

Structures of Ric-8A, a G protein chaperone and activator

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Ric-8A is a 60 kDa protein expressed in the cytoplasm of multicellular eukaryotic cells. Unrelated to G protein-coupled receptors, Ric-8A has *in vitro* activity as a guanine nucleotide exchange factor. As such, Ric-8A catalyzes the release of GDP of GDP from the alpha subunits of heterotrimeric G proteins (Ga), forming a nucleotide-free Ga:Ric-8A complex. In the presence of GTP or non-hydrolyzable GP analogs, the complex dissociates, releasing Ga•GTP and Ric-8A. Ric-8A controls the cellular abundance of Ga by inhibiting its ubiquitination, and acting as a chaperone. The mechanisms by which Ric-8A carries out these essential activities are unknown.

We present structural data derived from SAXS and single crystal X-ray diffraction to define the structure of Ric-8A and its complex with Ga. We examine the significance of this solid-state and solution-phase structural information to results that we have published on the dynamics behavior of the Ga:Ric-8A complex from DEER spectroscopy and hydrogen-deuterium mass spectrometry.