Raaijmakers[a], Anja Roos[b], Moh R. Daha[b], [a]*Dept Crystal and Structural Chemistry, Utrecht University, The Netherlands.* [b]*Dept Nephrology, Leiden University Medical Center, Leiden University, The Netherlands.* E-mail: p.gros@chem.uu.nl

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
Chairpersons: Glaucius Oliva, Andrew H.-J. Wang

MS72.29.1
Acta Cryst. (2005). A**61**, C92
Structural Studies on Carboxysomes
Cheryl A. Kerfeld, Michael R. Sawaya, Shiho Tanaka, Morgan Beeby, Janel Laidman and Todd O. Yeates, *Molecular Biology Institute, UCLA, Box 951570 Los Angeles, CA 90095-1570.* E-mail: Kerfeld@mbi.ucla.edu

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
Maria Jose Marcaida[a], Anastasia Callaghan[a], Walter Scott[b], Martyn Symmons[a], Vidya Chandran[a], Kenneth McDowall[c], Jonathan Stead[c], Ben Luisi[a], [a]*University of Cambridge, Department of Biochemistry, 80 Tennis Court Road, Cambridge CB2 1GA, U.K.* [b]*Department of Chemistry and Biochemistry, University of California at Santa Cruz, Santa Cruz, CA, U.S.A.* [c] *Astbury Centre for Structural Molecular Biology, University of Leeds, Leeds, LL57 2UW, U.K.* E-mail: ben@cryst.bioc.cam.ac.uk

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
Soichi Wakatsuki, *Photon Factory, Institute of Materials Structure Science, High Energy Accelerator Research Organization (KEK). Japan.* E-mail: soichi.wakatsuki@kek.jp

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

MS72.29.4
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The Structure of a Mitochondrial Peptidasome
Therese Eneqvist, Kenneth A. Johnson, *Department of Biochemistry and Biophysics, Stockholm University, Stockholm, Sweden.* E-mail: eneqvist@dbb.su.se

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

more than 10,000Å^3 that shields the proteolytic site. The fact that proteolysis occurs inside a closed chamber is reminiscent of the proteasome structure and for that reason we introduced a new term: the peptidasome. The chamber has no obvious opening for the substrate to enter; yet a bound peptide is found inside and amino acids separated by almost 800 residues in sequence form the active site. The structure suggests a novel mechanism for access to the active site, involving hinge-bending motions that cause the peptidasome to open and close in response to substrate binding.

Keywords: crystallographic structure, peptide degradation, metalloproteinases

MS72.29.5

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Molecular Machines and Tropical Pathogens

Wim Hol, Junpeng Deng, Jan Abendroth, Daniel Mitchell, Marissa Yanez, Claudia Roach, Brian Krumm, Stewart Turley, *Dept of Biochemistry and HHMI, University of Washington, Seattle, WA USA.* E-mail: wghol@u.washington.edu

The "Type 2 Secretion System" (T2SS) from Vibrio cholerae, enterotoxigenic E. coli (ETEC) and related pathogens is responsible for secreting proteins like cholera toxin (CT) and heat-labile enterotoxin (LT). The T2SS consists of 14-16 different proteins, and spans the inner as well as the outer membrane. We have expressed many components of the T2SS from several bacteria including soluble proteins, integral membrane proteins and multi-protein complexes. Several crystal structures have been elucidated which gives initial insight into the architecture of the inner membrane subcomplex.

The editosome is essential for Trypanosomatids, which are causative agents of sleeping sickness, Chagas' disease and leishmaniasis. For several mitochondrial proteins the pre-mRNA needs to be edited substantially. The editing information is encoded in numerous small "guide RNAs" which are used by the "editosome" to create a mature messenger. The editosome consists of over a dozen different proteins. The structures of editosome ligase and TUTase provide the first views of parts of this complex machinery.

