

# Cooperative assembly of $\beta$ -barrel pore-forming toxins

Nguyen V.T., Kamio Y.

Dept. of Microbial Biotechnology, Grad. School of Agricultural Science, Tohoku University, Sendai 981-8555, Japan; Dept. of Biochem. and Plant Physiol., Ctr. Molec. Biol. and Cell Technol., Hanoi University of Science, Viet Nam

**Abstract:** Bacterial  $\beta$ -barrel pore-forming toxins are secreted as water-soluble monomeric proteins and assemble into  $\beta$ -barrel-shaped pores/channels through membranes of target cells, causing cell death and lysis. The pore assemblies that undergo various intermediate stages are symbolized by the association of multi-subunit structures in cells. Crystal structures of water-soluble monomers and membrane-embedded oligomeric pores, and recent studies involving biochemical detection and direct visualization of the sequential assembly of the toxin monomers have solved the mystery of how the pores are formed. Here, we review the mechanism of the cooperative assembly of several toxins of interest to explain the nature of the activities of the toxins. © 2004 The Japanese Biochemical Society.

**Author Keywords:** Cooperative assembly; Membrane binding; Oligomerization; Pore-forming toxins; Single-molecule imaging

**Index Keywords:** aerolysin; bacterial toxin; clostridium perfringens toxin; hemolysin; leukocidin; monomer; oligomer; unclassified drug; beta sheet; cell death; channel gating; crystal structure; cytolysis; nonhuman; protein assembly; protein secretion; protein structure; short survey; solubility; target cell; Animals; Bacterial Toxins; Humans; Models, Biological; Protein Folding; Protein Structure, Secondary; Bacteria (microorganisms)

Year: 2004

Source title: Journal of Biochemistry

Volume: 136

Issue: 5

Page : 563-567

Cited by: 4

Link: Scopus Link

Chemicals/CAS: aerolysin, 53126-24-2; clostridium perfringens toxin, 71329-60-7; leukocidin, 1406-83-3; Bacterial Toxins

Correspondence Address: Kamio, Y.; Dept. of Microbial Biotechnology, Grad. School of Agricultural Science, Tohoku University, Sendai 981-8555, Japan; email: [ykamio@biochem.tohoku.ac.jp](mailto:ykamio@biochem.tohoku.ac.jp)

ISSN: 0021924X

CODEN: JOBIA

DOI: [10.1093/jb/mvh160](https://doi.org/10.1093/jb/mvh160)

PubMed ID: 15632294

Language of Original Document: English

Abbreviated Source Title: Journal of Biochemistry

Document Type: Short Survey

Source: Scopus

Authors with affiliations:

- Nguyen, V.T., Dept. of Microbial Biotechnology, Grad. School of Agricultural Science, Tohoku University, Sendai 981-8555, Japan, Dept. of Biochem. and Plant Physiol., Ctr. Molec. Biol. and Cell Technol., Hanoi University of Science, Viet Nam
- Kamio, Y., Dept. of Microbial Biotechnology, Grad. School of Agricultural Science, Tohoku University, Sendai 981-8555, Japan

References:

