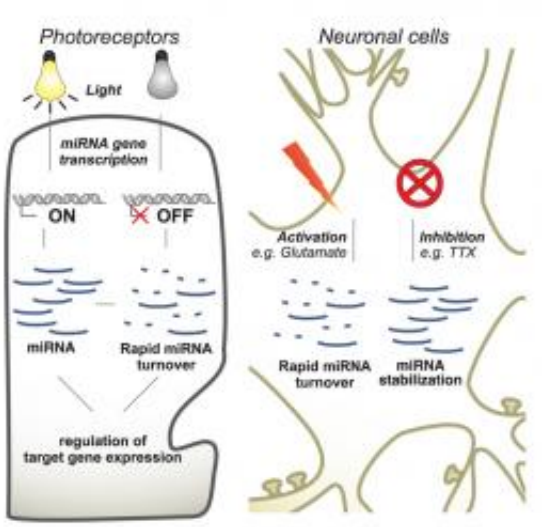
MicroRNA expression and turnover are regulated by neural activity in the retina and brain

May 17 2010



(PhysOrg.com) -- Scientists from the Friedrich Miescher Institute for Biomedical Research (FMI) found that microRNAs, small RNA regulators of gene expression, are up- and down-regulated in the retina during light-dark adaptation and in response to synaptic stimulation in hippocampal and cortical neurons. This important discovery provides an unexpected function for microRNAs: it shows that they are able to regulate rapidly the expression of synaptic proteins, which are involved in synapse plasticity and memory formation.

Bring a neurobiologist and an expert in microRNA biology together and you will merge two fields at the frontiers of life science and create research hypothesis that could be tremendously successful but which could just as easily fail. "Our initial idea was very speculative. We had no certainty what so ever that this project could be successful," say Witold Filipowicz and Botond Roska, Group Leaders at the Friedrich Miescher Institute for Biomedical Research and corresponding authors of a recent publication in *Cell*. "But we had the tools and the expertise to test it." And so they did, with groundbreaking results.

A team of scientist around Witold Filipowicz and Botond Roska, also including collaborators from other FMI groups, showed that levels of microRNAs, tiny RNA regulators of gene expression, respond to different types of stimulation in neurons. They could show that in the nerve cells of the mouse retina, the levels of a set of clearly defined microRNA species increase rapidly upon stimulation with light due to upregulated transcription.and that a glutamate transporter Slc1a1, a protein important for synaptic transmission, is controlled specifically by these microRNAs that are up regulated by light.

The FMI scientists also discovered that microRNAs in neurons, both retinal and non-retinal, turn over very rapidly and that microRNA decay is tightly regulated by neuronal activity. "So far microRNA molecules have been considered very stable with half-lives extending even to days",explains Witold Filipowicz. "To find now a subset of microRNAs that are reversibly up- and down-regulated in the retina during light-dark adaptation, and in other neurons in response to synaptic stimulation, changes our perception of the role of microRNAs in neurons and in the processes in the brain."

"Have we found a mechanism that explains gene regulation generally in the retina and the brain? I don't think so. But it is a mechanism that plays a role and that should not be neglected in future studies of synaptic

plasticity and memory formation," explains Botond Roska. It will be particularly important for gene regulation in the long processes - axons and dendrites - of neuronal cells, which often extend very far from the nucleus, and are therefore less responsive to transcriptional control of gene expression.

Three years after the initiation of the study it turns out that the futuristic fusion of neurobiology and RNA research produced pioneering results. Witold Filipowicz adds: "It is the strength of the FMI that it fosters such collaborations across the boundaries of disciplines and thereby supports projects that may seem a little risky but may also allow a crucial step forward in the understanding of the processes in our cells."

The Friedrich Miescher Institute is part of the Novartis Research Foundation.

More information: Publication in Cell - www.cell.com/abstract/S0092-8674%2810%2900357-0

Provided by Friedrich Miescher Institute for Biomedical Research