2025 MRC 하계 심포지엄

Biomedical Applications of Nanoparticles

2025.08.14.(목) 14:00~

부산대학교 경암의학관 1층 제1강의실

과학기술정보통신부 Ministry of Science and ICT
NRF 한국연구재단 National Research Foundation of Korea
부산광역시 BUSAN METROPOLITAN CITY
CANCER CELL DIVERSITY CDMRC
BrainKorea 21 FOUR
부산대학교 GRAND 융합의과학 교육연구단

센터장 인사말

안녕하세요? 종양학의 난제인 암세포 다양성 극복을 위한 분자제어기술 연구를 진행한 지 이제 4년이 지나가고 있습니다.
종양 내부의 암세포 다양성 뿐만 아니라, 종양 간의 다양성은 종양 치료의 매우 힘든 장벽임에 틀림이 없습니다. 간암에서의 암세포 다양성 극복을 위해 다양한 방안을 모색하던 중, 지질나노입자(Lipid Nanoparticle)에서 새로운 가능성을 발견하였습니다. 코로나 사태를 극복하는 과정 중에, 지질나노입자의 가능성을 충분히 보았습니다. 그래서 이번 심포지엄에서는 지질나노입자 관련 국내 전문가들을 모시게 되었습니다. 오늘 이 자리를 계기로 저희 센터가 암세포 다양성 극복을 위한 새로운 계기를 마련할 수 있기를 기대합니다.

오늘 이 자리가 저희 센터 내부 뿐만아니라, 국내외 학계 및 산업계가 상호협력하는 자리가 되길 기원합니다. 학계에서 개발한 새로운 기술들이 산업화될 수 있도록, 산업계에서 도와줄 수 있기를 바라고, 산업계의 노하우와 고민이 학계로 전달되어 새로운 연구가 진행될 수 있기를 기대합니다. 상호 간의 협력과 공동연구는 종양학의 난제를 풀어 나가는 아주 중요한 디딤돌이 될 것입니다.

감사합니다.

2025. 08. 14

부산대학교 암세포다양성분자제어연구센터
오세옥 배상

2025 부산대학교 MRC 하계 심포지엄
Biomedical Applications of Nanoparticles

Program

2025년 8월 14일 (목) 오후 2시~		
14:00 ~ 14:05	개회사	**오세옥** 교수 센터장
14:05 ~ 14:10	축사	**조원호** 교수 부산대학교 의과대학장
14:10 ~ 14:40	Emerging Ionizable Lipids: Innovations and Applications in Gene and Cell Therapry	**이혁진** 교수 서울대학교
14:40 ~ 15:10	Personalized extracellular vesicle and nanoparticle for osteoarthritis	**이수홍** 교수 동국대학교
휴 식		
15:25 ~ 15:55	Lipid Nanoparticle Technology for RNA Delivery: Toxicity-Minimizing Lipid Nanoparticles	**방은경** 박사 KIST
15:55 ~ 16:25	Development of Potent Lipid Nanoparticles for Target Specific mRNA Delivery	**손지연** 팀장 녹십자
16:25 ~ 16:55	Development of mRNA Structures and Delivery Strategies for Modulating Immunogenic Responses	**이규리** 교수 고려대학교
16:55 ~ 17:00	폐회사	**권상모** 교수 부산대학교 BK21 사업단장
저녁 만찬		

2025 부산대학교 MRC 하계 심포지엄
Biomedical Applications of Nanoparticles

Session1 **초청강연**

Emerging Ionizable Lipids: Innovations and Applications in Gene and Cell Therapry

이혁진 교수
서울대학교 첨단융합학부

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2025 – Professor, Seoul National University
2012 - 2025 Distinguished Professor, College of Pharmacy, Ewha Womans University
2009 - 2012 Postdoctoral Associate, Langer Lab, MIT

