

microRNAs: fine regulators of synaptic transmission

by Gerhard Schratt

More than one hundred billion nerve cells are packed in the brain of an adult as compactly as possible. Correct interconnections among these nerve cells are critical for cognitive performances, such as learning and memory, and defects in their interconnections underlie a series of neurological diseases such as autism and epilepsy. Individual nerve cells communicate via synapses, highly specialized contact sites where messengers are released, which dock as mediators onto dendritic processes of other nerve cells, thereby transmitting signals. Synapses not only link nerve cells together, they can also store information: the number and strength of these connections determine how efficiently information can pass through the brain and be accessed.

Our research focuses on the molecular mechanisms that are important for the alteration (plasticity) of synapses and thus for learning and memory processes. It has long been known that the protein machinery in dendritic processes plays a central role. Plasticity requires dynamic regulation of the protein make-up in dendritic processes by both protein synthesis and degradation. However, it is largely unknown which molecules are important for this regulation.

Recently, we were able to show that a new class of molecules, known as miRNAs (micro-ribonucleic acids), inhibit the synthesis of key proteins in dendritic processes, thereby preventing excess growth of the dendritic processes. This inhibition can be overcome by administering factors that are also released after stimulation of the synapse. miRNAs are tiny, 19- to 23-nucleotide-long ribonucleic acids, which, unlike messenger RNA (mRNA), are not translated into proteins but take on purely regulatory functions. miRNAs are located in almost every cell of the body, and they regulate a variety of biological processes, including the development of the heart, the metabolism of insulin, and the development of cancer. Hundreds of different miRNAs have been identified in various stages and regions of brain development; however, for the most part, their function has remained unclear.

Our new research results now suggest that a certain group of neuronal miRNAs make an important contribution to the plasticity of synaptic connections. miRNAs appear to achieve these effects by regulating a variety of proteins that affect the structure and function of synapses. On the basis of these observations, we are currently focusing on a variety of questions: How do miRNAs and their target mRNAs reach the

synapse? How are the expression and function of miRNAs regulated? What effect do miRNAs have on nerve conduction and ultimately cognitive performances? Can the capacity for synaptic plasticity be influenced by manipulating miRNAs in animal models?

Research on this fascinating class of molecules is certainly still in its infancy; however, it can be expected that future results will make important contributions to our understanding of molecular processes involved in learning and memory. Ultimately, miRNAs might also be of clinical interest for treatment of neurological diseases associated with impaired function of synaptic transmission.