- Alberts, B., Alexander, J., Lewis, J., Raff, M., Roberts, K., Walter, P., (2002) Molecular Biology of the Cell, 4th Ed., , Garland Science, New York
- Van Der Goot, G., (2001) Pore-Forming Toxins, , Springer-Verlag, Berlin, Heidelberg, Germany
- Parker, W.M., Cryptic clues as to how water-soluble protein toxins form pores in membranes (2003) *Toxicon*, 42, pp. 1-6
- Song, L., Hobaugh, M.R., Shustak, C., Cheyley, A., Bayley, H., Gouaux, E., Structure of staphylococcal  $\alpha$ -hemolysin, a heptameric transmembrane pore (1996) *Science*, 274, pp. 1859-1866
- Olson, R., Nariya, H., Yokota, K., Kamio, Y., Gouaux, E., Crystal structure of staphylococcal LukF delineates conformational changes accompanying formation of a transmembrane channel (1999) *Nat. Struct. Biol.*, 6, pp. 134-140
- Pedelacq, J.D., Maveyraud, L., Prevost, G., Baba-Moussa, L., Gonzalez, A., Courcelle, E., Shepard, W., Mourey, L., The structure of a *Staphylococcus aureus* leucocidin component (LukF-PV) reveals the fold of the water-soluble species of a family of transmembrane pore-forming toxins (1999) *Struct. Fold Des.*, 7, pp. 277-287
- Parker, M.W., Buckley, J.T., Postma, J.P., Tucker, A.D., Leonard, K., Pattus, F., Tsernoglou, D., Structure of the *Aeromonas* toxin proaerolysin in its water-soluble and membrane-channel states (1994) *Nature*, 367, pp. 292-295
- Rossjohn, J., Feil, S.C., McKinstry, W.J., Tweten, R.K., Parker, M.W., Structure of a cholesterol-binding, thioactivated cytolysin and a model of its membrane form (1997) *Cell*, 30, pp. 685-692
- Tomita, T., Kamio, Y., Molecular biology of the poreforming cytolysins from *Staphylococcus aureus*  $\alpha$ -hemolysin and  $\gamma$ -hemolysins and leukocidin (1997) *Biosci. Biotechnol. Biochem.*, 61, pp. 565-572
- Sugawara-Tomita, N., Tomita, T., Kamio, Y., Stochastic assembly of two-component staphylococcal  $\gamma$ -hemolysin into heteroheptameric transmembrane pores with alternate subunit arrangements in ratios of 3:4 and 4:3 (2002) *J. Bacteriol.*, 184, pp. 4747-4756
- Miles, G., Movileanu, L., Bayley, H., Subunit composition of a bicomponent toxin: Staphylococcal leukocidin forms an octameric transmembrane pore (2002) *Protein Sci.*, 11, pp. 894-902
- Gouaux, E., Hobaugh, M.R., Song, L.,  $\alpha$ -hemolysin,  $\alpha$ -hemolysin, and leukocidin from *Staphylococcus aureus*: Distant in sequence but similar in structure (1997) *Protein Sci.*, 6, pp. 2631-2635
- Parker, M., Van Der Goot, F.G., Buckley, J.T., Aerolysin-the ins and outs of a model channel-forming toxin (1998) *Mol. Microbiol.*, 19, pp. 205-212
- Fivaz, M., Abrami, L., Tsitrin, Y., Van Der Goot, F.G., Not as simple as just punching a hole (2001) *Toxicon*, 39, pp. 1637-1645
- Shepard, L.A., Shatursky, O., Johnson, A.E., Tweten, R.K., The mechanism of pore assembly for a cholesteroldependent cytolysin: Formation of a large prepore complex precedes the insertion of the transmembrane beta-hairpins (2000) *Biochemistry*, 39, pp. 10284-10293
- Kaneko, J., Ozawa, T., Tomita, T., Kamio, Y., Sequential binding of staphylococcal  $\gamma$ -hemolysin to human erythrocytes and complex formation of the hemolysin on the cell surface (1997) *Biosci. Biotechnol. Biochem.*, 61, pp. 846-851

- Nguyen, T.V., Kamio, Y., Higuchi, H., Single-molecule imaging of cooperative assembly of  $\gamma$ -hemolysin on erythrocyte membranes (2003) EMBO J., 19, pp. 4968-4979
- Abrami, L., Van Der Goot, F.G., Plasma membrane microdomains act as concentration platforms to facilitate intoxication by aerolysin (1999) J. Cell Biol., 147, pp. 175-184
- Ferreras, M., Frank, H., Serra, M.D., Colin, D.A., Prevost, G., Menestrina, G., The interaction of *Staphylococcus aureus* bi-component  $\gamma$ -hemolysins and leucocidins with cells and lipid membranes (1998) Biochim. Biophys. Acta, 1414, pp. 108-126
- Walker, B., Krishnasasty, M., Zorn, L., Bayley, H., Assembly of the oligomeric membrane pore formed by Staphylococcal alpha-hemolysin examined by truncation mutagenesis (1992) J. Biol. Chem., 267, pp. 21782-21786
- Rossjohn, J., Raja, S.M., Nelson, K.L., Feil, S.C., Van Der Goot, F.G., Parker, M.W., Buckley, J.T., Movement of a loop in domain 3 of aerolysin is required for channel formation (1998) Biochemistry, 37, pp. 741-746
- Nguyen, T.V., Higuchi, H., Kamio, Y., Controlling pore assembly of staphylococcal  $\gamma$ -hemolysin by low temperature and by disulfide bond formation in double-cysteine LukF mutants (2002) Mol. Microbiol., 45, pp. 1485-1498
- Valeva, A., Weisser, A., Walker, B., Kehoe, M., Bayley, H., Bhakdi, S., Palmer, M., Molecular architecture of a toxin pore: A 15-residue sequence lines the transmembrane channel of staphylococcal alpha-toxin (1996) EMBO J., 15, pp. 1857-1864
- Monma, N., Nguyen, T.V., Kaneko, J., Higuchi, H., Kamio, Y., Essential W177 and R198 residues of LukF for phosphatidylcholine-binding and pore-formation of Staphylococcal  $\gamma$ -hemolysin on human erythrocyte membranes (2004) J. Biochem., 136, pp. 427-431
- Walker, B., Braha, O., Cheley, S., Bayley, H., An intermediate in the assembly of a pore-forming protein trapped with a genetically-engineered switch (1995) Chem. Biol., 2, pp. 99-105
- Gu, L.Q., Braha, O., Conlan, S., Cheley, S., Bayley, H., Stochastic sensing of organic analytes by a pore-forming protein containing a molecular adapter (1999) Nature, 398, pp. 686-690

Download: 0782.pdf