The fragile X mental retardation syndrome protein interacts with novel homologs FXR1 and FXR2

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Fragile X Mental Retardation Syndrome is the most common form of hereditary mental retardation, and is caused by defects in the FMR1 gene. FMR1 is an RNA-binding protein and the syndrome results from lack of expression of FMR1 or expression of a mutant protein that is impaired in RNA binding. The specific function of FMR1 is not known. As a step towards understanding the function of FMR1 we searched for proteins that interact with it in vivo. We have cloned and sequenced a protein that interacts tightly with FMR1 in vivo and in vitro. This novel protein, FXR2, is very similar to FMR1 (60% identity). FXR2 encodes a 74 kDa protein which, like FMR1, contains two KH domains, has the capacity to bind RNA and is localized to the cytoplasm. The FXR2 gene is located on human chromosome 17 at 17p13.1. In addition, FMR1 and FXR2 interact tightly with the recently described autosomal homolog FXR1. Each of these three proteins is capable of forming heteromers with the others, and each can also form homomers. FXR1 and FXR2 are thus likely to play important roles in the function of FMR1 and in the pathogenesis of the Fragile X Mental Retardation Syndrome.