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Structure and Assembly of a Bacterial Type IV Secretion Core Complex. Remi Fronzes[a], Gabriel Waksman[a]. [a]*Institute of Structural and Molecular Biology, Birkbeck and UCL, Malet Street, London, WC1E 7HX, United Kingdom.*
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Type IV secretion systems (T4SSs) are molecular machines used for the transport of macromolecules across the bacterial cell envelope in Gram-negative bacteria. T4SSs are highly versatile. Conjugative T4SSs translocate DNA from a donor to a recipient bacterium and contribute to bacterial genome plasticity, spread of antibiotic resistance or other virulence trait among bacterial pathogens. In some bacteria such as *Helicobacter pylori* (Cag PI), *Brucella suis* (VirB/D), or *Legionella pneumophila* (Dot, Icm), T4SSs are directly involved in pathogenicity as they mediate the secretion of virulence factors (DNA or toxins) into host cells. The archetypal T4SS, the VirB/D system, was defined in *Agrobacterium tumefaciens* where it is naturally responsible for the delivery of the T-DNA to the plant host-cell. The *A. tumefasciens* VirB/D system comprises 12 proteins (VirB1 to 11 and VirD4). In the past few years, atomic structures of isolated components such as VirD4, VirB11, VirB5, virB8, virB10 and virB9 have become available and have provided seminal insights into the mechanism of T4SS assembly and substrate secretion. However, no structural data was available concerning the assembly of the complex, particularly at the level of both bacterial membranes where the T4SS is supposed to form pores/channels. We here present the cryoEM structure of a 1 MDa complex composed of VirB7, VirB9 and VirB10 homologues from the *E. coli* conjugative plasmid pKM101 T4SS. The molecular characterization of this ternary complex provides key insights into the type IV secretion systems architecture and assembly

[1] Fronzes R., Schaefer E., Saibil H., Orlova E. and Waksman G., *Science*, **2009**, 323, 266.

Keywords: secretion systems; type IV secretion; structure

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Structure of the Catalytic Subunit of Telomerase; a Major Target for Cancer and Aging Therapies. Andrew Gillis[a], Anthony Schuller[a], Emmanuel Skordalakes[a]. [a]*The Wistar Institute, 3601 Spruce St, Philadelphia, PA 19104, USA.*
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A common hallmark of human cancers is the overexpression of telomerase, a ribonulceoprotein complex responsible for maintaining the length and integrity of chromosome ends. Telomere length deregulation and telomerase activation is an early and perhaps necessary step in cancer cell evolution. In fact ~90% of human tumors show high levels of telomerase activity when it is dormant in most somatic cells. Efforts to elucidate in detail the complex mechanism of telomere replication by telomerase as well as attempts to discover cancer and aging therapies that target this enzyme have been hindered to a certain extend by the absence of structural information. We recently determined the high-resolution structure of the catalytic subunit of telomerase from *Tribolium castaneum [1]*. The structure reveals a number of novel and unexpected results that greatly enhance our understanding of telomerase action on telomeres. The protein consists of four highly conserved domains, organized into a ring-like structure that shares common features with retroviral reverse transcriptases, viral RNA polymerases and to a certain extend bacteriophage, B-family DNA polymerases. Domain organization places motifs implicated in substrate binding and catalysis in the interior of the ring, which can accommodate seven-to-eight bases of double stranded nucleic acid. Modeling of an RNA/DNA heteroduplex in the interior of this ring reveals a perfect fit between the protein and the nucleic acid substrate and positions the 3'-end of the DNA primer at the active site of the enzyme providing some evidence for the formation of an active telomerase elongation complex.

[1] Gillis, A.J., A.P. Schuller, and E. Skordalakes, *TERT. Nature*, **2008**. 455(7213): p. 633-7.

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Structural Studies of Candida Albicans Pathogenicity Factors: ALS Adhesins Family. Paula S. Salgado[a], Robert Yan[a], Lois Hoyer[b], Emesto Cota[a]. [a]*Division of Molecular Bioscience, Imperial College London, London, UK.* [b]*Department of Pathobiology, University of Illinois at Urbana-Champaign, Urbana, Illinois, USA.*
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Adherence to host cells is one of the key determinants of pathogenesis, yet limited information has been published on the structure and mechanism of fungal adhesins. C. albicans is a common human commensal that can cause a range of infections, from skin/mucosal 'thrush' to severe systemic candidiasis. The ALS family of surface glycoproteins is sufficient to confer key adhesive properties. These adhesins are able to bind a broad range of targets in host cell surfaces and the extracellular matrix [1, 2]. Moreover, they bind to small peptides and unstructured regions in folded domains in a stable, reversible and specific manner [3]. This seems to confer C. albicans with a unique mode of binding, eliminating the need of specific surface complementarity, as observed in most pathogen/host cell interactions. ALS adhesins consist of 3 domains: ~30kDa N-terminal, central Thr-rich domain with a variable number of 38aa repeats and a STN-rich membrane-anchoring C-terminal of variable length [4]. The N-terminal is proposed to be sufficient for adhesion and is, therefore, a possible target for new therapeutic strategies. Preliminary NMR data from NT-ALS1 reveals an IgG superfamily secondary structure topology, identical to that of the fibrinogen-binding regions