NEWS

# Molecular mechanisms: New pathway for fragile X treatment

BY **JESSICA WRIGHT**

2 DECEMBER 2010

Startling sound: Inhibiting the ERK1/2 pathway in fragile X mice prevents them from having seizures in response to loud noises.

Inhibiting the ERK1/2 pathway — which regulates the synthesis of other proteins — can **rescue some of the effects** of fragile X syndrome, according to a study published 17 November in the *Journal of Neuroscience*. The ERK pathway could provide a novel target for fragile X therapies.

Fragile X syndrome is caused by lack of the fragile X mental retardation protein, or FMRP, which controls the production of several proteins important at the synapse, the junction between neurons. Some therapies for fragile X syndrome **target the mGluR receptor**, which also regulates protein synthesis.

In the new study, researchers show that protein synthesis overall is higher in a slice of the hippocampus removed from the brains of fragile X mice. Inhibiting both the mGluR receptor and ERK1/2 — a pathway that mGluR activates — restores protein synthesis to normal levels, the researchers show. By contrast, inhibiting mTOR1 — another pathway also thought to be involved in fragile X syndrome — does not restore protein synthesis.

Injecting an inhibitor of the ERK pathway into the brains of fragile X mice also prevents seizures triggered by loud noise — a known characteristic of this mouse model.

The researchers show that the loss of FMRP does not increase mGluR and ERK1/2 signaling overall. Rather, it may make the cells more sensitive to proteins regulated by these pathways.