Investigating MeCP2 Regulation of L1CAM Gene Expression in Neural Stem Cells Derived from a Patient with Rett Syndrome

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Mutations in the MeCP2 gene are the most common cause of Rett Syndrome (RTT), a severe form of autism diagnosed primarily in girls. The MeCP2 gene product, MeCP2, is a transcriptional regulatory protein that influences the expression of several genes required for neural development. L1 CAM is a cell adhesion molecule responsible for neurite outgrowth, which is deficient in neural stem cells derived from a patient with Rett Syndrome. This suggests that expression of the gene encoding L1 CAM is impaired in the MeCP2 mutant background. I investigated the level of expression of the L1CAM gene in neural stem cells derived from a patient with Rett Syndrome (RTT cells). Using the pTet-off system, I varied the level of wild-type MeCP2 gene expression in RTT cells maintained in tissue culture and measured the effect on the level of L1 CAM protein synthesis. Finally, I used an expression plasmid to overexpress the L1CAM gene in the RTT cells and measured the effect on neurite outgrowth. I found that L1 CAM protein levels were lower in RTT cells than in wild-type neural stem cells, indicating that expression of the L1CAM gene is impaired in the MeCP2 gene mutant background. More L1 CAM protein was produced in the RTT cells when the expression of the MeCP2 gene was increased. The average length of neurites from the RTT cells increased when the L1CAM gene was overexpressed. The experimental results indicate that MeCP2 influences the expression of the L1CAM gene, resulting in the deficiency in L1 CAM protein levels in a MeCP2 mutant background. Moreover, the overexpression of the L1CAM gene increases neurite outgrowth in the RTT cells. I will continue to investigate the role of MeCP2 and L1 CAM in the pathology of Rett Syndrome and pursue new avenues of treatment.

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