NEWS

Molecular mechanisms: Fragments of RNA regulate synapse

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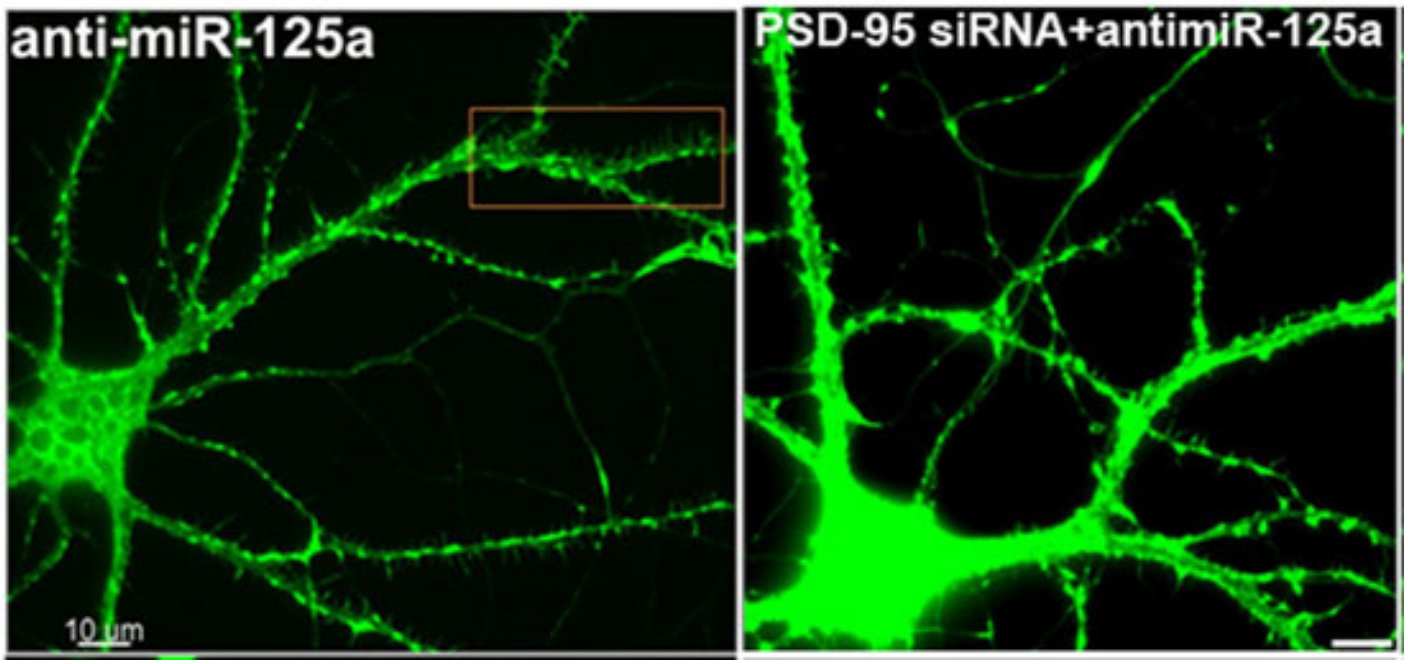

