect for anti-HCC approach. We enhanced the intracellular expression of the ribozyme at transcriptional/post-transcriptional level and improved tumor selectivity via introduction of microRNA target site at the 3' end of the ribozyme. Then, systemic administration of adenovirus encoding our refined ribozyme achieved great anti-tumor efficacy and improved ability to specifically target tumor without hepatotoxicity in vivo. Minimal liver toxicity, tissue distribution and clearance pattern of the recombinant adenovirus were observed in normal animals administered either systemically or via the hepatic artery. Post-transcriptionally regulated RNA replacement strategy mediated by a cancer-specific ribozyme provide a clinically relevant, safe, and efficient strategy for HCC treatment.

P-15

# *Anticancer effects of hASC-EV, not hUC-EV: A double-edged sword effect in normal and cancer cells*

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Human adipocyte mesenchymal stem cell-derived extracellular vesicle, hASC-EV, is characterized about 100-150nm range of heterogeneous sizes with small membrane vesicles originated plasma membrane and collected from human adipocyte mesenchymal stem cell. Each exosome has its own functions as transferring their biological materials to induce biological process like replications, growth, apoptosis and necrosis. hASC-EV was provided by collaborators and already proven its various functions which include anti-inflammatory, anti-liver fibrosis and anti-lung fibrosis by them. In this study, we tested hASC-EV's anticancer function with inhibiting cancer cell proliferation and increasing normal cell duplication, these were a double-edged sword effect in normal and cancer cells in vitro. We also tested human umbilical cord-derived MSC extracellular vesicle (hUC-EV) as a negative control for anticancer effects. The action of hUC-EV was not any double edged-sword effects like hASC-EV but decreased proliferation both cancer and normal cells. Apoptosis was increased in CIP2A positive cells in MRC5 and A549 co-cultures by hASC-EV treatment rather than hUC-EV. Moreover, the tumor size of the A549 xenograft mice decreased statistically significantly and remained small for 37 days after 5 intravenous administrations with 1x109 particles hASC-EV. But same times and same particle number of hUC-EV administration did not shown any positive effect in A549 xenograft mice model. These animal results were similar with the cell results of hASC- and hUC-EV. The results showed that hASC-EV induced apoptosis into A549 cells rather than MRC5 cells in the co-culture system and significantly reduced A549 tumor size in xenografted mice. Thus hASC-EV has anticancer effects with a double edged-sword in normal and in cancer cells.

Key words
Adipocyte mesenchymal stem cell, umbilical cord mesenchymal stem cell, extracellular vesicle, A549 xenograft mice model

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P-16

# *Signaling pathways involved in HMGB1-dependent NADPH oxidase in monocytes*

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The effects of vascular inflammation on monocytes are modulated by reactive oxygen species (ROS) and also involve high mobility group box 1 (HMGB1) engagement. However, its role in the HMGB1-induced generation of ROS in monocytes is still unclear. Thus, this study investigated the source and mechanisms of ROS generation in monocytes stimulated with HMGB1. Monocytes were cultured using THP-1 cells (a human monocytic leukamia cell line), and stimulated with HMGB1 (100 ng/ml), and ROS production were analyzed by flow cytometry. The expression of p47phox and mitogen-activated protein kinases in HMGB1-stimulated VSMCs was analyzed by Western blots. Exposure of THP-1 cells to HMGB1 showed an increased production of ROS, which was attenuated by NADPH oxidase inhibitors. Linked to these results, we aimed to the signal transduction pathways involved in the activation of NADPH oxidases. In cultured human THP-1 cells stimulated with HMGB1 (100 ng/ml), ROS production was markedly increased. However, both these effects were markedly attenuated in cells pretreated with the inhibitors of ROS [N-acetyl cysteine (NAC)] and NADPH oxidase [diphenyleneiodonium chloride (DPI) and apocynin (APO)]. Moreover, HMGB1-induced expressions of p47phox phosphorylation were markedly attenuated in MAPKs inhibitors pre-treated cells, and phosphorylation of MAPKs expressions were reduced in receptors for advanced glycation end-product (RAGE)-inhibited cells. Likewise, in RAGE-inhibited cells, HMGB1-induced ROS production was significantly reduced in cells.
Taken together, it was indicated that activation of the MAPKs/p47phox cascade plays a central role in HMGB1/RAGE-induced ROS generation and suggests the existence of a ROS inflammatory amplification feedback loop in monocytes. Altogether, these results suggest that RAGE plays a critical role in HMGB1-induced ROS generation in monocytes through activation of NADPH oxidase.

P-17

# *A role for LTB4 induced MCP-1 production in HMGB1-exposed vascular smooth muscle cells*

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Although Monocyte chemotactic protein-1 (MCP-1) is best known for its ability to recruit mononuclear cell, few studies have examined the effects of this chemokine on others cells in the vascular response to injury. Given the importance of high mobility group box 1 (HMGB1) in vascular injury and inflammation, this study determined MCP-1 expression in VSMCs exposed to HMGB1, and also evaluated the role of 5-lipoxygenase (5-LO) signaling pathways in HMGB1-induced MCP-1 expression. VSMCs were ex plant cultured using rat thoracic aorta, and stimulated with HMGB1 (30 ng/ml). The expression of 5-LO and MCP-1 in HMGB1-stimulated VSMCs was analyzed by Western blots. LTB4 and MCP-1 production were determined by ELISA. In cultured rat aortic VSMCs stimulated with HMGB1 (30 ng/ml), the expression of 5-LO was markedly increased in a dose- and time-dependent manner, as well as production of leukotriene B4. Likewise, MCP-1 expression and production in HMGB1-stimulated VSMCs were markedly increased, which was significantly attenuated in cells treated with zileuton (100 μM), a 5-LO inhibitor as well as in cells deficient of 5-LO. In response to LTB4, MCP-1 expression in VSMCs was increased dose-dependently, which was attenuated in cells treated with U75302 (10 μM), a LTB4 receptor 1 (BLTR1) inhibitor as well as in cells deficient of BLTR1. It was suggested a potential importance of LTB4 in MCP-1 expression in VSMCs.

Our results suggested that 5-LO-derived LTB4 produced by HMGB1-stimulated cells increased MCP-1 expression in VSMCs of the injured vasculatures. Thus, the LTB4-BLTR1 signaling axis in VSMCs might serve as a potential target for future therapeutic strategies for vascular inflammation in the injured vasculatures.

