

Microsymposium

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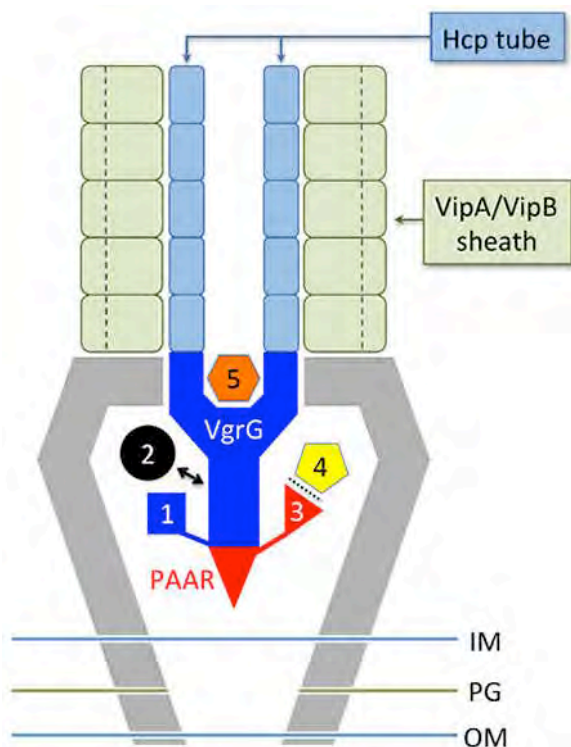
Central spike proteins of contractile ejection systems

M. Shneider^{1,2}, S. Buth¹, B. Ho³, M. Basler³, J. Mekalanos³, P. Leiman¹

¹Ecole Polytechnique Federale de Lausanne (EPFL), Institute of Physics of Biological Systems, Lausanne, Switzerland, ²Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Laboratory of Molecular Bioengineering, Moscow, Russia, ³Harvard Medical School, Department of Microbiology and Immunobiology, Boston, USA

Contractile tails of bacteriophages and related systems - R-type pyocins, the *Serratia entomophila* antifeeding prophage, the Photorhabdus Virulence Cassette, and the Type VI Secretion System (T6SS) - contain a special spike-shaped protein complex, which is involved in breaching the target cell envelope during infection. We have identified the genes and determined crystal structures for several spike proteins from phages, pyocins, and T6SS, and established a paradigm for their organization and function. The architecture of spike proteins is remarkably well conserved at the level of tertiary structure, but the corresponding genes and amino acid sequences have undergone huge rearrangements with domains becoming separate genes that are very far away from each other in the genome. Large bacteriophages and T6SS have the most complex spikes, in which the tip is a small protein that forms a very sharp conical extension on the spike. The membrane-attacking tip is stabilized by a buried Fe or Zn ion. The spike tip proteins belong to the PAAR (Proline-Alanine-Alanine-arginine) repeat domain superfamily with several thousand members in the GenBank. PAAR repeat proteins from T6SS are often extended by a domain with a putative effector function (nuclease, DNases, peptidases, etc.) or by a transthyretin domain. PAAR knockout mutants of *Vibrio cholerae* and *Acinetobacter baylyi* have either reduced or completely abolished T6SS activity, showing that PAAR proteins are essential for T6SS function and can play an important role in building of the T6SS machine and/or target cell membrane piercing. The unique HMM profile of PAAR repeat proteins makes it possible to identify their orthologs in all T6SS and contractile tail phages including T4, phiKZ, P1, etc. Complete structures (including the tip protein) of phage T4 central spike and T6SS spike of *Vibrio cholerae* will be presented and discussed.

[1] M. Shneider, S. Buth, B. Ho et al, *Nature*, 2013, 500, 350-353, [2] P. Leiman, M. Shneider, *Adv Exp Med Biol*, 2012, 726, 93-114, [3] C. Browning, M. Shneider, V. Bowman et al, *Structure*, 2012, 20, 326-339



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