has been performed and will be highlighted during presentation. The crystals just have been shipped to BM-14 beam line at France and results obtained will be elaborated during presentation. The structure studies of BRCA1 (1560-1859) will help in understanding the pathogenicity of mutations which may provide very important information for predisposing someone at the high risk of cancer.

Keywords: BRCA1, transactivation domain.

MS01.P20

Acta Cryst. (2011) A**67,** C222

The crystal structure of TBC domain of human GapCenA

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In eukaryotic cells, the centrosome serves as a main microtubule organizing centre and plays a key role in one of the most important process in biology, the cell division. It is composed of two orthogonally arranged centrioles surrounded by an amorphous mass of proteins termed the pericentriolar material. Despite its importance, little is known about its precise molecular structure. The ultimate goal of the Centrosome 3D project is to gain a better structural understanding of the centrosome function and its relation to a series of human pathologies including Parkinson and Huntington, Bardet–Biedl syndrome, development of cystic kidneys, and most notably, cancer.

GapCenA (RabGap1) is one of the centrosome associated protein, it activates the small GTPases, regulators of membrane trafficking and receptor localization in eucariotic cells. The human genome encodes at least 70 Rab GTPases and more than 50 putative Rab GTPase-activating proteins (GAPs). GapCenA is composed of 1069 amino-acid residues, contains PID (phosphotyrosine interaction domain) and TBC (Tre-2/Bub2/Cdc16) domains, as well as long coiled-coli C-terminal tail. After testing a number of different constructs of GapCenA we have managed to crystallize and determine the structure of the TBC domain to the resolution of 1.85 Å.

Keywords: biocrystallography, protein, X-ray_structure

MS01.P21

Acta Cryst. (2011) A**67,** C222

Expression, Purification, Crystallization and preliminar X-ray crystallographic analysis of Human Malonyl Coa Decarboxylase

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Malonyl Coa Decarboxylase (MCD), which catalyses the conversion of malonyl coa to acetyl coa, plays an important role in the pathways of the novo fatty acid biosynthesis and fatty acid oxidation. Malonyl coa is an allosteric inhibitor of Carnitine Palmitoyltransferase 1, the enzyme that normally control the flux throw the mitochondrial β-oxidation. In order to provide structural and function evidences of the molecular mechanism of malonyl coa decarboxylation, we have overexpressed and crystallized human MCD. The crystals belongs to the triclinic P1 space group with a unit cell a = 79.55 b = 103.58 c = 134.23 α = 95.40 β = 90.11 γ = 94.82. The self rotation function shows binary axes at 90º from each others which would agree with a tetramer in the crystal asymmetric unit, having D2 symmetry and a volume solvent content of about 75%. Structure determination (with phases obtained from selenomethionine derivative collected at the ESRF Grenoble) are in progress.

Keywords: malonyl coa decarboxylase, malonyl coa, fatty acids

MS01.P22

Acta Cryst. (2011) A**67,** C222

The crystal structure of the p27 component of human dynactin

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Dynactin, (or dynein activator), is a 1.2 MDa complex essential for the most aspects of cellular function of dynein in eukaryotic cells [1]. Dynein, a retrograde microtubule-based molecular motor, is not only essential for intracellular transport, but is also required for mitosis and for cell viability. Inhibition or depletion of dynactin, its partner complex, leads to loss of dynein function. Dynactin contains eleven different polypeptide chains, and the structure of most is either known or can be inferred from homologous proteins. However, the structure of the so-called pointed-end complex remains an enigma, although it is thought to participate in interactions with membranous cargo. Two components of this complex, the p25 and p27 proteins, show unique amino acid sequence features that suggest an unusual left-handed β-helix fold, so far seen in several prokaryotic enzymes [2]

We here report the crystal structure of human p27 protein determined to 2.15 Å resolution. The structure was successfully solved in the automated Molecular Replacement pipeline BALBES [3] even there is very limited amino acid sequence similarity of p27 to any of the structures in the PDB. As expected, the main domain displays a tertiary fold of the left-handed parallel β-helix (LβH) structural motif, encoded by the 'hexapeptide repeat' amino acid sequence motif.

The parallel β-helix is a highly repetitive fold, made up of parallel β-strands connected by turns or loops. Those structures coil up to form helical 'rungs'. The structure is stabilized mainly by interstrand hydrogen bonds. Each rung of the β-helix has 2 to 3 untwisted parallel β-strands interrupted by a loop region or one to two turns. The helical rungs are aligned and form a cross-β structure. In this form β-strands are linked by hydrogen bonds and are parallel to the axis of helix. This repetitive motif creates a hydrophobic core of a cylindrical shape. In the β-helix, the strands are almost planar, the surfaces of a helix are nearly flat, all of which results in forming a triangular prism shape.

The p27 protein represents the only one in the human proteome with the β-helix fold, although p25 is expected to be structurally related. The only other similar protein in any eukaryotic proteome is an antifreeze protein from spruce budworm, although it represents type I of LβH, and consists of five residues per strand (15 per rung), rather than six, as found in the p27 structure. There is a homodimer in the asymmetric unit of the p27 crystal, and its quaternary structure strongly suggests that the mutual disposition of the two molecules is representative of the structure of the p25/p27 heterodimer found in dynactin.

We hope that the three-dimensional model will assist in studies intended to unravel the details of interaction of dynactin with cargo particles.

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Keywords: dynactin, beta-helix fold, automated molecular replacement