2009 PhD KAIST, Daejeon, Korea
2004 MS Columbia University, NY, USA
2002 BS Johns Hopkins University, MD, USA

Awards:
2021 년 이달의 과학기술인상
2022 년 제 1 회 임성기재단 젊은연구자상
2022 년 국가연구개발 100 선 최우수성과
2023 년 대한민국 과학기술 포장

Research Interests:
Non-viral gene delivery, Gene therapy, RNA nanostructure

1) Substrate RNA nanostructure for gene therapy
2) IVT (in vitro transcripted) mRNA for gene and cell therapy
3) Non-viral gene delivery systems (Lipid nanoparticles)

Selected Publications:

1. Hee Jin, Michaela Jeong, Gyeongseok Lee, Minjeong Kim, Youngjo Yoo, Hyun Jin Kim, Jaeho Cho, Yun-Sil Lee, Hyukjin Lee. “Engineered Lipid Nanoparticles for the Treatment of Pulmonary Fibrosis by Regulating Epithelial-Mesenchymal Transition in the Lungs.” Adv. Funct. Mater. 2022
2. Kim M, Jeong M, Hur S, Cho Y, Park J, Jung H, Seo Y, Woo HA, Nam KT, Lee K, Lee H. “Engineered ionizable lipid nanoparticles for targeted delivery of RNA therapeutics into different types of cells in the liver.” Sci Adv. 2021
3. Jang B., Kim, B., Kim H., Kwon H., Kim M., Seo Y., Colas M,, Jeong H., Jeong E.H., Lee K., Lee H., “Enzymatic synthesis of self-assembled dicer substrate RNA nanostructures for programmable gene silencing”, Nano letters, 18(7), 4279-4284, 2018
4. Lee H. et al “Molecularly Self-assembled Nucleic Acid Nanoparticles for Targeted In Vivo siRNA Delivery”, Nature Nanotechnology 7, 389-393, 2012

Emerging Ionizable Lipids: Innovations and Applications in Gene and Cell Therapry

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The mRNA-based vaccines and therapeutics have opened a new era of immunization and disease treatment, with notable successes in combatting infectious diseases and even cancer. However, optimizing the delivery of mRNA payloads to target cells and modulating the immune response remains a critical challenge. In this study, we present our research on the development of immune modulating ionizable lipids and their incorporation into lipid nanoparticles (LNPs) for enhancing the efficacy and safety of mRNA vaccines and therapeutics. Our research focuses on designing and synthesizing a novel class of ionizable lipids, characterized by their pH-responsive charge-switching properties. Combinatorial synthesis of degradable ionizable lipids has been carried out using amine head groups with different lipid tail structures. These lipids enable efficient encapsulation of mRNA payloads, provide superior stability, and facilitate endosomal escape, leading to improved delivery of mRNA to the cytoplasm. Moreover, we have systematically tuned the physicochemical properties of these lipids to optimize their immune-modulating effects, tailoring the balance between pro-inflammatory and tolerogenic responses. To quantitatively assess the performance of these ionizable lipids, we conducted a series of in vitro and in vivo experiments using the lead mRNA/LNPs. Our results demonstrate that the incorporation of these novel lipids into LNPs significantly enhances mRNA translation and elicits a balanced immune response, characterized by increased antigen-specific T cell responses with pro-inflammatory cytokines. In summary, our research presents a significant advancement in the field of mRNA based vaccine and therapeutic development.

