National Cancer Center (NCC) Japan, NCC Seed Acceleration Program（NCC SAP）

Tumor-Selective pan-RAS-Degrading Protein Therapeutics

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Vision

- We developed RIDER (Receptor-guided Intracellular Degrader), a novel modality that combines tumor antigen–dependent delivery with targeted protein degradation.
- To develop a next-generation pan-RAS-degrading protein therapeutic for RAS-mutant refractory solid tumors, including pancreatic, colorectal, and lung cancers. By enabling tumor antigen–guided delivery and selective, degradation of intracellular RAS, this approach aims to overcome the key limitations of current RAS inhibitors: mutation-restricted use, acquired resistance, and toxicity caused by RAS inhibition in normal tissues.

Marketability

- RAS mutations are involved in approximately 20–30% of all cancers, representing an estimated 3–6 million patients annually worldwide. Current competitors include KRAS G12C inhibitors, pan-RAS inhibitors such as Daraxonrasib/RMC-6236, and KRAS G12D degraders such as Setidegrasib/ASP3082. However, these approaches do not provide tumor-cell selectivity.
- This program is positioned as a next-generation modality based on tumor-selective pan-RAS degradation, with potential opportunities in patients who are non-responsive, relapsed, or dose-limited with existing therapies.

Innovation

- RIDER （Receptor-guided Intracellular Degrader） is a new modality combining tumor antigen–guided delivery and intracellular degradation.
- It directly degrades KRAS, NRAS, and HRAS, rather than simply inhibiting RAS activity.
- Expected advantages include durable pan-RAS control, IC50 < 1 pM, and >1,000-fold antigen-dependent selectivity.

Partnering

【 Expected partners 】
Pharmaceuticals・ Biotech/Drug Discovery Service・ CMO/CDMO/CRO/SMO ・ Medical/Diagnosis/Research Devices ・ Venture capitals

【 Expectation 】
PK/PD analysis, GMP drug supply, safety/immunogenicity testing, indication expansion, fundraising, and commercialization support.

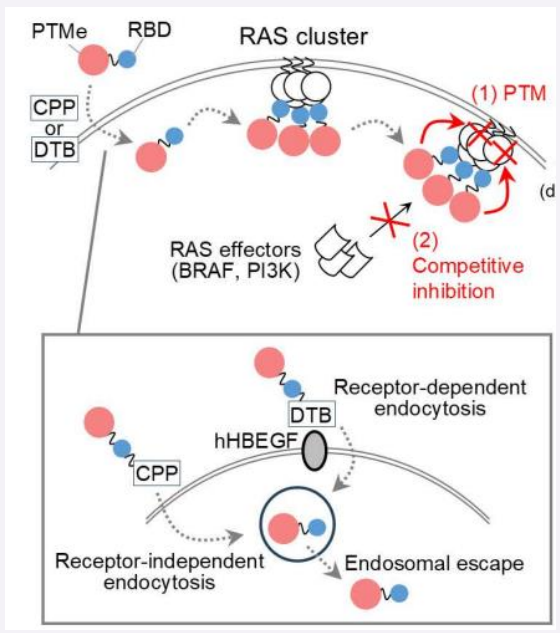
Research Outline

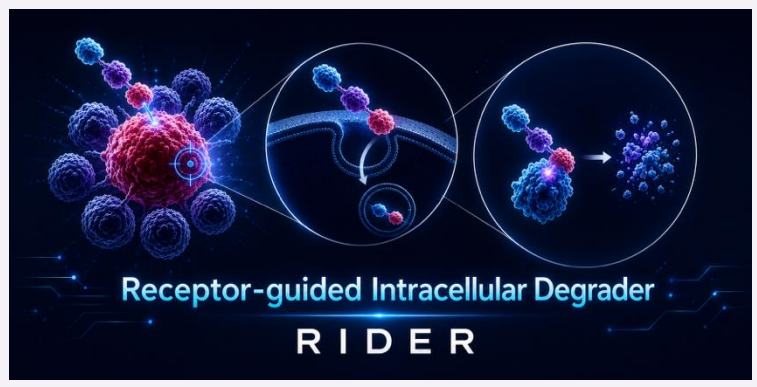
Key Words: #Protein therapeutics, #Targeted protein degradation, #pan-RAS degradation, #Tumor-selective delivery, #Genetic mutations, #Biomarkers, #Immune response

【Research Outline】
- This project develops a recombinant protein drug that selectively degrades intracellular RAS in RAS-mutant solid tumors.
- The molecule integrates tumor antigen binding, intracellular delivery, RAS binding, and RAS-degrading enzyme domains.
- It has shown fM–pM in vitro activity, >1,000-fold antigen-dependent selectivity, and xenograft antitumor efficacy.
- Next steps include linker optimization, lead selection, serum stability, PK/PD, safety/immunogenicity, and CMC/GMP development.

【References】

- Nomura, T.K. et al. (2026) Nature Communications
- Nomura, T.K. et al. (2021) Cell Chemical Biology 28(11):1581–1589.e6.





Protein-based pan-RAS inhibitor for RAS-driven cancers

KRAS signaling → Tumor growth | RRSP-RBD treatment → RAS cleavage → Signal OFF

Existing RAS inhibitors
- KRAS G12C focused
- Limited mutation coverage
- Resistance concerns

This seed
- Protein-based modality
- pan-RAS activity
- Immune related mechanism

Need
High unmet need in pancreatic, colorectal

Advantage
Broad RAS suppression and novel mechanism

Future
PK/safety, partnering

Seeking partners: Pharma / Biotech / CDMO / DDS / VC