Structural Analysis of *Listeria* Neutral Sphingomyelinase (SmcL)

Amy EA Openshaw[a], Paul R Race[a], Héctor Monzó[b], José A Vázquez-Boland[b], Mark J Banfield[a], *[a]ICaMB, Medical Sciences, Framlington Place, University of Newcastle, Newcastle-upon-Tyne, NE2 4HH. UK. [b]Veterinary Molecular Microbiology Section, University of Bristol, Langford, Bristol, BS40 5DU. UK.* E-mail: a.e.a.openshaw@ncl.ac.uk

Pathogenic *Listeria* secrete phospholipases that help mediate disruption of phagocytic vacuoles, promoting bacterial intracellular replication. One of these enzymes, SmcL from *Listeria ivanovii*, is a member of the family of Mg^{2+}-dependent neutral sphingomyelinases (nSMases). These enzymes disrupt membranes by catalysing the hydrolysis of sphingomyelin (SM) to ceramide and phosphocholine. SmcL shares >50% identity with *S. aureus* nSMase (β-toxin) [1] and shows distant sequence homology to mammalian nSMases. In humans and other mammals, ceramide generation by SMases initiates a signalling pathway implicated in a number of important cellular responses including apoptosis, the stress-response, cell differentiation and cell proliferation. All the members of the nSMase family, whether bacterial or eukaryotic, appear to have a conserved active site, and likely a conserved overall fold [2].

Single crystals of *Listeria ivanovii* SmcL are available. These crystals diffract X-rays to >1.8 Å at synchrotron radiation sources and display trigonal symmetry (space group $P3_{1/2}21$). Detailed analysis of the SmcL structure will provide details of an enzymatic mechanism with relevance to bacterial pathogenesis and the understanding of mammalian cell signalling.

[1] Gonzalez-Zorn B. *et al.*, Vazquez-Boland J.A., *Mol. Microbiol*. 1999, **33**, 510. [2] Rodrigues-Lima F., *J. Biol. Chem*., 2000, **275**, 28316.

Keywords: bacterial pathogenesis, cell signalling, phospholipase