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Core Mutations Switch Monomeric Protein GB1 into an Intertwined Tetramer

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The structure of a mutant immunoglobulin-binding B1 domain of streptococcal protein G (GB1), which comprises five conservative changes in hydrophobic core residues, was determined by NMR spectroscopy and X-ray crystallography. The oligomeric state and quaternary structure of the mutant protein are drastically changed from the wild type protein. The mutant structure consists of a symmetric tetramer, with intermolecular strand exchange involving all four units. Four of the five secondary structure elements present in the monomeric wild type GB1 structure are retained in the tetrameric structure, although their intra- and intermolecular interactions are altered. Our results demonstrate that through the acquisition of a moderate number of pivotal point mutations, proteins such as GB1 are able to undergo drastic structural changes, overcoming reduced stability of the monomeric unit by multimerization. The present structure is an illustrative example of how proteins exploit the breath of conformational space.

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