P-18

# *Potential of mTOR as the therapeutic target for blocking choroidal neovascularization*

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We recently demonstrated the therapeutic potential of shRNA abrogating mechanistic target of rapamycin (mTOR) delivered via recombinant adeno-associated virus (rAAV) against pathological retinal angiogenesis. In rat oxygen-induced retinopathy (OIR) and mouse laser-induced choroidal neovascularization (CNV) models, rAAV2-shmTOR reduced both neovascularization and inflammation. In addition, the intra-ocular delivery of rAAV-shmTOR induced efficient transduction of retinal endothelial cells and reduced extensiveness by laser injury with mTOR inhibition. To further explore the mechanism of anti-angiogenic role of rAAV2-shmTOR, we investigated endothelial cells in the presence of VEGF stimulation. rAAV2-shmTOR significantly reduces mTOR expression and downstream signaling cascades of mTORC1 and mTORC2 in HUVEC cells even under VEGF treatment conditions. Angiogenic features and proliferative activity of HUVEC cells stimulated by VEGF treatment were efficiently inhibited by rAAV2-shmTOR. Moreover, rAAV-shmTOR supported the maintenance of the integrity of the vascular endothelial cell barrier by sustaining tight junctions between HUVEC cells.
Taken together, these results demonstrate the potential of rAAV2-shmTOR as an efficient therapeutic strategy for retinal vascular disorders.

**Co-first authors:** Seho Cha and Won-il-Seo
**Co-corresponding authors:** Heuiran Lee and Beom Jun Lee

P-19

# *Manufacturing master cell banks of oncospreading dual-RRV producing cells*

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Retroviral Replicating Vectors (RRVs) can spread in tumor tissue because of their ability to infect and replicate in dividing cells. Since RRVs have been shown highly efficient transduction in tumors, it is possible to obtain the therapeutic effect through prodrug activator genes delivered by RRV vectors. In the previous study, we developed the GaLV-env-pseudotyped dual RRV vector system (sRRVgp-yCD & spRRVe-TK) encoding HSV1-TK and human codon optimized yeast CD genes, respectively, for cancer therapeutic agents. In our present study, we were willing to establish the virus producer cells (VPC) that can produce high titers of the dual RRVs and to manufacture master cell banks (MCBs) for clinical use. First, each of the dual RRVs (sRRVgp-yCD & spRRVe-TK) was separately transduced into retrovirus packaging cell line PG13. An then, PG13/env-HSV1-TK and PG13/gagpol-yCD VPCs were selected clonally and amplified for the screening of VPCs producing high titer retroviral vector particles. The biological titer and genome integrity of the selected VPC clones were evaluated. Currently, MCBs of the validated PG13/env-HSV1-TK and PG13/gagpol-yCD VPCs are under manufacturing in the GMP facility.

P-20

# *Wide-ranging effects of a novel mTOR-inhibiting gene therapeutic for diabetic retinopathy in a STZ-induced mouse model*

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Despite being a multifactorial condition, therapeutic interventions for diabetic retinopathy (DR) consist of laser photocoagulation or anti-VEGF drugs, treatment strategies that may not fully address the condition's complex pathophysiology, among other limitations inherent to the treatments themselves. However, a gene therapy focusing on a therapeutic target with broader effects, such as the mechanistic target of rapamycin (mTOR), may be a potential solution to overcome these concerns. Having previously demonstrated the suitability of a mTOR-inhibiting shRNA packaged in a recombinant adeno-associated virus to treat angiogenic retinal disorders, here we explore the effects of rAAV2-shmTOR-SD in a streptozotocin-induced diabetic mouse model. Delivered via intravitreal injection, the therapeutic virus vector was shown to effectively transduce mouse retinas and therein downregulate mTOR expression, which was elevated in sham-treated and control shRNA-injected (rAAV2-shCon-SD) control groups. mTOR inhibition lead to marked reductions in pericyte loss, vascular permeability, and cell layer thinning in the retina, three processes involved in DR progression. Immunohistochemistry showed that rAAV2-shmTOR-SD limited retinal angiogenesis and reduced pathogenic Müller cell activation and proliferation, thereby addressing DR-related activities linked to vision loss, while also having anti-apoptotic effects. Taken together, these results demonstrate the promise of rAAV2-shmTOR-SD as a potential gene therapeutic for DR.

**Co-first authors:** Steven Hyun Seung Lee, Joo Yong Lee
**Co-corresponding authors:** Keerang Park, Heuiran Lee

P-21

# *rAAV expressing soluble VEGF receptor-1 variant tested in a STZ-induced mouse model as a intravitreally-injected gene therapy for diabetic retinopathy*

**Steven Hyun Seung Lee[1,2,3*], Joo Yong Lee[4,5*], Im Kyeung Kang[2,3*], Jun-Sub Choi[1], Hee Jong Kim[1], Jin Kim[1], Seho Cha[1], Kyoung Jin Lee[2,4], Ha-Na Woo[2,4], Keerang Park[6**], Heuiran Lee[2,4**]**

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**Purpose:** In addition to laser photocoagulation, therapeutic interventions for diabetic retinopathy (DR) include anti-VEGF drugs, with both possessing distinct disadvantages. Specific to the latter is the necessity of frequent intravitreal injections, which may be burdensome to patients, adversely affecting patient compliance and treatment efficacy, and for which gene therapy may prove to be a favorable alternative. Here, we investigate the therapeutic potential of a recombinant AAV2 expressing a soluble variant of VEGF receptor-1 (rAAV2-sVEGFRv-1) in a long-term study.
**Methods:** C57/B6 mice were used to generate a streptozotocin-induced diabetic mouse model, which were administered with rAAV2-sVEGFRv-1 or a therapeutic dose of bevacizumab via intravitreal injections, with appropriate controls. Multiple studies have shown bevacizumab, which and is often used off-label due to the economic advantages it offers, to be as effective as approved therapeutics versus DR.
**Results:** rAAV2-sVEGFRv-1 effectively transduced the mouse retinas, was well-supported in target cell types, and its overall therapeutic efficacy compared favorably to bevacizumab in addressing various aspects of DR pathophysiology. rAAV2-sVEGFRv-1 reduced both retinal vascular leakage as well as pericyte loss, an important early feature of the condition. Limiting the extent to which retinal cell layer thinning occurred suggests the therapeutic virus vector possess neuroprotective qualities while also being anti-apoptotic, which is the mechanism of cell death by which neurodegeneration occurs in DR.
**Conclusions:** Taken together, these results demonstrate the great promise of rAAV2-sVEGFRv-1 as an effective and convenient gene therapy-based solution for the treatment of DR.

