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## Cholesterol-Dependent Cytolysins: from Water-Soluble State to Membrane Pore

Friday, 23 November 2018 12:00 (30 minutes)

Cholesterol-dependent cytolysins (CDCs) are a family of pore-forming toxins that punch holes in the outer membrane of eukaryotic cells. The CDCs exhibit a number of unique features amongst pore-forming toxins including an absolute dependence on the presence of cholesterol-rich membranes for their activity and the formation of oligomeric transmembrane pores greater than 150 Å in diameter. The first crystal structure of a CDC was that of perfringolysin O [1] and most of our understanding of CDC function is based on studies of this toxin [2-4]. We have subsequently determined structures of other family members that have confirmed that the 3D fold first seen in PFO is shared by all family members [5-9]. We have determined a number of CDC structures which are providing valuable insights into the role of receptor binding, oligomerisation and prepore assembly [8,9]. The conversion from water-soluble monomer to pore is highly complex: it is essential that the pore does not form prematurely otherwise the target cell won't be successfully breached [10]. The crystal structures of the water-soluble states of these toxins, together with cryo-electron microscopy, small angle X-ray scattering data, fluorescence spectroscopy and molecular dynamics simulations have proved very useful for modelling their membrane pores.

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