Docket #: S21-407

Targeted Purification and Profiling of Human Extrachromosomal DNA

Researchers at Stanford have developed a method for targeted purification of megabase-sized extrachromosomal DNA (ecDNA) by combining in vitro nuclease treatment and pulsed field gel electrophoresis. The method, termed ecDNA CRISPR-CATCH, results in strong enrichment of ecDNA molecules containing oncogenes from human cancer cells. It 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. EcDNA oncogene amplifications are present in half of human cancer types and up to one third of tumor samples and are associated with poor patient outcomes. Given the prevalence of ecDNA in cancer, there is an urgent need for better characterization of unique genetic and epigenetic features of ecDNA in order to understand how it may differ from chromosomal DNA and obtain clues about how it is formed and maintained in tumors. Using existing tools, isolation and targeted profiling of megabase-sized, clonal ecDNAs is currently challenging due to their large sizes and sequence complexity.

Related Technology
Stanford docket S21-317 describes a system that links inducible gene expression to the presence of ecDNA in cancer cells. The 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.

Stage of Development
Pre-clinical. The method has been shown to work with human cancer cells.

Applications

- ecDNA detection and ecDNA sequencing for patient selection or risk stratification
- Users can include researchers, companies developing therapeutics targeting ecDNA-related processes, and cancer diagnostic companies

Advantages

- 30x enrichment of ecDNA compared to whole genome sequencing
- Ability to detect subclonal mutations
- Ability to assign mutations to ecDNA vs. chromosomal DNA (phasing), determination of absolute ecDNA size for ecDNA heterogeneity, ecDNA methylation profiling, ecDNA reconstruction without chromosomal DNA contamination

Publications

- Hung, K.L., Luebeck, J., Dehkordi, S.R. et al. (2022). Targeted profiling of human extrachromosomal DNA by CRISPR-CATCH. *Nat Genet* 54, 1746–1754.

Patents

- Published Application: WO2023091825

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