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## Asia 3 Roundtable on Nucleic Acids 2024

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### Seung Ryul Han, Ph.D.

Research Institute,  
Rznomics Inc., Seongnam, 13486, Korea.  
Tel: +82-31-706-8732  
Email: [hansr1981@rznomics.com](mailto:hansr1981@rznomics.com)



2024-present	Director, Research Institute, Rznomics Inc.
2017-2023	Deputy Director, Research Institute, Rznomics Inc.
2014-2017	Senior Researcher, Department of Integrated Life Science, Dankook University
2014 PhD	Department of Molecular Biology, Dankook University
2009 MS	Department of Molecular Biology, Dankook University
2007 BS	Department of Molecular Biology, Dankook University

#### Research Interests:

Molecular Biology, RNA replacement enzyme, Gene therapeutics, RNA editing

#### Selected Publications:

1. Lee KH, Kim S, Song J, **Han SR**, Kim JH, , Lee **S-W\***, Efficient circular RNA engineering by end-to-end self-targeting and splicing reaction using *Tetrahymena* group I intron ribozyme, *Molecular Therapy Nucleic Acids* **2023**, 33, 587
2. **Han SR**, Lee CH, Im JY, Kim JH, Kim JH, Kim SJ, Cho YW, Kim E, Kim Y, Ryu J-H, Ju MH, Jeong JS, **Lee S-W\***, Targeted suicide gene therapy for liver cancer based on ribozyme-mediated RNA replacement through post-transcriptional regulation, *Molecular Therapy Nucleic Acids* **2021**, 23, 154
3. Lee CH, Han SR, **Lee S-W \***, Group I Intron-Based Therapeutics Through *Trans*-Splicing Reaction, *Progress in Molecular Biology and Translational Science*, **2018**, 159, 79
4. Lee CH, **Han SR**, **Lee S-W\***, Therapeutic applications of group I intron-based *trans*-splicing ribozymes, *WIREs RNA*, **2018**, 9, e1466

# Splicing ribozyme-based anti-cancer RNA editing therapeutics

Seung Ryul Han

Research Institute, Rznomics Inc., Seongnam, Korea

## Abstract

Trans-splicing ribozyme based on Tetrahymena group I intron catalytically enables to sense and reprogram target RNA into gene of interest. We have modified and optimized the ribozymes for therapeutic application by developing them with high target specificity and efficacy, targeting fidelity, and minimal off-target effects in cells. Based on the optimized splicing ribozyme, we are developing RNA editing technology through RNA replacement or repair as a gene therapeutic approach for diverse intractable human diseases including malignant, degenerative, and hereditary disorders. Here, I will introduce the features of the splicing ribozyme-based RNA editing approach and focus in particular on the recent progress of our leading pipelines for malignant diseases including hepatocellular carcinoma (HCC) and glioblastoma (GBM). We developed human telomerase reverse transcriptase (hTERT) mRNA targeted trans-splicing ribozyme harboring downstream therapeutic suicide gene, constructed a genetically modified replication-incompetent adenoviral vector encoding the ribozyme, called RZ-001, and tested its preclinical anti-cancer effects, biodistribution, and toxicity. The preclinical observations suggest that RNA editing strategy mediated by hTERT-targeted trans-splicing ribozyme could provide a clinically relevant, safe, and effective approach for cancer therapy. Based on the results, RZ-001 received IND approval for phase 1/2a clinical trials from the Korean Ministry of Food and Drug Safety and the US FDA for both HCC and GBM. Recently, RZ-001 received Orphan Drug Designation from US FDA for HCC patients. Moreover, Fast Track designation was secured from US FDA for GBM patients. This study and recent recognitions by the US FDA may raise the potential of splicing ribozyme-based RNA editing approaches as a safe and effective therapeutic option for patients with highly unmet medical needs.