Characterization of Disease-Causing Mutants of Phosphoglycerate Dehydrogenase

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Macular Telangiectasia type 2 (MacTel) is a rare, late-onset, macular degenerative disease associated with deficiency in circulating levels of serine. The enzyme phosphoglycerate dehydrogenase (PHGDH) is the rate-limiting enzyme in the serine synthesis pathway. It was previously identified that PHGDH is frequently mutated in patients with MacTel. Characterizing common mutations in PHGDH expressed in MacTel patients can help us understand how enzyme function relates to disease. In this study, we characterized two common loss of function mutations in MacTel patients, E297X and G228W, that resulted in a premature stop codon and a single amino acid substitution, respectively. Based on existing structural and functional data, we hypothesize that these mutations in PHGDH may impact the oligomeric structure of the enzyme. To test this hypothesis, PHGDH variants were expressed in *E. coli* BL21 cells, purified via Ni-NTA resin, and collected for further assay development. This study lays the foundation for studying the relationship between enzymatic function and oligomeric state of PHGDH and how it is impacted by loss of function mutations.