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FUNCTIONAL GENOMICS

Screening for lncRNA function

> 499 lncRNA loci were required for robust cellular growth

Biological functions are known for only a small number of long non-coding RNAs (lncRNAs). A study in *Science* now reports a highly specific, high-throughput CRISPR-based approach to screen for functional lncRNAs.

High-throughput functional screening of non-coding DNA using CRISPR–Cas9 is complicated by the fact that loss-of-function phenotypes require deletions that are larger than the small insertions and deletions typically generated. The team adopted the previously developed CRISPR interference (CRISPRi) method, which represses gene transcription by recruiting a catalytically inactive version of the Cas9 enzyme to the transcription start site (TSS) of genes using a single guide RNA (sgRNA).

Liu *et al.* first designed an sgRNA library targeting 16,401 lncRNA loci, with 10 sgRNAs aimed against each lncRNA gene TSS. The authors then used the sgRNA library to screen for lncRNA genes that alter cellular growth in seven human cell lines.

In total, 499 lncRNA loci were required for robust cellular growth, with the overwhelming majority (89%) of lncRNAs genes affecting growth in only one cell type. Of note, not a single lncRNA, of 1,329 lncRNA genes tested, modified growth across all cell lines, suggesting that lncRNA function is highly cell-type-specific.

Comprehensive validation studies confirmed the screens' results: the phenotypes were reproducible, transcriptome responses were correlated, and the knockdown of target transcripts was robust.

This systematic screening approach has expanded the number of known functional lncRNA genes and may serve as a useful tool for further analysis of lncRNA function.

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ORIGINAL ARTICLE Liu, S. J. *et al.* CRISPRi-based genome-scale identification of functional long noncoding RNA loci in human cells. *Science* http://dx.doi.org/10.1126/science.aah7111 (2016)