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"CRISPR-All" enables genetic screens combining different types of genetic perturbations

Stanford scientists have developed a strategy that enables simultaneous and combinatorial genetic screening across different types of genetic perturbations (gene knockouts, knock-ins, overexpression, and gene domain modification).

Genetic screens have revolutionized drug discovery by providing a powerful tool to systematically study the effects of various genetic perturbations. This strategy has identified numerous drug targets across therapeutic modalities, including small molecules, biologics, and cell therapies. However, there is no method for simultaneously screening different types of genetic perturbations together (e.g., knockouts, knockdowns, knock-ins, etc.), significantly limiting the scope of genetic screens.

To address this, Stanford researchers developed a method ("CRISPR-All") that allows for the simultaneous and combinatorial screening of different types of genetic perturbations. This technique uses a single standardized module architecture, with each module representing a different type of genetic perturbation (knockout, knock-in, knockdown, gene domain modification, etc.) Each module is barcoded and can be used with a cloning and expression architecture that allows any number of modules to be used individually or in combination.

Stage of Development
Proof of concept: demonstrated CRISPR-All screening in primary human T-cells

Applications

- Combinatorial screening of different types of gene modifications (knockout, knock-in, knockdown, overexpression, gene domain modification)

- Identification of optimal genetic modifications for cell therapies (e.g., CAR-T)
- Identification of novel drug targets
- Mechanistic insight into drug mechanism of action

Advantages

- Enables simultaneous and combinatorial screening of different types of genetic perturbations
- Modular architecture allows for an arbitrarily combinatorial number of genetic modifications
- Strategy uses amplification-free cloning
- Uses reusable component libraries

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