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**Co-corresponding authors:** Keerang Park, Heuiran Lee

P-22

# *Adeno associated virus 2-based gene therapy with coding survivial splicing variant DX2 of pro-apoptotic AIMP2 for treatment of neurodegenerative diseases*

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Pro-apoptotic gene AIMP2 is considered a critical causative gene for Parkinson disease(PD). Even in amytropic lateral sclerosis (ALS), AIMP2 is suspected of contributing to disease development in the tight interaction with lysyl tRNA synthetase. Nevertheless, it is difficult to directly target AIMP2 for the treatment of the diseases due to the housekeeping character and macro-complex-forming existence. Instead, AIMP2 has an antagonistic survival splicing variant, so called DX2. Thus, we developed DX2-coding AAV2 to target neurodegenerative disease such as PD and ALS. To prevent leakage of the transgene, miR142 target seq was added.

Neurodegenerative diseases are characterized by the loss of neuron cells such as dopaminergic neurons in Parkinson's disease (PD) and motor neurons in Amyotrophic lateral sclerosis (ALS). As AIMP2 can contribute to PD through promoting apoptosis following to aberrantly activating poly (ADP-ribose) polymerase 1 (PARP-1), DX2 blocks the AIMP2-induced neuronal apoptosis. As for ALS patients, the cause is unknown but some of patients carries mutations in specific genes such as TDP43 and SOD1, which lead to the loss of motor neurons. DX2 can bind to SOD1 prevent the loss of motor functions

Here, it is shown that DX2 contributes to cell survival by suppressing AIMP2-induced apoptosis, and to suggest AIMP2-DX2 as a novel therapeutics for neurodegenerative disease such as PD and ALS.

P-23

# *Viral vector-based diagnosis of circulating tumor cells*

**Jae Won Song[1,2], Sun Kyung Kim[1,2], Bada Lee[1,2], Peter Goughnour[1] Jong Man Park[3] and Jin Woo Choi[1,3] ***

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Cancer metastasis is the spread of cancer cells to distal organs or tissue, and is actively researched to understand and treat more advanced stages of cancer. Circulating tumor cells (CTCs) is a main factor that mediates cancer metastasis. They circulate in the blood making it suitable for liquid biopsy unlike tissue biopsy that is invasive and highly demanding for patients. In addition, it is more efficient to detect the comprehensive gene expression of tumor.
Epithelial cell adhesion molecule (EpCAM), which is well known to be highly expressed in epithelial cancer cells, is the current biomarker to detect CTCs, However, EpCAM expression is reduced in some CTCs that undergo epithelial-mesenchymal transition (EMT) before disseminating from primary tumor cells leading to false negative results. This is the main cause of false negative diagnosis in the previous CTC detection trials. Here, we present a novel method using adenovirus for detecting all types of CTCs. This technology uses a chimeric adenovirus 3/5 that has a cancer specific hTERT promoter with a green fluorescence protein (GFP) for easy detection in blood samples.
In this report, we verified the adenovirus 3/5 virus infection efficacy and cancer specificity. Since chimeric adenovirus 3/5 binds specifically to desmoglein-2 (DSG2) and CD46, it was shown that the expression of these receptors in each cell line were highly correlated with the infection rate of virus. The correlation between infection rate and mRNA/protein expression level was highest in DSG2 . The same method was also applied to detection of CTCs in patient's blood of prostate cancer and renal cell carcinoma. The number of CTCs was significantly decreased after prostatectomy and the number is correlated with the tumor stage of renal cell carcinoma.
Taken together, our novel method can be used for the prognosis and point of care for cancer patients.

P-24

# *Bi-specific RNAi to target mTOR and Androgen receptor for castration-resistant prostate cancer.*

**Soo Min Lee[1,3], Su Kyeong Kang[1,3], Ki Hwan Um[2] and Jin Woo Choi[1,3] ***

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RNA interference (RNAi) is a mechanism that regulates mRNA stability and translation by silencing specific genes. RNAi has been extensively applied to various diseases such as cancer. However, there are technical limitations to such as off-targeting effects and low delivery efficacy. Also, in many diseases like cancer, as one gene is not a only cause of the disease development, it would be nice to target more than one gene. So, corporation of two shRNAs system is needed. However, in that cases, two respective promoters should be coded and that may lead positional hindrance effect each other.

To overcome these challenges, we developed a novel bi-specific shRNA system that both strands of shRNA (sense, anti-sense) are designed to respectively bind to each mRNA and finally down-regulate two different gene without any off-target effects. In addition, as our technology only needs one promoter, the expression level can be balanced. As for delivery issue, we incorporated our technology into adenovirus to assist its delivery into the cells.

castration-resistant prostate cancer (CRPC) is an incurable type of prostate cancers with a low survival rate. CRPC doesn't respond to anti-androgen receptor (AR) therapy but AR still work as a main cancer-driving gene. Especially network of CRPC is reorganized into mTOR. Therefore, co-targeting AR and mTOR is considered as highly potent therapeutic strategy. Further, we used the genetically modified oncolytic virus as a carrier of bi specific siRNA on mTOR and AR, which facilitates delivery of RNAi in target cells. As the results, mTOR and AR are knocked down sufficiently in CRPC cell lines 72 hours after virus infection and cancer cell suffered from apoptosis and the proliferation was decreased subsequently. In mouse xenograft model, more regression of tumor size compared with the empty oncolytic virus. This suggests that our novel oncolytic virus loading mTOR-AR bi-specific RNAi have a possibility as a new therapeutic agent for CRPC patients.

P-25

# *Multiplexed genome engineering of human induced pluripotent stem cells*

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*# These authors equally contributed to this study.*

Clustered Regularly Interspaced Short Palindromic Repeats and Cas-associated (CRISPR/Cas) systems have been used as a versatile tool for genome editing in mammalian and plant cells. CRISPR/Cas genome editing enzymes consist in two parts: effector protein that results in DNA double strand break and single guide RNA (sgRNA) that addresses the ribonucleoprotein (RNP) enzymes to the intended sequence in the genome. Recently, various cell therapies are being developed by combining induced Pluripotent Stem Cells (iPSCs) and gene editing technology. In particular, the efficiency of gene editing is important when multiple gene editing is performed in a complex manner. We performed simultaneous multiplexed genome editing rather than sequential mutagenesis of each gene to avoid unwanted damage to the cells. At least two different sgRNA candidates for each target gene that might result in higher editing efficiency were designed using web-based tools, synthesized *in vitro*, and tested individually in HEK293T cells. After T7E1-based efficiency tests, the two sgRNAs per each gene were chosen. Total of 8 different RNP pairs were assembled *in vitro*, and introduced into HEK293T cells using electroporation. The four different RNP pairs with proven efficiency were introduced into iPSCs using electroporation to target four different genes. After two weeks, sixteen iPSCs colonies were picked and genomic DNA was isolated. PCR amplicons spanning the intended editing sites were amplified and subjected to next generation sequencing. Deep sequencing of the DNA from the 4 genes in iPSCs lines revealed one cell out of 16 tested to be homozygous mutations for each locus. Our experiences suggested that designing sgRNAs that should result in greater editing efficiency while minimized off-target effects accounts for overall success of genetically modified iPSCs.

