Docket #: S19-349

Large Scale Genomic Editing and Tracking using CRISPR-based Single-Cell Barcoding

Researchers at Stanford University have developed a scalable, single-cell barcoding system and method for genomic editing and tracking using cas12a-based compressive molecular probes. Human diseases involve millions or even billions of cells and complex pathophysiological processes, yet current laboratory methods are insufficient as they can only profile a small number of cells and are extremely labor- and cost-intensive. This severely limits our ability to systematically modify and edit the molecules within a cell to understand their function, and consequently limits our understanding of cellular and disease biology. To address this challenge, this novel barcoding system, based on CRISPR gene editing technology, leverages cas12a-based molecular probes to either edit or measure molecules within a cell, allowing for massive scale cell measurements at low cost. The probes are designed under a computational compression principle, similar to compressing an image on a computer to save space. The compressive molecular probes enable at least a two orders-of-magnitude (20-fold to 100-fold) boost to the number of cells that can be edited or measured. Thus, it could be used to scale up gene-editing and profiling methods.

The cas12a-based barcoding system has been tested and validated, enabling the recovery of single-cell lineages and transcriptional profiles in melanoma cells as well as identifying a drug that can play a protective role in severe COVID-19 based on high-throughput screening and clinical datasets. These findings demonstrate the utility of this barcoding technology for large-scale profiling of single-cell gene expression, and it could further be used for genome-scale compressive CRISPR editing. The system is a transformative new way to collect large biomedical datasets at high-resolution, which are critical for understanding complex diseases such as cancer and neurological disorders.

Stage of Development
Proof of Concept / Computational

Figure:

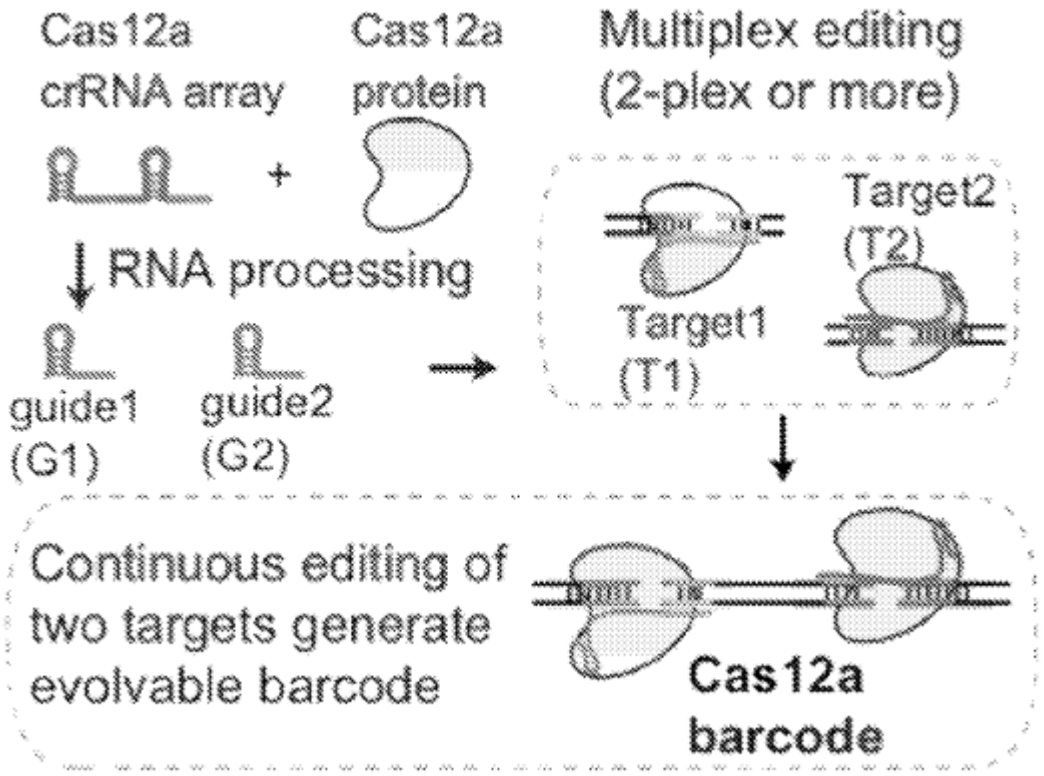

Figure description: An illustration of an exemplary design of a barcode system, in which a single CRISPR RNA (crRNA) array with two RNA guides (G1/G2) could be processed to edit two target sites within a cellular barcode sequence. Continuous editing generates evolvable barcodes.
Image credit: Patent Application No. WO 2022/226085 A1

Applications

- Single-cell genomics/proteomics, such as single-cell RNA-seq
- Gene-editing
- CRISPR screening

Advantages

- Scalable and low-cost profiling of single-cell gene expression - uses composite probe measurements to profile single-cell gene expression
- Scalable and low-cost gene-editing system - enables genome-scale CRISPR editing in human cells

Publications

- Machine-learning-optimized Cas12a barcoding enables the recovery of single-cell lineages and transcriptional profiles
- Integrative analysis of functional genomic screening and clinical data identifies a protective role for spironolactone in severe COVID-19

Patents

- Published Application: WO2022226085

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