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

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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.

[1] J. Rossjohn et al., Cell 89, 685 (1997).
[2] O. Shatursky et al., Cell 99, 293 (1999).
[3] R.J. Gilbert et al., Cell 97, 647 (1999).
[4] M.P. Christie et al., Biophys. Revs., in press (2018)
[5] G. Polekhina et al., PNAS 102, 600 (2005).
[6] S.C. Feil et al., Structure 20, 248 (2012).
[7] S.C. Feil et al., J. Mol. Biol. 426, 785 (2014).
[8] S.L. Lawrence et al., Sci. Reps. 5, 14352 (2015).
[9] S.L. Lawrence et al., Structure 5, 1488 (2016).
[10] K.R. Wade et al., Proc. Natl., Acad. Sci. 112, 2204 (2015).

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