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P-27

# *Cancer Immunotherapy by Combinational Delivery of SAHA and siRNA using Anti-PD-L1-Targeted Immunoliposomes*

**Ji-Eun You[a] and Keun-Sik Kim[a]**

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Cancer immunotherapy is a powerful treatment modality with active on-going preclinical and clinical developments of multiple therapeutic pipelines. Recently, programmed death ligand-1 (PD-L1) emerged as a central element in cancer treatments targeting immune checkpoints. The PD-L1 monoclonal antibodies that block the PD1/PD-L1 pathway can delay tumor growth efficiently but has critical disadvantages such as low selectivity and high immune mediated systemic toxicity. In this study, we developed active targeting liposome loaded histone deacetylase inhibitor (HDACi) and PD-L1 siRNA for synergistic anticancer immunotherapeutic effect. The aim of the study was to determine the antitumor effect of combined chemo-gene therapy in non-small cell lung cancer (NSCLC). The PD-L1-targeted immunoliposomes were ~100 nm in diameter with unimodal size distribution. These immunoliposomes demonstrated a significant increase in cellar association and the combined delivery of the PD-L1-targeted immunoliposomes containing HDACi (SAHA) or anti-PD-L1 siRNA were also significantly more cytotoxic than only one-drug treatment. We also validated a significant increase of cytokines of CD8+ T cell responses following treatment with SAHA (Vorinostat) and anti-PD-L1 siRNA. Theses immunoliposomes for dual-drug (SAHA and siRNA) delivery have promising potential for clinical applications and possibly provides a well-controlled design for combination therapy with chemotherapeutic and siRNA therapeutic drug for further exploration.

**Key words:** HDACi, Immunoliposomes, Immunotherapy, PD-L1, SAHA, siRNA

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P-28

# *6-O-galloylsalidroside, an active ingredient from Acer tegmentosum, ameliorates alcoholic steatosis and liver injury in a mouse model of chronic ethanol consumption*

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We previously reported that Acer *tegmentosum* extract, which is traditionally used to treat liver disease in Korea, might improve metabolism, and suppress inflammation in the liver. The active ingredient, 6-O-galloylsalidroside, was isolated from A. *tegmentosum*. We hypothesized that 6-O-galloylsalidroside could produce the desirable pharmacological benefits to ameliorate physiological conditions caused by chronic alcohol consumption. We investigated whether 6-O-galloylsalidroside can regulate alcoholic fatty liver and repair liver injury in mice. During chronic-plus-binge ethanol-feeding in mice, 6-O-galloylsalidroside was administered orally once per day for 11 days. Target RNA expression was determined by real-time PCR. Intrahepatic lipid accumulation caused by alcohol consumption was measured in vivo with 1H magnetic resonance imaging. Hepatic steatosis was observed histologically in tissue samples by staining with hematoxylin, eosin, and Oil Red O. The serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured with a Konelab system, and the triglyceride content was measured in liver homogenates by an enzymatic peroxide assay. 6-O-galloylsalidroside appeared to alleviate alcohol-induced steatosis, implied by decreased hepatic and serum triglyceride levels despite ethanol feeding. 6-O-galloylsalidroside treatment correlated with a decrease in Cd36 RNA expression, potentially inhibiting the development of alcoholic steatosis through the hepatic de novo lipogenesis pathway. Furthermore, treatment with 6-O-galloylsalidroside inhibited the expression of cytochrome P4502E1 and attenuated hepatocellular damage, reflected by a reduction in ALT and AST levels. These findings suggest that 6-O-galloylsalidroside extracted from A. *tegmentosum* has the potential to serve as a bioactive agent for the treatment of alcoholic fatty liver and liver damage.

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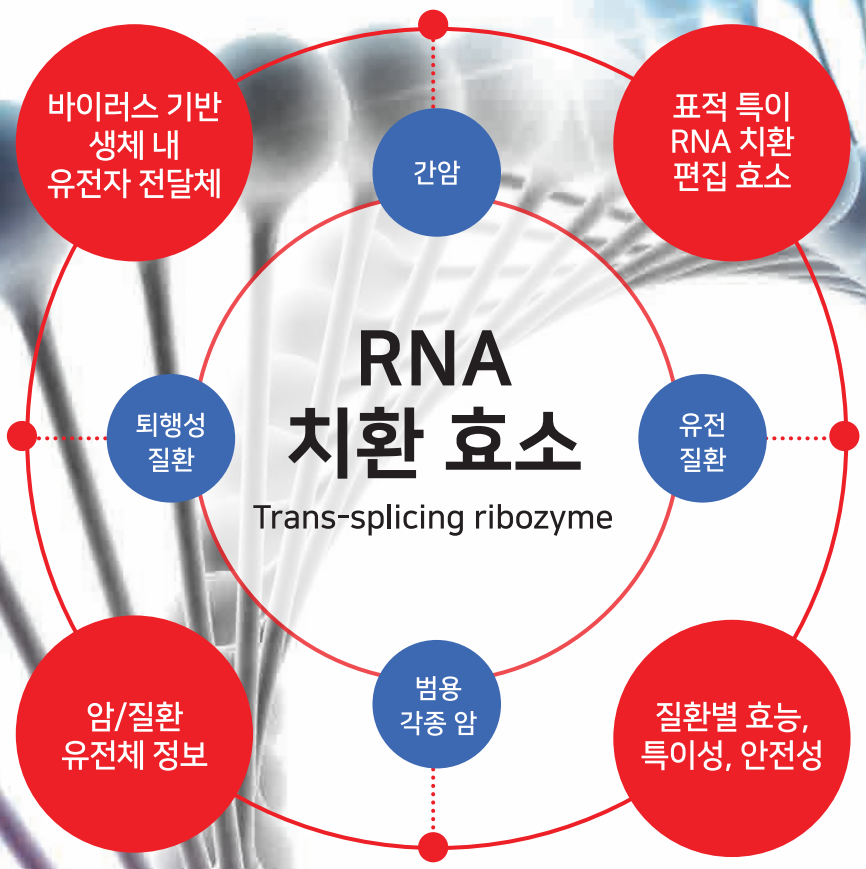


