Investigating MeCP2 and JNK3 reciprocal regulation in human cellular models for Rett Syndrome

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The c-Jun N-terminal Kinase family, activated by a wide range of cellular stress factors, is involved in neuronal maturation and neuroinflammation. Our studies belong to a wider project aimed to investigate the therapeutic role of a JNK inhibitor DJNKI1 (Borsello-Mario Negri), whose neuroprotective effect on mouse model of Alzheimer Disease and cerebral ischemia has been proved. Our aim was to investigate on a human cellular model, the molecular mechanisms and possible interactions linking MeCP2 to JNKs. An *in vitro* model of Rett Syndrome (SKNBE-2(c) and HEK293t cell lines, transfected with MeCP2-WT or MeCP2-R168X) was generated. To verify if MeCP2 regulated JNK expression, the level of JNK proteins and mRNA was evaluated by western blot and real time PCR. No significant difference was disclosed. Immunofluorescence assays showed that JNK localization was not affected in the MeCP2-R168X cells. However, because JNKs proteins predominantly function as kinases, we hypothesized that MeCP2 and JNKs directly interacted. Immunoprecipitation assays on HEK293t cells, co-transfected with MECP2 and JNK3 plasmids revealed no direct interaction. In parallel, Real Time PCR on patients' blood revealed increased levels of JNK mRNA, compared with pediatric controls (still in progress). Nevertheless our studies show that the occurrence of a MECP2 mutation does not vary JNK expression, its localization and the interaction among the two proteins, the drug could improve the damages caused by the MeCP2 acting on other molecules which link MeCP2 and JNK, but not directly. Further experiments, also using different human model have to be carried on.