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Session 2 **초청강연**

Personalized extracellular vesicle and nanoparticle for osteoarthritis

이수홍 교수
동국대학교 의생명공학과

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Dr. Soo-Hong Lee is a Professor in the Department of Medical Biotechnology at Dongguk University. He earned his B.S. (1994), M.S. (1997), and Ph.D. (2002) degrees in Chemistry from Hanyang University. Following his doctoral studies, he worked as a Postdoctoral Research Associate at the Korea Institute of Science and Technology (KIST) and Rice University. Dr. Lee began his academic career in the Department of Biomedical Science at CHA University, where he served as an Assistant Professor (2006–2010) and later as an Associate Professor (2010–2014). He was granted tenure and promoted to Full Professor in 2015. His research focuses on biomaterials, tissue engineering, stem cell engineering, and cell therapy. He has published over 170 scientific papers, which have been cited more than 10,431 times (h-index = 49). Additionally, he holds more than 60 granted or pending patents. Dr. Lee has received numerous prestigious awards, including: Grand Prize from the Korean Society for Biomaterials (2023), Medipost Independent Investigator Award from the Korean Tissue Engineering and Regenerative Medicine (KTERM) Society (2022), Best Scientist Award from Dongguk University (2021), Independent Investigator Award from the Korean Society for Biomaterials (2017), Contribution Award from the KTERM Society (2017), Ministerial Citation from the Ministry of Science (2014), Best Research Evaluator Award from the National Research Foundation (2013), Macromolecular Rapid Communication Young Scientist Award (2010), Best Scientist Award from CHA University (2009), National R&D 100 Best Researches Award from the Ministry of Education, Science, and Technology (2008), R&D 100 Best Researches Award from the Korean Research Foundation (2008)

Selected papers

1. Deogil Kim, Min-Ju Lee, Yoshie Arai, Jinsung Ahn, Gun Woo Lee, **Soo-Hong Lee*** “Ultrasound-triggered three-dimensional hyaluronic acid hydrogel promotes in vitro and in vivo reprogramming into induced pluripotent stem cells” Bioactive Materials Volume 38 (2024)
2. Alvin Bacero Bello, Kevin Kent Vincent Canlas, Deogil Kim, Hansoo Park*, **SooHong Lee ,*** "Stepwise dual-release microparticles of BMP-4 and SCF in induced pluripotent stem cell spheroids enhance differentiation into hematopoietic stem cells". Journal of Control Release. Volume 371 (2024)
3. Deogil Kim, Byung-Hyun Cha, Jinsung Ahn, Yoshie Arai, Bogyu Choi*, **Soo-Hong Lee*** “Physicochemical Properties in Three-Dimensional Hydrogel Modulate Cellular Reprogramming into Induced Pluripotent Stem Cells” Advanced functional materials, 200741 (2021)
4. Yoshie Arai, Bogyu Choi, Byoung Ju Kim, Sunghyun Park, Hyoeun Park, James J. Moon, **Soo-Hong Lee*** “Cryptic ligand on collagen matrix unveiled by MMP13 accelerates bone tissue regeneration via MMP13/Integrin α3/RUNX2 feedback loop” Acta Biomaterialia, 15;125:219-230, (2021)
5. Byung-Hyun Cha, Jin-Su Kim, Alvin Bello, Geun-Hui Lee, Do-Hyun Kim, Byoung Ju Kim, Yoshie Arai, Bogyu Choi, Hansoo Park, **Soo-Hong Lee*** “Efficient isolation and enrichment of mesenchymal stem cells from human embryonic stem cells by utilizing the interaction between integrin α5β1 and fibronectin” Advanced Science, 7(17): 2001365 (2020)

Personalized extracellular vesicle and nanoparticle for osteoarthritis treatment

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Soo-Hong Lee*

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I would like to introduce stem cell membrane-based nanoparticles for personalized osteoarthritis treatment. Traditional drug delivery systems for OA treatments face limitations due to rapid clearance within the joint and low biocompatibility. Moreover, the inflammation associated with OA exacerbates tissue damage and delays the regenerative capacity of therapeutics. In the first topic, to overcome these limitations, an OA-specific drug delivery system designated dCOL2-CM-Cur-PNPs is developed herein to target OA cartilage for anti-inflammatory and cartilage regeneration purposes. This system is constructed using cell membranes obtained from induced pluripotent stem cell-derived mesenchymal stem cells (iMSC-CMs), poly(D,L-lactide-co-glycolide) (PLGA) nanoparticles loaded with the well-known anti-inflammatory and cartilage-regenerating agent curcumin (Cur-PNPs), and damaged type II collagen (dCOL2)-targeting phospholipids.