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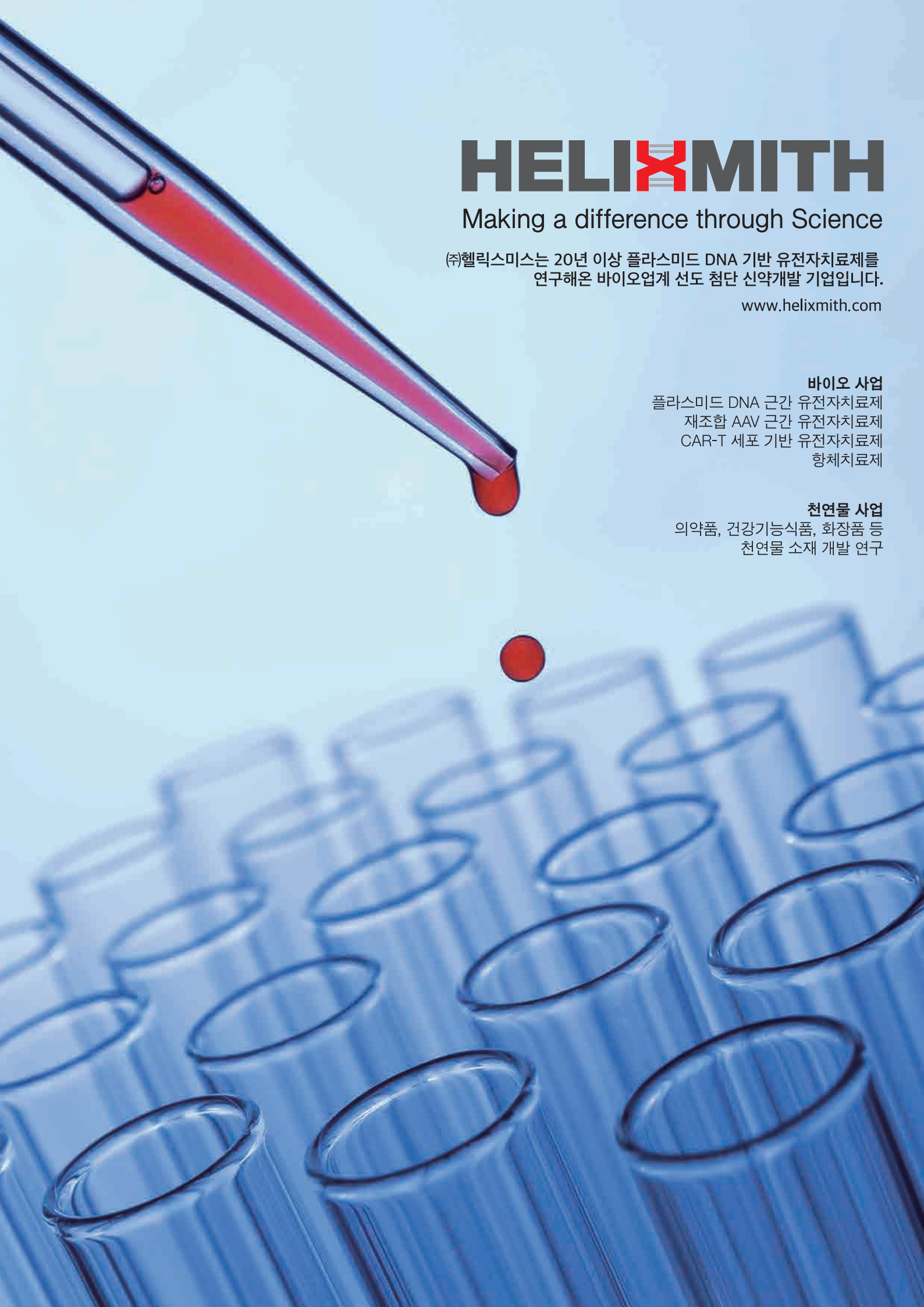
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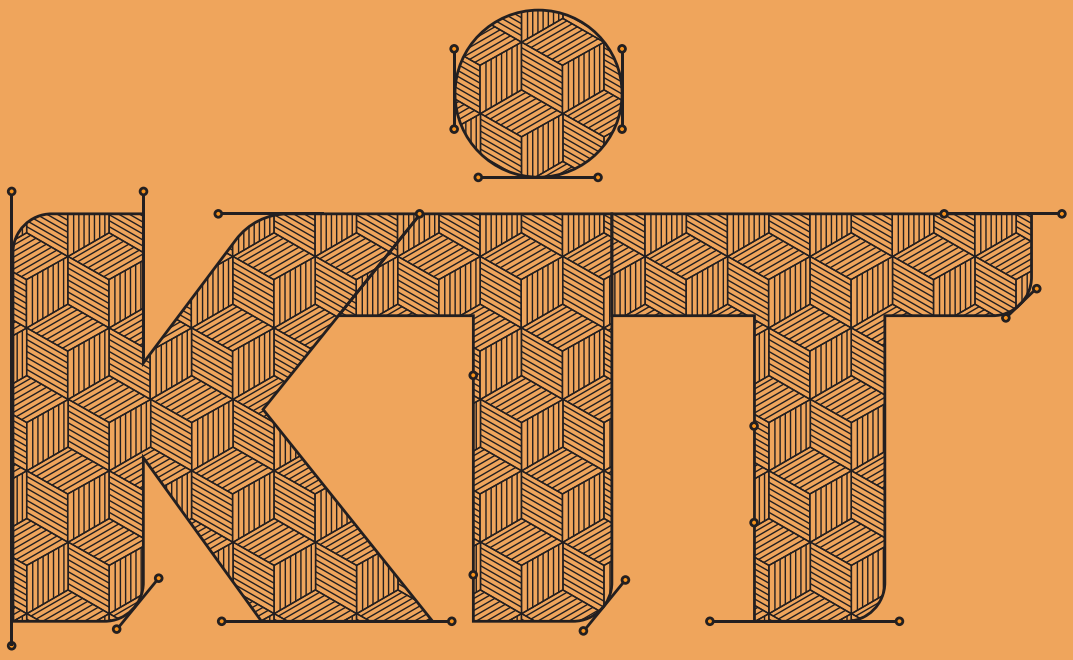

