Docket #: S21-317

DNA Element Responsive to Extrachromosomal DNA in Cancer Cells

Researchers at Stanford have developed a system that links inducible gene expression to the presence of extrachromosomal DNA (ecDNA) in cancer cells. Their novel, inducible DNA element (or gene switch) can be linked to reporter genes for drug screening and linked to therapeutic genes for the treatment of cancer. Circular ecDNA encoding oncogenes are a prevalent feature of cancer genomes and potent driver of cancer progression. However, the presence of ecDNA requires laborious methods for detection, and no existing method directly links a desired gene expression program to the presence of ecDNA in cancer cells. The Stanford invention comprises a promoter of the Plasmacytoma variant translocation 1 (PVT1) lncRNA gene operably linked to a heterologous nucleic acid sequence. The nucleic acid sequence can encode reporter proteins, cytotoxic proteins, proteins that induce an immune response or encode a viral protein required for replication of an oncolytic virus. This work may be leveraged to selectively kill or induce immunity against cancer, and to screen relevant ecDNA-targeting drug compounds.

Related Technology
Stanford docket S21-407 describes a method for targeted purification and profiling of megabase-sized human ecDNA. The method, termed ecDNA CRISPR-CATCH, allows targeted purification of ecDNA from human cancer cells and can be used to identify genetic variants and differences in methylation profiles between ecDNA and chromosomal DNA isolated from the same cancer cell, and for non-invasive in vitro assays to diagnose cancer.

Stage of Development
In vitro

Applications

- **Linkage to a reporter gene to detect ecDNA+ cancer cells**. This system may be used for high throughput screening of drug compounds that target ecDNA+ cancer cells.
- **Linkage to a therapeutic gene, such as a gene that kills cancer cells**. Because the DNA element only induces gene expression in cells with ecDNA, the cell killing will be selective to cancer cells.
- **Lingkage to a therapeutic gene that induces immune response**. Because the DNA element only induces gene expression in cells with ecDNA, the induced immunity will be selectively directed against cancer cells.

Advantages

- No existing DNA element or gene switch with selectivity to ecDNA is known.

Publications

- Hung, King L., et al. "ecDNA hubs drive cooperative intermolecular oncogene expression." *Nature* 600.7890 (2021): 731-736.

Patents

- Published Application: WO2023064778
- Published Application: 20250304952

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