have been shown to control MT dynamics by local influences on microtubule assembly and to be responsible for 'search-and-capture' of microtubule targets, such as the cell cortex and chromosomes. However, the molecular mechanisms by which +TIPs perform these functions are not clearly understood. +TIPs include structurally unrelated proteins such as EB1, cytoplasmic linker proteins (CLIPs), the dynein-dynactin complex. Here we report the crystal structure of the C-terminal zinc-binding motif of CLIP-170 in complex with the microtubule-binding (CAP-Gly) domain of p150 Glued solved by multiple-wavelength anomalous diffraction using the zinc atom. The structure reveals that CLIP-170 binds p150Glued via the same surface as another +TIP, EB1. Using biochemical and biophysical approaches, we investigated protein interactions involving CLIP-170 and found that an intramolecular interaction area overlaps with EB1- and microtubule-binding sites in an analogous manner to p150Glued.

Keywords: cytoskeleton, crystal structure, NMR

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Topological classification of protein

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Classification of the protein crystal structure is one of the important studies in molecular biology. SCOP [1], CATH [2], and FSSP [3] are known as some of the data base where the classification is based on the amino acid sequence, the secondary structure, and the protein structure. The classification of the graph with respect to the genus obtained by embedding the graph into two dimensional surface is a fundamental problem in the topological combinatorics. The genus is a measure to distinguish the graph complexity. The method is applied to classify the crystal [4]. One of the most interesting applications is the classification of RNA structure by the pseudo-knot [5]. In this study we apply the method to protein classification. The diagram of genus versus hydrogen-bond plot shows a rich structure. The fine structure of the motif can be distinguished well. In the classification of the protein mutant, which is defined as single or several amino-acid structural polymorphism, even the "zero amino-acid structural polymorphism" can be classified in several categories. In the analysis of the disulfide-bond formation facilitator (human), the data can fit well by the straight line in the diagram of genus versus hydrogen-bond plot. The result shows that the mutant can be classified further families. The method opens to construct the periodic table of protein.

[1] SCOP, http://scop.mrc-lmb.cam.ac.uk/scop.
[2] CATH, http://www.cathdb.info/latest/index.html.
[3] FSSP, http://www2.ebi.ac.uk/dali/fssp/fssp.html.
[4] M. Yamanaka and A. Tanaka, cond-mat/0510161.
[5] M. Bon, G. Vernizzi, H. Orland, and A. Zee, q-bio/060732.

Keywords: protein structure and folding, topological aspects of structure, biological macromolecules

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Structural insights into the mitochondrial import complex, TIM9.10

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Over 99% of human mitochondrial proteins are synthesised from nuclear DNA and must be imported as immature precursors *via* a coordinated series of specific, tightly regulated events. Encoded topological signals ensure nascent proteins are ushered to their correct mitochondrial destination. Proteins destined for the inner or outer mitochondrial membranes contain internal targeting information. After transfer through the outer membrane's general import pore, preproteins encounter TIM9.10, a hetero-hexamer of two homologous polypeptides, Tim9 and Tim10. TIM9.10 mediates preprotein passage across and within the intermembrane space. Inner membrane carrier proteins (*e.g.* metabolite carriers) are transferred to the inner membrane translocase, Tim22, for insertion, whereas β -barrel proteins of the outer membrane are transferred to the sorting and assembly machinery, SAM. We have determined the structure of the hTIM9.10 assembly to 3.5 Å resolution and can now verify key contacts in our 2.5 Å structure from *Saccharomyces cerevisiaea*. The molecular assembly has a unique α -propeller topology in which alternating Tim9 and Tim10 subunits alternate about a central pseudo-hexad. Each subunit of the hexamer has a helix-loop-helix topology, and a highly conserved twin CX3C motif present in both forms two intra-chain disulfides that define a central loop. The six loops come together to to form one face of the core assembly, below which tentacle-like helices emanate. Helical protrusions in the structures of other chaperones have been implicated in substrate binding so we are now combining structural and biochemical approaches to investigate chaperone-substrate interactions in our system.

Keywords: membrane trafficking, mitochondria, chaperone

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Structural basis for peroxisomal localization of tetrameric carbonyl reductase

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Peroxisomal matrix proteins are nuclear-encoded and synthesized in the cytosol. There are two well-characterized classes of peroxisome targeting signals (PTS), known as PTS1 and PTS2. Proteins carrying one of these signals are recognized in the cytosol by soluble PTS receptors, Pex5p for PTS1 and Pex7p for PTS2. The PTS1 is a carboxy-terminal sequence ending in the tripeptide Ser-Lys-Leu (SKL) or some conservative variant. All proteins bearing the PTS1 do not undergo cleavage of the targeting sequence upon transport into the peroxisome. Pig heart peroxisomal carbonyl reductase (PerCR) is a 100 kDa homotetrameric enzyme and exhibits NADPH-linked reductase activity towards alkyl phenyl ketones, alpha-dicarbonyl compounds, and all-trans-retinal. It belongs to the short-chain dehydrogenase/reductase (SDR) family, and its sequence comprises a C-terminal SRL tripeptide, which is a variant of the PTS1, SKL. PerCR is imported into peroxisomes of HeLa cells when the cells are transfected with vectors expressing the enzyme.