In the second topic, I will talk about extracellular vesicles(EVs) to promote cartilage regeneration. For clinical application, scalable production of EVs is essential, and their therapeutic efficacy is largely influenced by the properties of the parent cells. Therefore, enhancing the functional characteristics of the source cells is a critical challenge in EV-based therapy. Three-dimensional (3D) spheroid cultures have been proposed as an effective strategy to enhance EV yield and chondrogenic differentiation by promoting cell–cell and cell–extracellular matrix interactions. Nevertheless, conventional 3D culture systems are often limited by uneven nutrient distribution, leading to necrotic core formation and reduced cellular homogeneity within the spheroids. To address these limitations, we developed a novel strategy using human mesenchymal stem cells (hMSCs) combined with TGF-β1-coated microparticles (T/MPs) to form uniform, cartilage-like 3D spheroids (3D-T/MP). In conclusion, our study presents an improved 3D culture platform that enhances the homogeneity and regenerative capacity of EVs, enabling efficient production of therapeutic

EVs for OA treatment. These approaches provide promising potential as a next-generation platform for promoting cartilage regeneration through OA-specific therapy.

Keywords: *Stem cell membrane-based nanoparticles, Osteoarthritis-specific drug delivery, Anti-inflammations, 3D spheroid, Extracellular vesicles(EVs), Cartilage regeneration.*

References

[1] Sunjun Lee, Bowon Kim, Min-Ju Lee, Deogil Kim, Sunghyun Park, Jinsik Kim, Yoshie Arai*, Soo-Hong Lee* (2025) Curcumin-PLGA NPs coated with targeting biomimetic personalized stem cell membranes for osteoarthritis therapy. Journal of Control Release, Volume 381, 113625.

[2] Byung-Hyun Cha, Jin-Su Kim, Alvin Bello, Geun-Hui Lee, Do-Hyun Kim, Byoung Ju Kim, Yoshie Arai, Bogyu Choi, Hansoo Park, Soo-Hong Lee* (2020) Efficient isolation and enrichment of mesenchymal stem cells from human embryonic stem cells by utilizing the interaction between integrin α5β1 and fibronectin. Advanced Science, 7(17): 2001365.

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Biomedical Applications of Nanoparticles

Session 3 **초청강연**

Lipid Nanoparticle Technology for RNA Delivery:

Toxicity-Minimizing Lipid Nanoparticles

방은경 선임연구원
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EDUCATION

Ph.D. 2010	under the Supervision of Professor Byeang Hyean Kim, Department of Chemistry, POSTECH, Pohang, Rep. of Korea
Diploma 2003	Cum Laude, under the Supervision of Professor Byeang Hyean Kim, Department of Chemistry, POSTECH, Pohang, Rep. of Korea (Cum Laude)

RESEARCH EXPERIENCE

2025. 03 – Present	Principal Researcher, Medicinal Materials Research Center, Korea Institute of Science and Technology (KIST), Rep. of Korea
2018. 08 – 2025. 02	Senior Researcher, Brain Science Institute, KIST, Rep. of Korea
2014. 11 – 2019. 10	Presidential Post-Doc Fellowship. Korea Institute of Science and Technology, Rep. of Korea.
2013. 09 – 2014. 10	Star Post-Doc Program. Korea Institute of Science and Technology, Rep. of Korea.
2011. 01 – 2013. 07	Post-Doc. Department of Organic Chemistry, University of Geneva, Geneva, Switzerland, with Professor Stefan Matile.
2010.03 –12	Post-Doc. Department of Chemistry, POSTECH, Pohang, Rep. of Korea, with Professor Byeang Hyean Kim.

TEACHING EXPERIENCE

2012. 11 – 2013. 02	Teaching Assistant for Organic Synthesis Laboratory, University of Geneva, Geneva, Switzerland.
2003. 03 – 2003. 06	Teaching Assistant for General Chemistry Lecture, POSTECH, Pohang, Rep. of Korea.
2003. 09 – 2003. 12	Teaching Assistant for Organic Chemistry II Lecture, POSTECH, Pohang, Rep. of Korea.

