Docket #: S24-393

DNA Elements for Episome Retention in Human Cells

Stanford scientists have developed a new DNA-based technology that allows therapeutic genes to be maintained in human cells for extended periods without altering the cell's chromosomes. A major challenge in gene and cell therapy is that most non-viral DNA introduced into cells is quickly lost as cells divide, making it difficult to achieve lasting therapeutic effects. Traditional methods often rely on viruses to keep therapeutic DNA in cells, but these can trigger immune responses or cause unintended changes in the genome.

The Stanford team identified naturally occurring human DNA sequences, called "retention elements," that act as anchors to help therapeutic DNA persist in dividing cells. These elements work by attaching the therapeutic DNA to the cell's chromosomes during cell division, ensuring it is passed on to daughter cells. Because these retention elements are derived from human DNA and do not integrate into the genome, they offer a safer, non-viral alternative for long-term gene delivery.

This technology could enable more reliable and sustained treatments for a range of diseases, including cancer, by supporting durable expression of therapeutic proteins or cell reprogramming factors in patient cells.

Stage of Development: Preclinical

Applications

- **Gene and cell therapy:** Enables durable expression of therapeutic proteins (e.g., CAR-T cells, cytokines) or reprogramming factors without viral vectors.
- **Biomanufacturing:** Rapid creation of producer cell lines for monoclonal antibodies or recombinant proteins.

- **Research Tools:** Engineered episomes for sustained transgene expression in mammalian, insect, or human cell lines.

Advantages

- Avoids risks associated with viral vectors
- Provides additive effect as combined retention elements enhance episome persistence
- Offers a safer, scalable solution for durable genetic engineering

Publications

- Sankar, V., Hung, K.L., Gnanasekar, A. et al. Genetic elements promote retention of extrachromosomal DNA in cancer cells. *Nature* (2025).

Patents

- Published Application: WO2026227008

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