



**RELATIONSHIP BETWEEN PROTEIN STRUCTURE AND PATHOGENICITY FOR
PRNP VARIANTS ASSOCIATED WITH CREUTZFELDT-JAKOB DISEASE (CJD)
AND GERSTMANN-STRÄUSSLER-SCHEINKER (GSS) DISEASE**

**Chelsea Li (Dr. Julio Facelli, Rolando Hernandez)
Department of Biomedical Informatics, University of Utah**

PRNP is a gene coding for the major prion protein that is composed of 253 amino acids. This protein has a role in neuronal development and synaptic plasticity along with myelin sheath maintenance and homeostasis. Various mutations of PRNP can lead to genetic prion diseases, Creutzfeldt-Jakob disease (CJD) and Gerstmann-Sträussler-Scheinker (GSS) are two prion diseases that are the focus of this analysis. CJD patients develop rapid dementia with a short survival time, while GSS patients who may have similar symptoms have survival times that can last 3-10 years. To understand the role of mutations of these two clinically different neurodegenerative diseases, protein structure prediction can be used to analyze how changes of the amino acid sequence affect structure. From Swiss Uniprot, the canonical sequence of PRNP was obtained. Using I-TASSER we predicted the 3D structures of PRNP for, both the canonical amino acid sequence and those obtained by single substitutions for each variant that have been reported to cause either CJD or GSS. The protein structures were compared to the wild-type structure and among themselves. Further investigation for this study will include using more tools to assess pathogenicity and deeper analysis and comparison between each of the variants along with seeing how the major prion protein interacts with other proteins to develop a potential pathway that it interacts.

This research was supported by a Supplement to the NLM Training grant T15 LM00712418, with additional support from the Utah Center for Clinical and Translational Science funded by NCATS award 1ULTR002538. Computer resources were provided by the University of Utah Center for High Performance Computing, which has been partially funded by the NIH Shared Instrumentation Grant 1S10OD02164401A1.