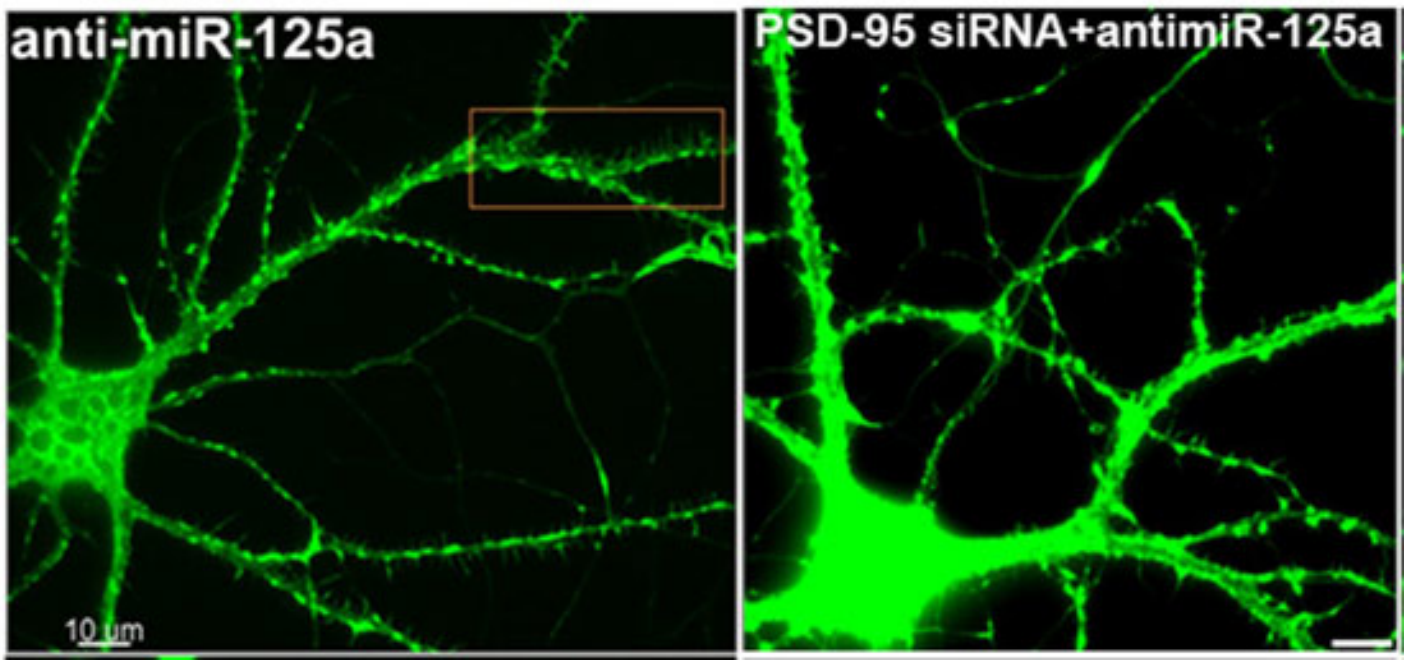

Fine-tuning function: Blocking an RNA fragment increases the density of dendritic spines (left), which can be rescued by preventing expression of an autism-associated protein (right).

Small fragments of RNA, called microRNAs, can fine-tune the levels of proteins at the junctions between neurons in response to cell signals, according to a study published 10 June in *Molecular Cell*[1].

The study reveals an elegant molecular mechanism by which microRNAs cooperate with the fragile X mental retardation protein, or FMRP, to regulate function at the synapse, the junction between neurons. MicroRNAs regulate gene expression by interfering with mRNAs, the RNA messages that code for protein.

Previous studies have implicated **lower-than-normal levels of microRNAs** in the brains of people with certain neurological disorders, such as schizophrenia and bipolar disorder.

The new study found that miR-125a, a microRNA, localizes at dendrites, the signal-receiving ends of neurons. Lack of this microRNA leads to denser dendritic spines and higher levels of postsynaptic density-95, or **PSD-95**, an autism-associated protein that organizes the connections at synapses.

Previous studies have shown that FMRP **lowers the levels of proteins** that function in the

postsynaptic density, a **complex of proteins** including PSD-95 that regulates learning and memory.

The new study suggests a model in which both FMRP modified with a phosphate group and the microRNA bind to PSD-95 mRNA and block PSD-95 protein production.

A signal transmitted through a receptor called mGluR1 results in removal of the phosphate group from FMRP. This in turn leads to the release of both FMRP and miR-125a from the PSD-95 mRNA, recovering PSD-95 protein production.

The results show how signaling through mGluR receptors can regulate the levels of PSD-95. Pharmaceutical companies are **targeting mGluR receptors** as a treatment for fragile X syndrome.

References:

1. Muddashetty R.S. *et al. Mol. Cell* **42**, 673-688 (2011) **PubMed**