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Structural Studies of Streptolysin O from *Streptococcus pyogenes*

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Cholesterol-dependent cytolysins (CDCs) constitute a family of bacterial toxins that form pores in many cell types. CDCs are secreted as water-soluble monomers, bind to cholesterol-rich membranes, oligomerise and insert into cell membranes. The presence of membrane cholesterol is required for the formation of large pores in cell membranes. In order to convert from a soluble monomeric protein into a membrane pore conformational changes of the three-dimensional structures of these toxins have to occur. Here, we present the three-dimensional structure of streptolysin O (SLO) from *Streptococcus pyogenes*. Comparison with other CDCs structures shows that the overall fold is similar but the C-terminal domain exhibits a different orientation with respect to the rest of the molecule. Additionally, the highly conserved region called the undecapeptide motif, which is involved in membrane recognition, adopts a different conformation in SLO compared to perfringolysin O (PFO), although the sequences in this region between the two toxins are identical.

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