

carbohydrate recognition domains, locating both sugar binding sites face to face. Sequence evidence suggests other tandem-repeat galectins have the same arrangement. We show that the galectin domain binds carbohydrates containing lactose and N-acetyl-lactosamine units, and we present structures of the galectin domain with lactose, N-acetyl-lactosamine, 3-aminopropyl-lacto-N-neotetraose, and 2-aminoethyl-tri(N-acetyl-lactosamine), confirming the domain as a bona fide galectin domain.

Bacteriophages are the most numerous organisms in the biosphere. In spite of their biological significance and the spectrum of potential applications, little high-resolution structural detail is available on their receptor-binding fibres. We present the crystal structure of the receptor-binding tip of the bacteriophage T4 long tail fibre, which is highly homologous to the tip of the bacteriophage lambda side tail fibres. This structure reveals an unusual elongated six-stranded anti-parallel beta-strand needle domain containing seven iron ions coordinated by histidine residues arranged co-linearly along the core of the biological unit. At the end of the tip, the three chains intertwine forming a broader head domain, which contains the putative receptor interaction site. The structure reveals a previously unknown beta-structured fibrous fold, provides insights into the remarkable stability of the fibre, and suggests a framework for mutations to expand or modulate receptor-binding specificity.

Keywords: host cell attachment, beta-structure, tandem-repeat galectin

MS.29.3

Acta Cryst. (2011) A67, C76

The cell fusion proteins of the “FF” family are homologous to class II viral fusion proteins

Félix A. Rey,^a Jimena Perez-Vargas,^a Thomas Krey,^a Benjamin Podbilewicz,^b ^a*Institut Pasteur, CNRS URA 3015, Unité de Virologie Structurale, 75015, Paris, (France).* ^b*Department of Biology, Technion - Israel Institute of Technology, Haifa, 32000, (Israel).* E-mail: rey@pasteur.fr

Structural studies of viral membrane fusion proteins have provided key information to understand the process of virus-cell membrane fusion, which is important during virus entry. Similar principles were inferred from structural studies of SNARE proteins, responsible for fusion of intracellular vesicles with their target membranes within the cell. No data are currently available on cellular fusion proteins responsible for cell-cell fusion, a process that is of high relevance during developmental biology and organogenesis.

We report here the crystal structure of a cell fusion protein from the nematode *C. elegans*, termed “Eff-1”, where it plays a key role during organogenesis. This protein is the prototype of the “Fusion Family” (FF) of proteins recently described. The structure provides unanticipated evolutionary links with the class II viral fusion proteins observed in regular enveloped viruses. Eff-1 folds as three beta-sheet-rich domains, assembled as a trimer organized as in the post-fusion structures of the alphaviruses and flaviviruses envelope proteins. This type of fusion proteins had so far been observed only in regular envelope viruses, where they make an icosahedral coat completely enclosing the viral membrane in their pre-fusion form. This presentation will describe the structure and provide a model for its putative mechanism of action.

Keywords: cell-cell fusion, developmental biology, structural biology, class II viral fusion proteins

MS.29.4

Acta Cryst. (2011) A67, C76

Structural basis for the inhibition of apoptosis by Epstein-Barr virus BHRF1

Marc Kvensakul,^{a,b} Andrew H Wei,^b Jamie I Fletcher,^b Simon N Willis,^b Lin Chen,^b Andrew W Roberts,^b David CS Huang,^b Peter M Colman,^b ^a*La Trobe Institute of Molecular Sciences, La Trobe University, Melbourne, Victoria, (Australia).* ^b*The Walter & Eliza Hall Institute of Medical Research, Parkville, Victoria, (Australia).* E-mail: m.kvensakul@latrobe.edu.au

Viruses must evade host apoptotic defences to ensure their own survival. Despite the complexity of mammalian cell death processes, viruses have evolved successful mechanisms for subverting the apoptotic machinery, including homologs of the mammalian pro-survival protein Bcl-2. The ubiquitous Epstein-Barr virus (EBV), a member of the gamma-herpesviruses, infects the epithelium of the oropharynx and resting B cells. Acute infection manifests as infectious mononucleosis or glandular fever, whereas chronic EBV-associated transformation is associated with Burkitt’s lymphoma, Hodgkin’s disease and nasopharyngeal carcinoma. EBV BHRF1 is a sequence, structural and functional homologue of Bcl-2, however its mechanism of action remained unclear. Previous structural studies indicated that BHRF1 lacks an accessible BH3 binding groove, and shows only weak affinity for BH3 ligands. We show that BHRF1 is a potent inhibitor of apoptosis, and confers chemoresistance in mouse lymphoma models similar to mammalian Bcl-2. Next, we determined the crystal structures of BHRF1 in complex with Bim and Bak BH3 peptides and show that in contrast to previous predictions, BHRF1 interacts with these proteins in a manner similar to its mammalian counterparts. Structure-based mutagenesis enabled us to address the molecular mechanisms underlying BHRF1 activity. We demonstrate that BHRF1 can prevent Bak activation by direct interaction, but prevents Bax activation indirectly by sequestering the BH3-only proteins Bim, Puma and tBid. Unlike mammalian pro-survival proteins, BHRF1 does not interact with the selective/sensitizer BH3-only proteins. These studies indicate that BHRF1 might be targeted by small molecule mimetics of BH3-only proteins.

[1] M. Kvensakul, A.H. Wei, J.I. Fletcher, S.N. Willis, A.W. Roberts, D.C. Huang, P.M. Colman, *PLoS Pathogens* **2010**, *6*(12):e1001236.

Keywords: viral, cancer

MS.29.5

Acta Cryst. (2011) A67, C76-C77

Crystal structure of the N-terminal domain of HIV-1 capsid in complex with an assembly-inhibiting nanobody

LuisCastillo,^a JonasHelma,^b PabloGuardado,^c UlrichRothbauer,^b Felix Rey,^c Heirich Leonhardt,^b Hans-Georg Kräusslich,^a ^a*Department of Infectious Diseases, Virology, Universitätsklinikum, Heidelberg, (Germany).* ^b*Biozentrum, Ludwig Maximilians Universität, München, (Germany).* ^c*Unité de Virologie Structurale, Institut Pasteur, Paris, (France).* E-mail: luis.castillo@med.uni-heidelberg.de

HIV-1 maturation from a non-infectious into an infectious agent is accompanied by morphological changes in its capsid shell, which undergoes a protease-mediated conversion from a spherical into a conical shape; therefore capsid assembly is a target for development of antiviral drugs. Here we report the crystal structure at 2.0 Å resolution of the N-terminal domain of HIV-1 capsid in complex with a nanobody capable of inhibiting mature and immature particles in vitro.