RESEARCH INTERESTS

Organic syntheses, Drug delivery systems, Biological applications of organic materials, Bio-organic chemistry, Nucleic acid chemistry, Supramolecular chemistry

PUBLICATIONS

1. S. Yoo, J. Youn, N. Kim, G. Keum, H. Park, E.-K. Bang, "Artificial intelligence-driven discovery of novel scaffolds for selective TLR7 antagonists and their application in enhancing mRNA translation efficiency", *Eur. J. Pharm. Sci.* **2025**, *212*, 10712.
2. Y.-S. Lee, M. S. Cheong, J. Lee, E.-K Bang, S. I. Park, H.-J. Park, S.-H. Bae, S. B. Youn, G. Roh, S. Lee, Y. Cho, D. Ha, A. Oh, S.-Y. Lee, E.-J. Choi, H. Choi, S. Jo, Y. Lee, J. Kim, H. W. Kwak, Y.-J. Bang, D. Lee, H. Shim, Y. K. Park, G. Keum, J.-H. Nam, W. Kim, "Immunogenicity and protection of a triple repeat domain Ⅲ mRNA vaccine against zika Virus", *Vaccine*, **2025**, *43*, 126518.
3. J. H. Ahn, J. S. Lee, G. Roh, N. Y. Lee, H. J. Bae, E. Kwon, K. M. Han, J. E. Kim, H. J. Park, S. Yoo, S. P. Kwon, E.-K. Bang, G. Keum, J. H. Nam, B. C. Kang, "Impact of administration routes and dose frequency on the toxicology of SARS-CoV-2 mRNA vaccines in mice model", *Arch. Toxicol.* **2024**, doi:10.1007/s00204-024-03912-1.
4. S. Yoo, M. Faisal, S.-H. Bae, K. Youn, H.-J. Park, S. P. Kwon, I. K. Hwang, J. Lee, H. J. Kim, J.-H. Nam, G. Keum, E.-K. Bang, "Novel less toxic, lymphoid tissue-targeted lipid nanoparticles containing a vitamin B5-derived ionizable lipid for mRNA vaccine delivery", *Adv. Healthcare Mater.* **2024**, doi: 10.1002/adhm.202403366.
5. J. Lee, J. M. An, J. Kim, E.-K. Bang, D. Kim, "A hybrid formulation of porous silicon nanoparticle with carboxymethyl cellulose for enhanced drug loading", *Mater. Lett.* **2024**, 371, 136929. doi: 10.1016/j.matlet.2024.136929.
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7. S. Lee, H. Yoon, S. H. Hong, S. P. Kwon, J. J. Hong, H. W. Kwak, H. J. Park, S. Yoo, S. H. Bae, H. J. Park, J. Lee, Y. J. Bang, Y. S. Lee, J. Y. Kim, S. Yoon, G. Roh, Y. Cho, Y. Kim, D. Kim, S. I. Park, D. H. Kim, S. Lee, A. Oh, D. Ha, S. Y. Lee, M. Park, E. H. Hwang, G. Bae, E. Jeon, S. H. Park, W. S. Choi, H. R. Oh, I. W. Kim, H. Youn, G. Keum, E.-K. Bang, J. H.

Rhee, S. E. Lee, J. H. Nam. “mRNA-HPV vaccine encoding E6 and E7 improves therapeutic potential for HPV-mediated cancers via subcutaneous immunization”, *J Med Virol.* **2023**. *95(12)*, e29309. doi: 10.1002/jmv.29309.

