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## Asia 3 Roundtable on Nucleic Acids 2024

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2017-	Rznomics Inc.
2014-2017	Department of Integrated Life Science, Dankook University, Senior Researcher
2014 PhD	Dankook University
2009 MS	Dankook University
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#### Research Interests:

Molecular Biology, RNA replacement enzyme, Gene therapeutics

#### 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

# **Anti-cancer RNA editing therapy based on telomerase reverse transcriptase (TERT) mRNA-splicing ribozyme**

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## **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.