Hartford Union High School SMART Team
H Bertucci, M Bertucci, T Dorosz, T Hart, A Heimermann, M Lentz, T Rusch, J Schultz, N Weber, and H Weiss

Advisor: M Arnholt

Mentor: Dr. G Makky, PhD, Marquette University

The Role of MeCP2 Mutations in a Reg-Rett-Able Syndrome

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Rett Syndrome affects about one in every 10,000 to 15,000 births. It is a genetic neurodevelopmental disorder that mainly occurs in females. Affected males die in infancy because the syndrome exhibits an X-linked dominant pattern of inheritance. Rett Syndrome is caused by mutations in the X-linked Methyl CpG binding protein 2 (MeCP2) coding gene. MeCP2 is necessary for epigenetic regulation of gene expression. This protein represses transcription by acting as a molecular bridge between methylated DNA and a complex of co-repressor proteins including histone deacetylases and Sin3A. Mutations of MeCP2 cause overexpression of several genes during brain development. MeCP2 is a 52-kDa protein with two functional domains: the transcriptional repressor domain (TRD) and the methyl-CpG binding domain (MBD). Within the MBD, mutations of Arg106, Arg133, Phe155, and Thr158 result in a decreased binding affinity of MeCP2 to methylated DNA: 2-fold for mutated Thr158 and 100-fold for the remaining mutated amino acids. The MBD has three beta sheets with Thr158 located on the c-terminal end. Here, hydrophilic residues interact specifically with the methylated DNA. The Hartford Union High School SMART (Students Modeling A Research Topic) Team designed a model of MeCP2 using 3D printing technology to represent the MBD-methylated DNA complex. The model highlights the amino acids involved in the interaction between MeCP2 and methylated DNA. Modeling the structure of MeCP2 allows for a more detailed understanding of the interaction between MeCP2 and DNA. This information will be crucial for designing treatments or interventions to improve the quality of life for Rett syndrome patients.