OPTOGENETICS

Controlling mRNA localization with light

An optogenetic approach allows researchers to probe how mRNA localization affects cellular processes.

The tight regulation of gene expression is crucial for normal cellular physiology, and although much is known, this is still an area of intense research. Cells can regulate gene expression by controlling where mRNAs are located and translated, yet tools for studying how this spatial restriction affects cell function are limited.

Heo and colleagues at the Korea Advanced Institute of Science and Technology have developed numerous optogenetic tools to modulate protein activity in cells. To extend optogenetic technology to studying mRNA localization, the researchers created mRNA-LARIAT, an extension of their previously developed light-activated reversible inactivation by assembled trap (LARIAT) technology.

In LARIAT, proteins of interest are reversibly sequestered into intracellular clusters by using CRY2 and CIB1 proteins,

which dimerize in the presence of blue light. LARIAT uses CIB1 fused to a multimeric protein coexpressed with CRY2 fused to a target protein. In the presence of blue light, clusters are formed by dimerization of CRY2 and CIB1 cross-linking the multimers formed by the multimeric protein.

In mRNA-LARIAT, mRNAs of interest are genetically tagged with binding sites for the MS2 cap protein (MCP) and bound by MCP-GFP, which is in turn bound to CRY2 fused to an anti-GFP nanobody. This complex is coexpressed with multimeric proteins fused to CIB1. When blue light is added, clusters form that sequester the mRNAs. The researchers have also shown that untagged RNAs can also be targeted by using RNA-targeting Cas9 in place of the MS2 system for sequestration.

Heo and colleagues have demonstrated that target mRNAs are reversibly targeted to clusters after blue-light treatment followed

by periods in the dark. The researchers measured translation under blue light and found that the sequestered mRNAs showed a clear decrease in translation efficiency. The team then used mRNA-LARIAT to study whether the localization of β -actin mRNA is involved in fibroblast migration. Typically, β -actin mRNA localizes to the leading edge in migrating cells. Light-induced sequestration decreased migration and considerably reduced stable focal adhesions, thus suggesting a crucial role for newly synthesized actin at these sites.

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Research paper

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