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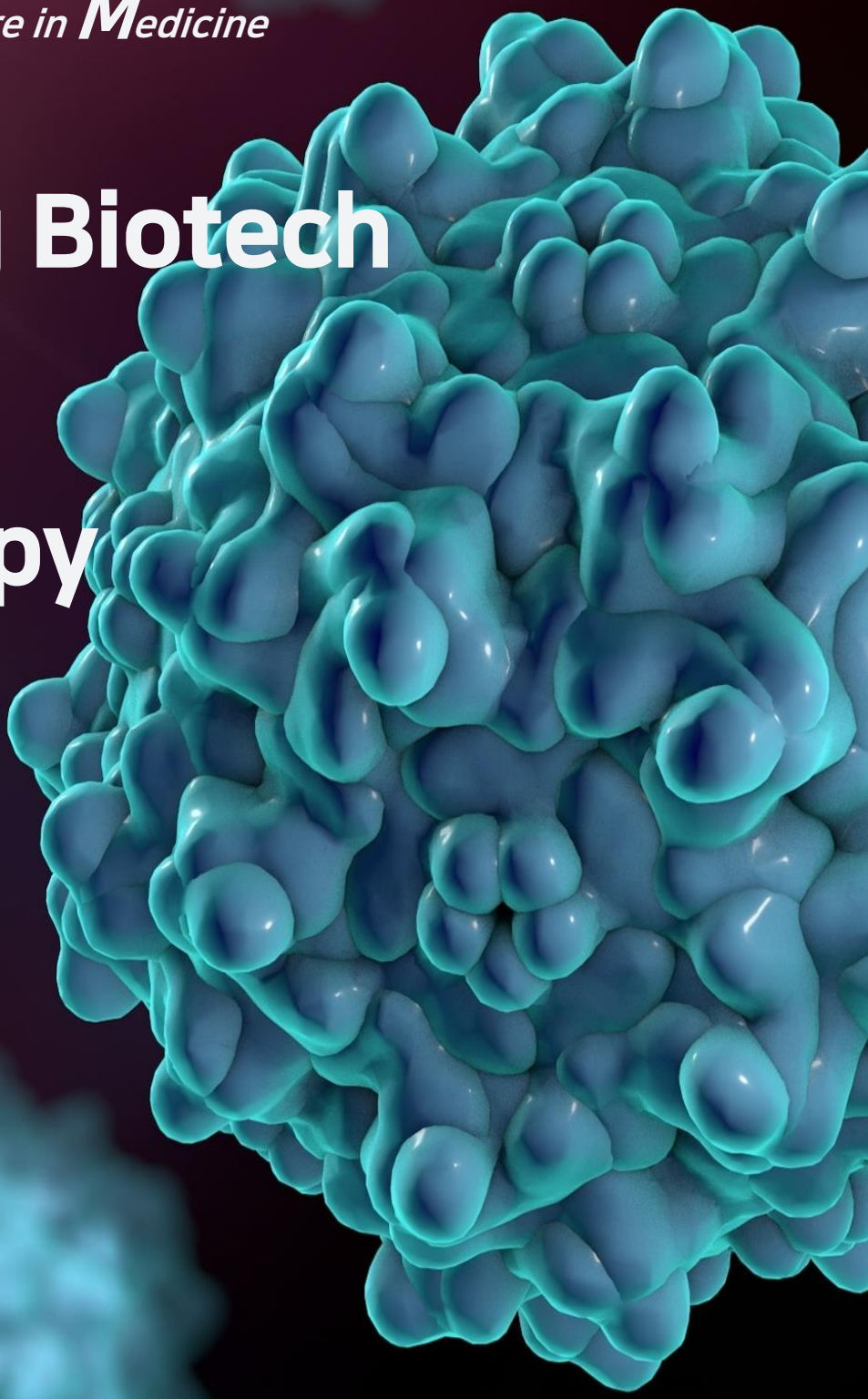


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국내 유일의 유전자치료제 & 세포치료제 전문

# CMO & CRO(CDMO)

**CAR-T GMP 제조 및 분석 (RCR & RCL)**

**CMO**
Contract Manufacturing Org.

- 바이오 의약품 위·수탁 제조
- 원료의약품/임상용의약품
- 글로벌 GMP 제조/공정개발

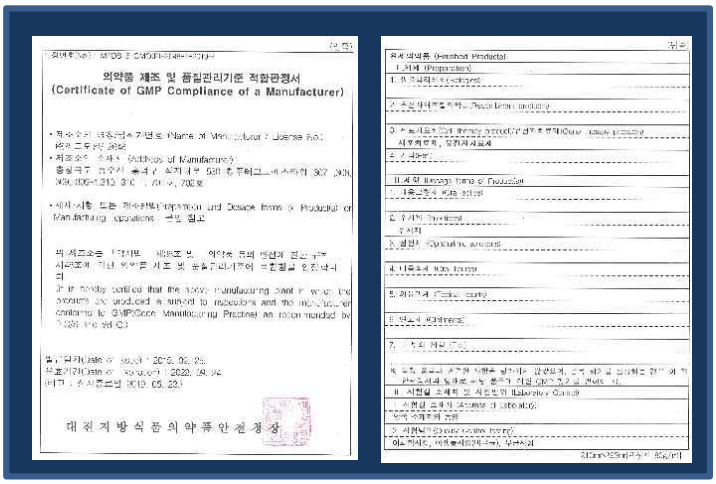
**CRO**
Contract Research Org.

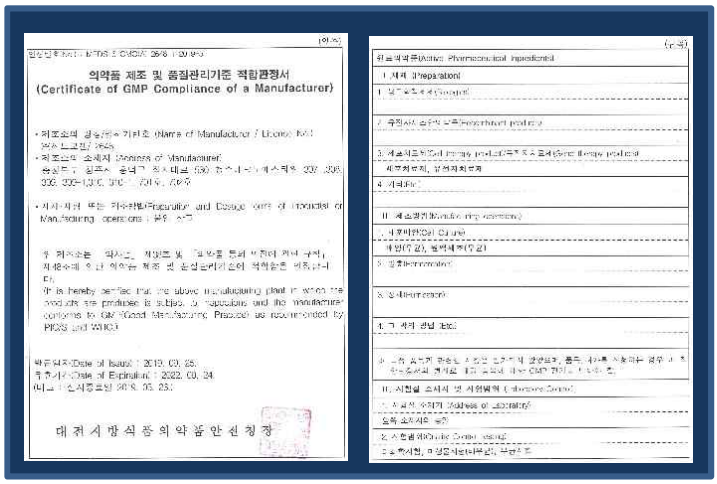
- 특성분석 (Characterization)
- 안전성·안정성평가 (Bio-safety, stability)
- Virology testing

**CAR-T**
개인 맞춤형 유전자치료제

- CAR-T 위·수탁제조
- CAR-T 품질평가분석


## 의약품 제조 및 품질관리기준 적합판정서




주식회사 씨드모젠 Tel. 043-231-2277 Fax. 043-236-2277 E-mail. cdmogen@cdmogen.com

**올릭스 주식회사는 비대칭형 RNA 간섭 (RNAi)을 이용한 기술로 다양한 질환에 대한 신약을 개발**하는 기업입니다. '아시아 최초 원천특허를 확보한' 올릭스는 최근까지 노인성 황반변성 치료제 프로그램(OLX301A), 망막하섬유화증 치료제 프로그램(OLX301D) 등을 프랑스 안과 전문기업 Théa에 약 9000억 규모로 기술이전 계약을 확장 체결하는 등 신약개발을 선도해 나가고 있으며 이를 바탕으로 향후 RNAi 신약 개발 시장의 First Mover가 되고자 합니다.

