

Abstract 40

ANALYSIS OF THE EXPRESSION PROFILE OF mRNAs AND microRNAs IN FRAGILE X SYNDROME.

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Fragile X syndrome (FXS) is caused by the absence of the FMRP protein. FMRP is involved in multiple pathways of mRNA metabolism and stability [Zalfa et al., 2007]. Indeed, FMRP has been shown to be associated to microRNAs (miRNAs) in mammals [Jin et al., 2004], possibly regulating neuronal mRNA translation or stability. We performed microarray experiments to characterize the transcriptional profile of lymphoblastoid cell lines from 4 FXS, 3 controls and 2 unmethylated full mutation (UFM) carriers. Bioinformatic analysis yielded a list of genes either up- or down-regulated in FXS lymphoblasts, compared to controls. We selected 8 genes for validation and confirmed that 5 of these were actually differentially expressed. We also analyzed the miRNA expression profile in lymphoblasts from 6 FXS, 6 controls and 3 UFM carriers. We observed internal homogeneity in each of the three groups (FXS, controls and UFM) and confirmed the inter group difference ($p < 0.05$). We identified few differentially expressed miRNAs in the three groups and found that some corresponding mRNA targets were accordingly modified, as shown by the mRNA profiling experiments. Interestingly, 5 of the selected miRNAs also bind to the 3' UTR of the *FMR1* gene. These experiments may lead to the identification of FXS pathogenetic pathways, eventually allowing pharmacological therapy of FXS, in spite of the absence of FMRP.

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