

Mecp2-null mice provide new neuronal targets for Rett syndrome.

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BACKGROUND: Rett syndrome (RTT) is a complex neurological disorder that is one of the most frequent causes of mental retardation in women. A great landmark in research in this field was the discovery of a relationship between the disease and the presence of mutations in the gene that codes for the methyl-CpG binding protein 2 (MeCP2). Currently, MeCP2 is thought to act as a transcriptional repressor that couples DNA methylation and transcriptional silencing. The present study aimed to identify new target genes regulated by *Mecp2* in a mouse model of RTT. **METHODOLOGY/PRINCIPAL FINDINGS:** We have compared the gene expression profiles of wild type (WT) and *Mecp2*-null (KO) mice in three regions of the brain (cortex, midbrain, and cerebellum) by using cDNA microarrays. The results obtained were confirmed by quantitative real-time PCR. Subsequent chromatin immunoprecipitation assays revealed seven direct target genes of *Mecp2* bound in vivo (*Fkbp5*, *Mobp*, *Plagl1*, *Ddc*, *Mllt2h*, *Eya2*, and *S100a9*), and three overexpressed genes due to an indirect effect of a lack of *Mecp2* (*Irak1*, *Prodh* and *Dlk1*). The regions bound by *Mecp2* were always methylated, suggesting the involvement of the methyl-CpG binding domain of the protein in the mechanism of interaction. **CONCLUSIONS:** We identified new genes that are overexpressed in *Mecp2*-KO mice and are excellent candidate genes for involvement in various features of the neurological disease. Our results demonstrate new targets of MeCP2 and provide us with a better understanding of the underlying mechanisms of RTT.