

HUMAN DISEASE

An eye on RNA

In the cytoplasm of eukaryotic cells, accumulations of mRNAs and proteins, termed RNA granules, are involved in post-transcriptional regulation; for example, they can be sites of mRNA decay or storage. The importance of post-transcriptional regulation, which is far less understood than transcriptional regulation, is highlighted by a recent paper showing that specific RNA granules influence organogenesis and that their disruption can cause human disease.

Lachke and colleagues identified mutations in the gene encoding Tudor-domain-containing protein 7 (TDRD7) as a cause of paediatric cataracts and risk factor for glaucoma. They also showed that mice with a mutation in this gene develop cataracts and glaucoma. They found that TDRD7 is specifically expressed in lens fibre cells during development and localizes to a subset of RNA granules.

TDRD7-containing granules frequently colocalize with the RNA-binding protein STAU1, which is associated with mRNA decay and other aspects of RNA metabolism.

So does mutation of TDRD7 affect gene expression? Lachke *et al.* found that knocking down TDRD7 in human and mouse lens cells resulted in substantial reduction in the number of RNA granules that form on exposure to stressful stimuli, known as stress granules. Microarray analysis of *Tdrd7*-knockdown cells and lens cells from *Tdrd7*-null mice revealed dysregulation of many genes that are known to be involved in lens development. Two of the downregulated genes are *Crybb3*, one of the crystallin genes, and the stress-responsive heat shock gene *Hspb1*. High levels of crystallin are needed for lens transparency and HSBP1 stabilizes crystallin proteins. Therefore, a plausible model is that TDRD7 normally helps to stabilize these mRNAs, so loss of

TDRD7 causes cataracts owing to insufficient crystallin.

These findings show how RNA granules can have tissue-specific regulatory functions that are conserved across species. It will be interesting to discover whether similar processes underlie other diseases.

Mary Muers

ORIGINAL RESEARCH PAPER Lachke, S. A. *et al.* Mutations in the RNA granule component TDRD7 cause cataract and glaucoma. *Science* **331**, 1571–1576 (2011)

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