Folding stability analysis of FKBP12 by mutation of charged residues. JYOTICA BATRA, HUAN-XIANG ZHOU, Florida State University, Institute of Molecular Biophysics and Department of Physics — The folded conformation of a protein is stabilized by hydrophobic and electrostatic interactions. Our group has developed theoretical methods for calculating effects of charged residues on folding stability. To test these methods and to better understand electrostatic effects, we have carried out measurements of wild-type and charge-mutated variants of the 12 kD FK506-binding protein (FKBP12). The charge mutations were selected based on sequence comparison with a close homologue, FKBP12.6. The experimental results provide some support of theoretical calculations but also identify shortcomings for further improvement. We are in the process of generating a hyper-stable variant of FKBP12 by accumulating individual stabilizing substitutions with FKBP12.6.

Date submitted: 09 Aug 2005

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