RNAs taking center stage

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RNAs, serving as a mere intermediary between DNA and proteins, were long regarded as a poor relation by researchers, attracting little interest. However, following the discovery of small RNAs known as microRNAs, they have increasingly been moving into the limelight. MicroRNAs bind to messenger RNA (mRNA), thereby regulating the translation of genes into proteins.

Recently, various studies have shown that the production of microRNAs is tightly controlled, but their subsequent fate was not clear. It was assumed that mature microRNAs remained stable in the cell for days, and that their possible functions were therefore restricted: a microRNA persisting for a relatively long period cannot be involved in any processes in the cell requiring rapid adaptation.

Regulated regulators

The study carried out by Helge Grosshans, a Research Group Leader at the Friedrich Miescher Institute, Switzerland, has now finally shifted attention away from DNA, spotlighting the key role played by microRNAs in the theater of cellular processes.

As Grosshans and his team report in the current issue of the renowned journal *Nature*, they discovered a mechanism for active degradation of microRNAs and showed that this mechanism is itself regulated. Explaining his findings, Grosshans says: “What was formerly conceived of as a direct, straightforward pathway is gradually turning out to be a dense network of regulatory mechanisms: genes are not simply translated

into proteins via mRNA. MicroRNAs control the translation of mRNAs into proteins, and proteins in turn regulate the microRNAs at various levels.” In addition, the FMI researchers showed in the nematode *Caenorhabditis elegans* that, via regulation of degradation, it is possible to influence microRNA activity. This means that microRNAs may, after all, be involved in the regulation of rapidly occurring processes.

Targeted degradation of disease-causing RNAs

But the findings are also relevant in another respect. As microRNAs have been implicated in the development of diseases, efforts to date have focused on replacing disease-causing microRNAs with other microRNAs, or inactivating them with the aid of complementary RNA strands. Unfortunately, it is extremely difficult to deliver RNAs to target cells for therapeutic purposes. Accordingly, the prospects of success for these novel treatment approaches have been uncertain. In his study, however, Grosshans identified a protein that specifically degrades microRNAs. If it now proves possible to specifically activate or inhibit this protein and its partners, that could provide an approach which is closer to classical and well-established forms of therapy. Grosshans comments: “We now assume that a large number of human genes are regulated by microRNAs, so the regulatory mechanism we’ve discovered has a great potential to significantly influence numerous processes in human cells."

The meteoric rise of microRNAs

MicroRNAs are short, single-stranded RNA molecules which interact with mRNAs in a sequence-dependent manner. They thus inhibit translation of mRNAs into proteins. MicroRNAs were first described in 1993 in the nematode *Caenorhabditis elegans*. They were subsequently also shown to play an important role in regulating development processes

and in pathogenesis in higher organisms. The findings of recent years and now also Helge Grosshans's study have shifted attention away from DNA toward RNAs, which are taking center stage. The term "microRNA" was only introduced in 2001.

More information: Chatterjee S & H. Grosshans (2009) Active turnover modulates mature microRNA activity in C. elegans. *Nature*, 24 August 2009, doi:10.1038/nature08349

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