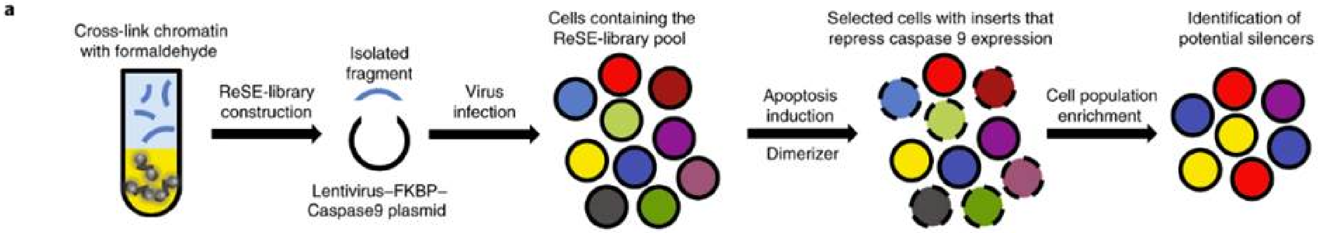
Docket #: S18-182

Systematic Identification of Silencer Elements in the Human Genome

Researchers at Stanford have developed, for the first time, a high-throughput method to systematically detect and identify silencer elements in the human genome. This method measures the repressive ability of silencer elements (ReSE) by screening for genomic fragments that repress the transcription of an inducible cell death protein. Genomic silencers – noncoding regions that repress gene expression—are an important class of regulatory elements, but systematic methods of identification and analysis have been lacking to date. As such, silencers have been understudied. ReSE is a robust screening system developed to meet this need. ReSE utilizes a lentiviral system to test the ability of candidate genomic fragments to repress the caspase-based 'kill switch' for the enrichment of potential silencers. Systematic identification of silencers in the genome using the ReSE screen may not only provide insights into the biology of the genome, but also assist in personalized medicine.



Outline of the screen design (Image credit: Pang and Snyder, *Nature Genetics*)

Stage of Development

Using this method the researchers identified more than 5,000?tissue-specific candidate silencer elements in the human genome. Overall, their study demonstrates that tissue-specific silencing is widespread throughout the human genome and probably contributes substantially to the regulation of gene expression and human biology.

Applications

- To identify and define the function of silencer regions
- Can be used to test if non-coding regions gain or lose repressive activity, especially the non-coding regions enriched for disease related mutations, SNPs, INDELs or other genomic structural variants

Advantages

- Systematic and high-throughput
- No comparable method exists

Publications

- Pang, B., Snyder, M.P. Systematic identification of silencers in human cells. *Nat Genet* **52**, 254–263 (2020). https://doi.org/10.1038/s41588-020-0578-5

Patents

- Published Application: WO2021155369
- Published Application: 20230104317

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