올릭스와 함께 차세대 신약개발을 개발하는데 동참하고자 하는 열정을 가진 인재분들의 많은 지원바랍니다.

## 상세 채용 분야

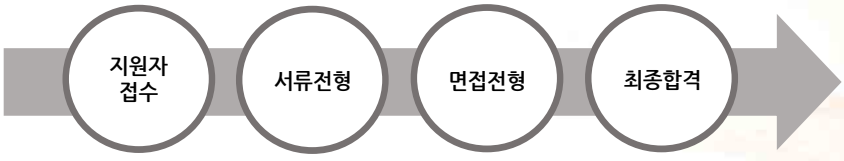
| 직무 | 담당업무 | 자격요건 | |
|---|---|---|---|
| 연구 | □ RNAi 신약 약리/약효 연구<br>- 신약 개발 개별 프로그램(표적장기/표적질환)약리/약효 연구 총괄<br>- 표적 질환 : 안과질환/대사질환/호흡기질환/신경계질환 등<br>- 기 연구개발 프로그램 약리/약효 연구 신규 적응증/타겟 발굴 연구<br>- 신약 후보물질 작용기전 연구<br>- 질환 동물모델 구출 및 in vivo 약효평가<br>- PK/PD 분석 및 예비 독성평가 | □ 필수 요건<br>**경력 사항** : 박사학위 후 3년 이상<br>**학 력** : 박사 이상<br>**전 공** :<br>- 생명과학 관련 전공 (생화학, 분자생물학 등 생물학 관련 전공)<br>- 표적장기 및 표적질환 관련 전공 (SCI급 관련 논문 게재 1편 이상) | □ 우대 조건<br>- 표적 질환 치료제 개발 프로젝트 리딩 유경험자<br>- RNA 관련 연구 유경험자<br>- 영어 우수자 |
| | □ RNAi 신약 원천기술 연구<br>- RNAi 원천기술 토대 신약 연구 개발<br>- 핵산 약물 선도/후보물질 도출 및 작용기전 연구<br>- 핵산 약물 생체 내 delivery 및 유도체 연구 개발<br>- 핵산 약물 치료제 기반기술(구조기술 등) 연구 | □ 필수 요건<br>**경력 사항** : 5년 이상<br>**학 력** : 박사 이상<br>**전 공** :<br>- 생명과학 관련 전공 (생화학, 분자생물학 등 생물학 관련 전공)<br>- 분자생물학 및 동물실험 경력자 | □ 우대 조건<br>- RNA 관련 연구 유경험자<br>- 영어 우수자 |
| 개발 | □ 독성<br>**1. 독성시험 관리**<br>- 독성시험 개발 전략 수립<br>- 독성시험 monitoring, 데이터 분석, 보고서 검토<br>- 국내외 CRO 정보 수집 및 계약 관리<br>- Project management<br>- CRO audit<br>- 예산관리<br>**2. 독성시험 관련 인허가 업무**<br>- 허가 문서 작성 및 검토<br>- 규제기관 대응<br>- 독성시험 보고서 관리<br>**3. 기타**<br>- 비 임상시험 규제변화 및 정보 확인<br>- 비 임상시험 관련 SOP 관리 | □ 필수 요건<br>**경력 사항** : 석사 후 7년, 박사 후 3년 이상 제약회사/CRO 경험<br>**학 력** : 석사 이상<br>**전 공** : 의학, 화학, 바이오, 생물공학 및 약학 관련 | □ 우대 조건<br>국내외 인허가 유경험자 |
| | □ PK/TK분석 (책임이상)<br>- 내부 혹은 외부에서 진행되는 PK 시험 디자인 및 분석<br>- 비임상, 임상 시험 중 PK/TK 부분 검토<br>- 생체시료 중 시험물질 정량분석법 개발/시료 분석 지원<br>- Immunogenicity 분석법 개발/시료 분석 지원<br>- 규제기관 제출 서류 중 해당 분야 작성<br>- 그 외 관련 업무 | □ 필수 요건<br>**경력 사항** : 석사 후 5년, 박사 후 1년 이상 제약회사/CRO 경험<br>**학 력** : 석사 이상, 박사 우대<br>**전 공** : 생명과학 관련 전공<br>**외 국 어** : 전화회의 가능 수준 | □ 우대 조건<br>Kinetics전공 박사학위 소지자 |

## 지원 방법 및 기타

· **제출 서류** : 자사양식 (홈페이지 https://www.olixpharma.com 접속 >> Careers >> 채용공고 >> 공고 클릭, '올릭스 입사지원서' 다운로드)

· **제 출 처** : 이메일 지원 (recruit@olixpharma.com)

· **채용 절차**

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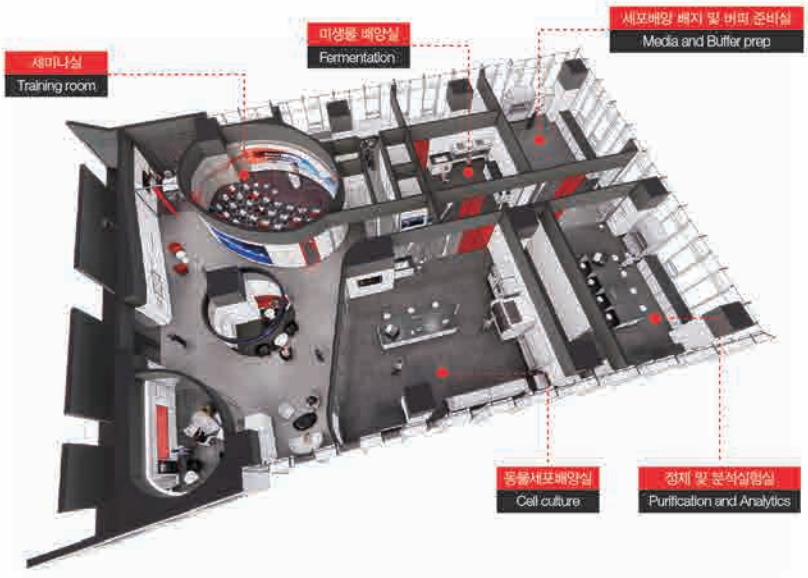