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9. H. Kim, R. Parida, K. Youn, S. C. Shin, G. Keum, J. Y. Lee, E.-K. Bang, S. Yoo, “Amyloid β Aggregate-Sensitive Red Fluorescent Dipolar Probes”, *ACS Appl. Opt. Mater.* **2023**, *1*(9), 1513.
10. H.-J. Park, Y.-J. Bang, S. P. Kwon, W. Kwak, S.-I. Park, G. Roh, S.-H. Bae, J.-Y. Kim, H. W. Kwak, Y. Kim, S. Yoo, D. Kim, G. Keum, E.-K. Bang, S.-H. Hong, J.-H. Nam. “Analyzing immune responses to varied mRNA and protein vaccine sequences”, *npj Vaccine*, **2023**, *8*, 84.
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3 July 2025

Lipid Nanoparticle Technology for RNA Delivery: Toxicity-Minimizing Lipid Nanoparticles

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The rapid advancements in mRNA vaccine technology, exemplified by the development of COVID- 19 vaccines, have highlighted both the potential and challenges of lipid nanoparticles (LNPs) as delivery platforms. While LNPs have proven effective in enabling mRNA delivery, concerns regarding their toxicity and adverse immune responses persist, necessitating innovative approaches to enhance their safety profile.

This presentation introduces novel lipid-based strategies for minimizing toxicity in LNP platforms. First, we incorporated trehalose glycolipids into LNP formulations, replacing a part of ionizable lipids. These formulations significantly mitigated toxicities, including those affecting the liver, spleen, and heart, while sustaining strong mRNA delivery efficacy and immune efficiency. Second, we developed vitamin B5-derived ionizable lipids, which demonstrated reduced toxicity while maintaining high mRNA encapsulation efficiency, effective delivery to lymphoid tissues, and robust immune responses. By leveraging biocompatible lipid designs, our research highlights the transformative potential of LNPs for safer mRNA-based therapeutics. These advancements represent critical steps toward developing toxicity-minimized LNP platforms for mRNA vaccines and other applications.

2025 부산대학교 MRC 하계 심포지엄
Biomedical Applications of Nanoparticles

Session 4 **초청강연**

Development of Potent Lipid Nanoparticles for Target Specific mRNA Delivery

손지연 팀장
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(Last Updated: 2025-05-14)

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Research Area: [Nanomedicine/Drug delivery]

• mRNA Drug Delivery with Lipid Nanoparticles for Vaccines and Therapeutics

- Lipid Design: Specialized in designing ionizable lipids for LNPs, with 6 patents filed.
- LNP Design: Developed LNPs tailored for specific delivery routes and target cells, with 2 patents filed.
- LNP Formulation & Process Development (GMP facility).

• siRNA Drug Delivery with Polymer/Lipid Nanoparticles (PNP) for Cancer Therapeutics

- Polymer/Lipid Nanoparticle Design: Extensive experience in designing and formulating polymer/lipid nanoparticles, with 9 patents filed.
- Process Development/Manufacturing & Pre-CTD Documentation: Led the development and manufacturing processes, including preclinical documentation for Clinical Trial Applications.
- GLP Toxicology Study: Directed GLP toxicology studies in the USA

• Virus Delivery with Polymer/Lipid Nanoparticles for Cancer Therapeutics

- Polymer/Lipid Nanoparticle Design: Focused on the design of nanoparticles for virus, with 2 patents filed.
- Oncolytic Virus Production, Polymer/Lipid Nanoparticle Formulation & Process Development

Patents Publications

[GC Biopharma, Korea]

1. Lipid nanoparticles using cationic cholesterol for local delivery for nucleic acid delivery. Korea patent 10-2022-0083137

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[Samyang Biopharmaceuticals Corp., Korea]

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Development of Potent Lipid Nanoparticles for Target Specific mRNA Delivery

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Lipid nanoparticles (LNPs) – a clinically approved drug delivery carrier of nucleic acid therapeutics and vaccines – are composed of four components: 1) ionizable lipid, 2) helper lipid, 3) cholesterol, and 4) PEGylated lipid. Among them, the ionizable lipid (e.g., MC3 (OnpattroTM), SM-102 (Spikevax TM), and ALC-0315 (ComirnatyTM)) plays a crucial role in complexation with nucleic acid and its endosomal escape, directly impacting the level of protein expression when utilized for mRNA delivery.

