Docket #: S23-163

Manipulating Spatial RNA Localization

Researchers at Stanford have developed an inducible and programmable CRISPR-mediated transcript organization (CRISPR-TO) method for repositioning RNAs to various desired subcellular compartments.

Spatial RNA transcriptomics, including subcellular mRNA localization, is a core mechanism for spatiotemporal regulation of gene expression and protein synthesis. For example, neurons with large axons tend to spatially localize key mRNAs to the tip of axons to coordinate axon guidance and growth cone development. Mounting evidence has begun to correlate the dysregulation of mRNA localization to an increasing number of diseases, in particular neurological diseases. However, despite decades of effort, the mechanistic and functional importance of RNA spatial localization has only been explored for a few key examples, largely due to a lack of efficient and programmable approaches that allow for the manipulation of any endogenous RNA localization in cells.

Stage of Development
Research – in vitro

Stage of Research
The inventors have developed methods of localizing RNA in a cell in which a localization polypeptide and RNA carrier polypeptide form an intracellular molecular transport dimerization pair. The method is both inducible, and can deliver a guide RNA to various subcellular locations within a cell.

Technology Reference Numbers
CZ Biohub SF ref. no.: CZB-282S
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Applications

- Using CRISPR-TO to efficiently manipulate the spatial localization of repetitive reporter mRNAs.
- Localization of GAPDH mRNAs or GCN4 reporter mRNAs to p-bodies, stress granules, minus ends of microtubules, plus ends of microtubules, tellers and nuclear stress bodies in HeLa cells.
- Localization of endogenous mRNAs to the projections of primary neurons.
- The recruitment of mRNA to the terminals of neuronal projections in primary mouse hippocampal neurons.
- Localization of OMM mRNA to promote the import of translated proteins into mitochondria.

Advantages

- Highly-versatile RNA localization technology that can be widely applied in different types of animal cells, and localized effectively to a wide variety of different subcellular compartments.

Patents

- Published Application: WO2025096250

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