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Inverted Solubility of the Pro 23 to Val Mutant of Human γD Crystallin– Altered Phase Diagram from a Single Amino Acid Substitution and the Effect of PEG J.J. MCMANUS, A. LOMAKIN, M. BASAN, O. OGUN, MIT, Department of Physics, CMSE and Materials Processing Centre, A. PANDE, J. PANDE, Dept. of Chemistry, SUNY, Albany., G.B. BENEDEK, MIT, Department of Physics, CMSE and Materials Processing Centre — Many genetic cataracts are the result of single point mutations in the amino acid sequence of lens crystallin proteins. The P23T mutation in human γD-crystallin (HGD) is associated with several different cataract phenotypes. The solubility of the protein shows an inverse temperature dependence. This is in contrast with the native protein. The replacement of Thr23 with a Ser or a Val residue shifts the location of the inverted solubility line to higher concentrations [1]. We describe the phase diagram of the P23V mutant of HGD, which exhibits aggregation, crystallization and liquid-liquid phase separation (LLPS). We have used QLS to probe the interactions of the protein in the soluble region of the phase diagram. We have developed a model to describe the observed retrograde solubility of the protein. Using PEG we introduce a so-called "depletion interaction" to further investigate the origin of the retrograde solubility. [1] A. Pande, O. Anunziata, N. Asherie, O. Ogun, G.B. Benedek, J. Pande, *Biochemistry* **44**, 2491-2500 (2005).

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