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The complement system is a critical component of the mammalian immune defense against micro-organisms in plasma that links the innate and adaptive immune responses. It consists of >30 plasma proteins and cell-surface receptors. The three different pathways of activation converge in the activation of complement component C3. C3 is a 190 kDa plasma protein that, together with complement components C4 and C5, belongs to the α2-Macroglobulin family. C3 undergoes a series of proteolytic activation and degradation steps and interacts with several regulators of complement. Here we present the structure of a naturally occurring, proteolytic product of C3, called C3c, which constitutes ¾ of the total protein. This structure provides insight into C3 and its binding sites and provides the first insight into the core fold of the α2-Macroglobulin protein family.

The C3c structure shows a surprising domain composition and reveals that the two, β and α, polypeptide chains of mature C3 are heavily intertwined. The core of the protein consists of 8 homologous domains, which we refer to as macroglobulin (MG) domains. The domains display a fibronection type-3 (FN3) like fold but have no sequence homology and lack the FN3-motif.

The multi-domain structure, its potential domain-domain flexibility and the implications for complement activation and convertase formation will be discussed.

Keywords: immunology, complement, plasma proteins

MS72 HOT STRUCTURES IN PROTEIN CRYSTALLOGRAPHY
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Structural Studies on Carboxysomes
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Carboxysomes are microcompartments found in autotrophic bacteria; they function to sequester RuBisCO for optimal carbon fixation. Carboxysomes are essentially primitive organelles, composed entirely of protein. Genomic sequencing is revealing the surprisingly wide distribution of proteinaceous organelles that are structurally related to the carboxysome. In order to understand principles of carboxysome assembly and function, we have undertaken EM and crystallographic analyses of the carboxysome and its isolated component proteins and enzymes. We have determined the structures of two of the carboxysome shell components. Our data provide the first molecular details of carboxysome structure and assembly that show striking parallels to principles of viral architecture. Our data also provide insights into the structural basis of function, including import and export of substrate and products.

Keywords: carbon-fixation, biological macromolecules, organelle assembly

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Structure and Function of RNase E and the RNA Degradosome Assembly
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The essential enzyme RNase E is critical to RNA processing and decay regulation in *Escherichia coli*. The activity of RNase E affects the balance and composition of the transcript population, and the enzyme serves as the scaffold for a multi-component assembly known as the RNA degradosome. RNase E belongs to a widely occurring family of ribonucleases that cleave RNA internally, but whose catalytic power is determined by the 5'-terminus of the substrate, even if this lies at a distance from the cutting site. We report crystal structures of the catalytic domain of RNase E as trapped allosteric intermediates with RNA substrates. The structures explain why a tetrameric quaternary structure is required for activity, and how the recognition of the 5' terminus of the substrate triggers a conformational transition to initiate catalysis. The structure also sheds light on the question of how RNase E might selectively process, rather than destroy, specific RNA precursors. We have also solved the crystal structures of two other components of the degradosome (enolase and polynucleotide phosphorylase), and the cognate complex of enolase with a recognition site from RNase E. These structural data are used to propose a model for the organization and function of the RNA degradosome.

Keywords: gene regulation, RNA processing and decay, ribonuclease

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Crystal Structures of Proteins Involved in Membrane Traffic
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Membrane traffic plays crucial roles in cell functions such as post-translational modification of newly synthesized proteins, exocytosis and endocytosis, receptor recycling, autophagy and lipid transport. Vesicle transport mediates many of these trafficking events using an intricate network of protein-protein interactions of coat proteins, adaptor proteins (AP), cargo receptors, SNARE complexes, small GTPases, ubiquitin and various accessory proteins. I will present our most recent structures of proteins involved in membrane trafficking of proteins and lipids between different organelles: the endoplasmic reticulum, the trans-Golgi Network, endosomes and lysosomes. First, double-sided recognition of ubiquitin molecules by several adaptor proteins will be presented as a recurring structural motif, from the examples of the ubiquitin interacting motif (UIM) of Hrs (hepatocyte growth factor-regulated tyrosine kinase substrate), and the GAT domain of GGA (Golgi-localizing, γ-adaptin ear domain homology, ARF-binding) and others. Second, structures of proteins involved in the first phase of vesicle budding from the ER; a guanine nucleotide exchange factor, small GTPases, and cargo receptors such as yeast Emp46p and Emp47p will be described using examples selected from yeast and plant proteins.

Keywords: X-ray protein crystallography, protein transport, membrane traffic

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The Structure of a Mitochondrial Peptidasome
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The pitrilysin endometalloproteases perform an essential molecular scavenger function in the cell by removing potentially harmful peptides. Especially the insulin-degrading enzyme (IDE) has obtained much attention, in part due to IDE's ability to degrade the degenerative amyloid-ß peptide associated with Alzheimer's disease. Presequence protease (PreP) is an organellar homologue to IDE and was recently identified as a protease responsible for the degradation of targeting peptides in both mitochondria and chloroplasts. The ability of PreP to degrade small, unfolded peptides in mitochondria is of particular interest in light of recent findings, which link amyloid-ß to the mitochondrial toxicity associated with Alzheimer's disease.

The 2.1Å resolution crystal structure of PreP from *Arabidopsis thaliana* represents the first structure from the pitrilysin protease family. The 995-residue polypeptide forms an enclosed chamber of