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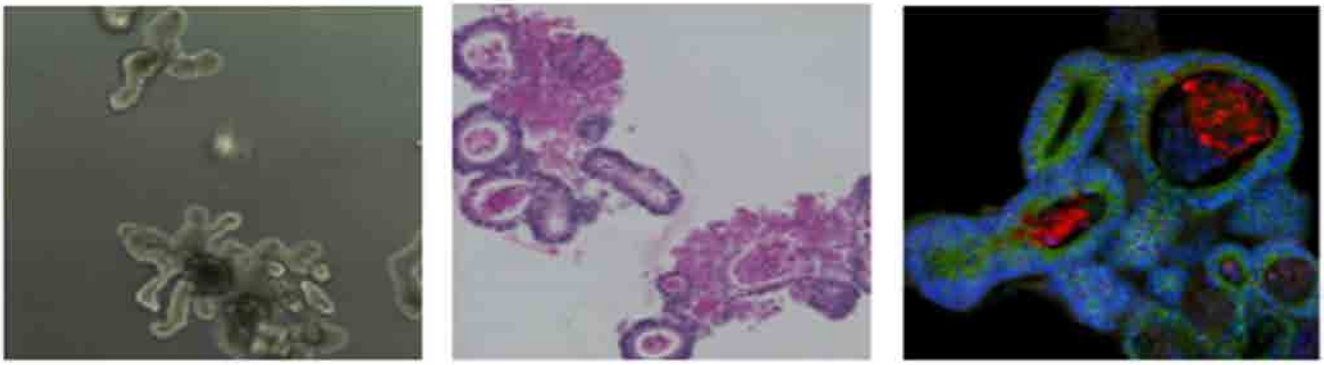
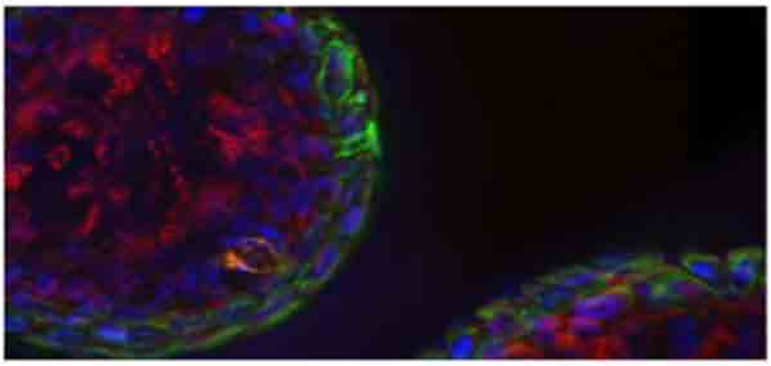


Intestinal organoids grown in Corning Matrigel matrix for organoid culture show typical budding morphology and marker expression (Vimentin, Mucin-2, Villin, Chromogranin, and Lysozyme)[3].



Airway organoids grown in Corning Matrigel matrix for organoid culture shown to express typical differentiation markers of basal (green), ciliated (red) and goblet (orange) cells[4].

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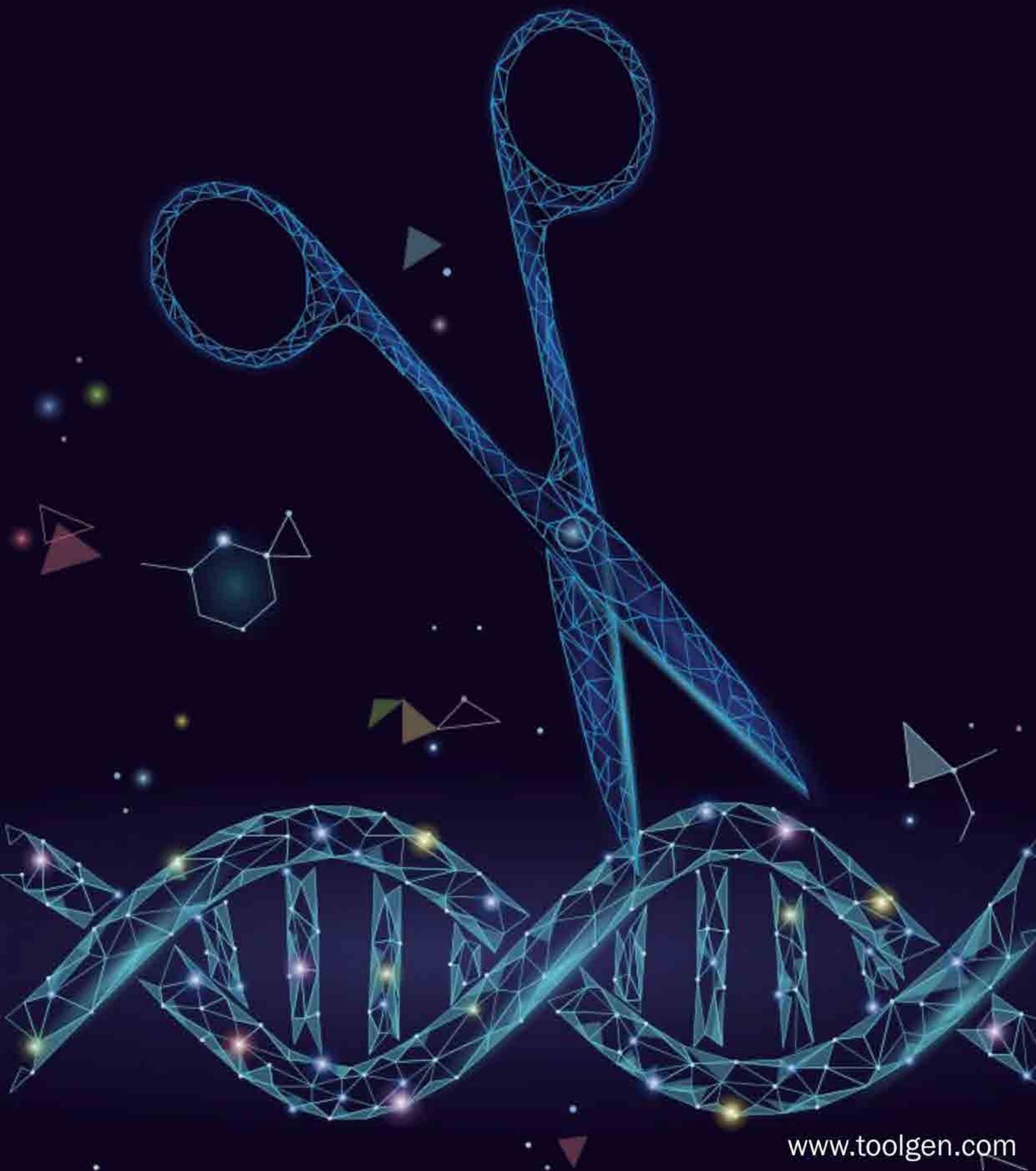

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