Docket #: S23-312

Methods for Ultra-High-Throughput Profiling of Nucleic Acid Binding or Modifying Proteins

Researchers at Stanford have developed a novel method for the mapping of nucleic acid binding or modifying proteins in a massively multiplexed manner.

Next generation sequencing (NGS) has allowed for sequence-agnostic sequencing and has revolutionized every area of biomedical science. One application of NGS is assaying the nucleic acid binding or modifying for a single protein interacting with thousands to millions of sequences simultaneously. However, increasing the number of proteins assayed has been difficult, costly, and labor-intensive. In another vein, microfluidics platforms have allowed for the parallel assessment of binding affinities of a several sequences with hundreds of transcription factors (TFs). Microfluidic technology has not yet been leveraged to assay the binding of many TFs to many sequences in parallel.

Stage of Development
Research - in vivo

Stage of Research
The inventors have developed a novel approach to assay many sequences and many proteins binding affinity at the same time. Specifically, they use a barcode and print approach that links particular members of pooled sequenced libraries to specific protein variants that interact with the particular library members. Briefly, a barcoded library of sequences and a library of proteins that are imprinted at discrete locations to provide a barcode of sorts for the protein variant are created and pooled. These libraries are then put through a microfluidic device separately such that each microfluidic droplet contains one protein variant and one sequence. These are then incubated with a capture agent that binds to variant proteins and the captured sequences bound to the variant proteins are sequenced. This allows for the

assessment of many different protein-sequence binding partners in a single assay.

Applications

- High throughput assessment of many different protein-sequence interactions in the same assay.

Advantages

- Can produce measurements of 100,000+ protein-sequence interactions in a single day.
- Reduces costs associated with performing many assays vs one assay with the proposed method.

Patents

- Published Application: WO2025137217

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