Docket #: S24-152

Human helicase-based system for enhanced gene integration

Stanford scientists have developed a gene integration system that uses human-derived helicases paired with CRISPR technology to enable precise insertion of long DNA sequences at targeted genomic locations. By utilizing endogenous cellular machinery, this approach may reduce immunogenicity concerns in gene therapy applications while achieving precise, efficient integration of therapeutic genes.

Current genome engineering methods like CRISPR-Cas9, TALENs, and ZFNs face several limitations in therapeutic applications. These systems often struggle with off-target effects, have limited capacity for integrating DNA sequences beyond a few thousand base pairs, and can trigger immune responses due to their non-human origins. Additionally, their efficiency can vary significantly across different cell types, constraining their therapeutic utility. The immune response triggered by foreign enzymes in current gene editing technologies presents particular challenges for clinical applications, where immune reactions can compromise both safety and efficacy. These limitations underscore the need for more precise, versatile, and immunologically compatible gene integration approaches.

Initial studies demonstrate that this helicase-based system effectively integrates large DNA sequences while maintaining targeting precision. When combined with CRISPR technology, the system achieved successful gene integration across multiple cell types. The use of human-derived helicase showed reduced immunogenic responses compared to conventional systems, suggesting potential advantages for therapeutic applications. This approach may address key technical barriers in gene therapy, biopharmaceutical research, and cell line development, particularly in applications requiring the integration of long genetic sequences.

Stage of Development:
Preclinical – in-vitro data
Continued research – Demonstration in vivo

Applications

- Gene therapy development for genetic disorders requiring large therapeutic genes
- Research tools for precise genome engineering in laboratory settings
- Cell line engineering for biopharmaceutical production
- Development of enhanced model organisms for disease research

Advantages

- Integration of extensive DNA sequences beyond the typical size limitations of current methods
- Enhanced targeting precision through combined helicase-CRISPR approach
- Reduced immunogenicity through use of human-derived helicase
- Demonstrated efficacy across multiple cell types
- Compatible with existing CRISPR-based targeting systems

Innovators

- Le Cong

Licensing Contact

Eileen Lee

Email