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High-throughput multiomic readout of RNA and gDNA within single cells

Stanford researchers have developed a single-cell technology for a targeted high-throughput multiomic readout of RNA and gDNA. This method allows for the simultaneous reading of RNA and gDNA with high-coverage in single cells and can identify variants in DNA and link them to their transcriptomic effects.

Most current methods to achieve simultaneous readout of both RNA and gDNA are laborious and low-throughput, making them unusable for screening purposes or other large-scale experimental approaches. Other more scalable methods have limited coverage and high sequencing costs. This method solves this problem.

This invention has numerous potential applications that involve linking genomic information to transcriptomic signatures. For example, genome wide association studies have provided information on the associations between distinct genetic loci and human diseases. Single nucleotide polymorphisms (SNPs) in cis-regulatory elements (CREs) can affect gene expression and contribute to disease mechanisms, but the majority of them are not well understood. Current methods to study CREs use CRISPRi to perturb them as a whole, which neglects the influence of individual SNPs on disease-relevant gene expression. This new method can be used to combine precision genome editing with a targeted scDNA-scRNA-seq readout to reliably link variable genomic editing outcomes with disease-relevant gene expression. Another potential application involves the profiling of patient tumor samples for mutational status and associated gene expression. Understanding the driving effects and gene expression changes that are associated with individual mutations could yield better predictive treatment strategies for cancer patients.

Stage of Development

- Proof of concept

Applications

- **Linking genomic information to transcriptomic signatures**
- **Characterizing patient samples for mutational status and associated gene expression**
    - Better predictions for treatment of cancer patients
    - Drive mechanistic insights of disease-relevant eQTL mappings
- **Enables performance of lineage tracing analysis using endogenous gDNA or mtDNA loci**

Advantages

- Directly reads out the loci of interest
- Targeted
- High sensitivity
- High-throughput
- Cost effective

Patents

- Published Application: WO2024243040

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