**Visualizing chaperone-mediated G protein folding and disruption by disease-causing mutations using cryo-EM**

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Guanine nucleotide binding proteins (G proteins) mediate a myriad of signals from hormones, neurotransmitters, chemokines, and sensory molecules. To perform this function, G protein complexes must be assembled from their nascent subunits. Assembly is initiated by the folding of the G protein β subunit (Gβ) into its β-propeller structure by the cytosolic chaperonin CCT. CCT is an essential protein chaperone with diverse folding substrates, including many proteins with β-propeller domains. Mutations in Gβ disrupt folding by CCT, resulting in diseases such as neuropathies and retinopathies. We have determined cryo-EM structures of human CCT in the process of folding Gβ5, a component of Regulator of G protein Signaling (RGS) complexes responsible for turning off G protein signals (Wang et al. 2023 *Mol. Cell* **83**, 3852-3868). These structures define the folding trajectory of Gβ5 and allow us to visualize CCT-mediated protein folding at the molecular level. We have recently extended this work to solve structures of disease-causing Gβ5 mutants that pinpoint disruptions in the Gβ5 folding trajectory, revealing the molecular defects and paving the way for targeted therapies to correct the folding flaws and the resulting diseases.