Keywords: type II secretion, RNA editing, tropical disease

MS73 MOLECULAR CRYSTALS WITH NOVEL PHYSICAL PROPERTIES

Chairpersons: Catalina Ruiz-Perez, Annie Powell

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New Synthetic Approaches Towards Supramolecular Multimetallic Systems with Interesting Magnetic Properties

Marius Andruh, *University of Bucharest, Faculty of Chemistry, Inorganic Chemistry Laboratory, Str. Dumbrava Rosie nr. 23, 020464-Bucharest, Romania,* E-mail: marius.andruh@dnt.ro

The search for new synthetic routes leading to solid-state architectures with pre-established functions and properties is the heart of crystal engineering. In the last 15 years or so, chemists learned a lot in manipulating the intermolecular forces, in order to design crystalline compounds with useful properties

We are currently developing a synthetic approach aiming at obtaining multimetallic complexes, which is based on the employment of homo- and heterobinuclear complexes as nodes. The following types of cationic species are used: (i) binuclear copper(II) species with end-off compartmental Schiff-base ligands; (ii) alkoxo-bridged copper(II) species; (iii) heterobinuclear 3d-3d' species with macrocyclic compartmental ligands;(iv) heterobinuclear 3d-4f species with side-off compartmental Schiff-base ligands. When the metallic ions are different and paramagnetic, the intra-node exchange interactions, as well as those between the resulting spins may lead to interesting magnetic properties. A particular case is the one concerning the 3d-4f binuclear nodes. The building principle is based on the employment of symmetrical (dicarboxylato anions, bis(4-pyridyl) derivatives) or of unsymmetrical spacers (e. g. the isonicotinate anion), which act selectively with the different (3d, 4f) metal ions.

Keywords: coordination chemistry compounds, coordination crystal engineering, magnetic exchange

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High Spin and Photomagnetic High Spin Molecules

Valérie Marvaud, *Laboratoire de Chimie Inorganique et Matériaux Moléculaires UPMC, Case 42, 4 place Jussieu, 75 252 Paris Cedex 05, France.* E-mail: marvaud@ccr.jussieu..fr

As part of our research activities devoted to molecular magnetism, we are interested in synthesising polynuclear compounds showing both large spin ground state and anisotropy. For this purpose, polycyanometalate precursors have been used successfully, with an effective control of the chemistry, which consist to firstly prepare polydentate ligands and their corresponding mononuclear complexes with varied metallic centre such as Mn^{II}, Ni^{II}, Co^{II}, Cu^{II}, before synthesising polynuclear compounds with tunable geometry. Thus, bi-, tri-, tetra-, hexa- and heptanuclear species have been obtained in this way with a spin state value ranging from 3/2 to 27/2.

The step by step rational synthesis allows us to synthesize as well hetero-trimetallic complexes such as CrNi2Mn4 (S=13/2) and several polynuclear species obtained from octacyanometalate precusors, for instance WCu6, WNi6 and WMn6 and the corresponding molybdenium species.

This part of the work devoted to octacyanometalate chemistry paves the way of photomagnetic Single Molecule Magnets. We already succeeded in getting the first photomagnetic high spin molecule !

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Keywords: molecular magnets, photochemistry, cyanide complex

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Crystal Structure-Mobility Correlation in TTF Based Organic Field-Effect Transistors

Concepció Rovira[a], Marta Mas-Torrent[a], Peter Hadley[b], Stefan T. Bromley[c], Jaume Veciana[a], [a]*ICMAB-CSIC, Bellaterra, Spain.* [b]*DUT, Delft, Netherlands.* [c]*UB, Barcelona, Sapin.* E-mail: cun@icmab.es

Organic Field Effect Transistors (OFETs) have attracted a great deal of interest over the last few years due to their unique processing characteristics and improved electronic mobility. The fundamental material characteristics of organic semiconductors are most clearly measured in single-crystals, but very few have been studied.

Recently, we have reported that crystals of the organic material dithiophene-tetrathiafulvalene (DT-TTF) have a high field-effect charge carrier mobility of 1.4 cm^2/Vs. [1] These crystals were formed by a simple drop casting method, making this material interesting to investigate for possible applications in low cost electronics.

Here, organic single-crystal field-effect transistors (OFETs) based on materials related to DT-TTF are presented and a clear correlation between the crystal structure and the electrical characteristics is observed.[2] The observed relationship between the mobilities in the different crystal structures is strongly corroborated by calculations of both the molecular reorganization energies and the maximum intermolecular transfer integrals.[2,3]

Interestingly, the most suitable materials described here exhibit mobilities among the highest reported for OFETs, and are the highest reported for solution-processed materials. [2,4]

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Keywords: OFETs, TTF derivatives, functional materials