Molecular Mechanisms for Cellular Protein Quality Control

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Cells have immensely crowded interiors and, to function successfully, they require quality control mechanisms to reorganise misplaced contents. The fate of hydrophobic proteins that have become exposed to the cytoplasm is decided by a collaboration between cochaperone SGTA (small, glutamine-rich, tetratricopeptide repeat protein alpha) and the BAG6 complex, whose operation relies on multiple transient and subtly discriminated interactions with diverse binding partners. These conspire to determine whether an exposed hydrophobic patch will be refolded by chaperones to safety within a protein's core, or delivered to an appropriate membrane or recycled via the ubiquitin/proteasome pathway. It seems these fates are under constant evaluation and can be changed or reversed in response to changing circumstances. I will present our latest structural and functional results on SGTA and its interactions (with an E3 ligase and a selection of hydrophobic substrates) using NMR spectroscopy and a range of complementary biophysical techniques such as Small Angle X-ray Scattering (SAXS), electron paramagnetic resonance (EPR) and native mass spectrometry.