To further advance the efficacy of mRNA therapeutics, an extensive library of novel ionizable lipids was constructed by rational design using combinatorial chemistry of head, linker, and tail groups. The lead compounds were identified through in-house screening methods for the physicochemical properties of LNP and their *in vitro* and *in vivo* mRNA delivery efficiency. The lead LNPs were comprehensively evaluated by preclinical studies in rodent and non-human primate models by intravenous administration, and the protein delivery efficiency and tolerability were found comparable to those of benchmark LNPs.

To expand the therapeutic utility of lead ionizable lipids, formulation composition screening was conducted to further control the delivery of LNPs to specific target organs, tissues, and cell types. Specifically, inhalable LNPs were designed for pulmonary delivery of mRNA via nebulization, and its superiority to the published benchmark LNPs was demonstrated.

Leveraging our findings, we strive to develop next-generation LNPs with significantly improved therapeutic utility.

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Keywords

LNP, Ionizable lipid, mRNA, therapeutic, vaccine, target cell/organ specific delivery, intravenous, intramuscular, inhalation

2025 부산대학교 MRC 하계 심포지엄
Biomedical Applications of Nanoparticles

Session 5 **초청강연**

Development of mRNA Structures and Delivery Strategies for Modulating Immunogenic Responses

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- Korea Society for Bioinformatics
- American Society of Gene and Cell Therapy (ASGCT)
- European Society of Gene and Cell Therapy (ESGCT)
- Controlled Release Society (CRS)

Research Interests

• **RNA therapeutics**: Development of novel RNA structures for regulating gene expression/inhibition and immune reactions. These include in vitro transcribed mRNA (IVT mRNA) for vaccine application/gene editing/cellular reprogramming/protein replacement,

siRNA/antisense oligonucleotides (ASO) for gene suppression and alternative splicing, and guide RNA for genome/RNA editing

• **Biomaterials for RNA Delivery**: Development of lipid and polymer based gene/cell delivery system for practical applications of gene/cell therapeutics. These include screening of novel lipid and polymer nanoparticles for RNA delivery into immune cells/non-immune cells/stem cells/cancer cells.

Publications (SCI(E))

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Development of mRNA Structures and Delivery Strategies for Modulating Immunogenic Responses

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Modulating the immunostimulatory properties of in vitro transcribed (IVT) mRNA is key to advancing mRNA-based therapeutics and vaccines. Balancing immune activation and translational efficiency is critical and varies by clinical goal. Vaccines require optimized translation and immune stimulation for efficacy, while mRNA therapeutics, like protein replacement therapies, focus on efficient protein expression with minimal immune activation. The objective is to create tailored strategies that reduce excessive immunostimulation, addressing diverse clinical needs. We have developed strategies to modulate the immunogenicity of mRNA-based therapeutics/vaccines. These involves the Additional Chimeric Element-incorporated mRNA (ACE mRNA), which incorporates RNA/DNA chimeric elements into unmodified IVT mRNA. This reduces type I interferon (IFN) responses and enhances protein expression, providing a novel approach to regulate immune reactions while improving translational efficiency. The second strategy is the Combined Hybrid Structure of siRNA-tailed IVT mRNA (ChriST mRNA), a hybrid construct combining siRNA and IVT mRNA functions. ChriST mRNA enables simultaneous expression and suppression of target proteins, enhancing the immunogenicity of Ψ-modified IVT mRNA. Lastly, we developed adjuvant-enhanced lipid nanoparticles (Pam3-incorporated LNPs) to boost mRNA-based cancer vaccine efficacy. These LNPs, containing the adjuvant Pam3, improve tumor antigen expression and significantly amplify immune activation, enhancing therapeutic outcomes. Collectively, these strategies advance mRNA technology to address diverse clinical needs.

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