Transport machineries in biomembranes utilizing 'charge zippers'

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We are studing membrane-active peptides and transmembrane proteins in their natural lipid environment, i.e. in macroscopically oriented lipid bilayers and in native biomembranes. Circular dichroism (including a synchrotron-CD beamline) is used to obtain qualitative data, solid-state NMR (with ^{19}F-, ^{2}H- or ^{15}N-labeling) yields more accurate structures as well as dynamical information, and MD simulations refine the overall picture. Membrane proteins are engaged in diverse transport processes of moving hydrophilic material across hydrophobic lipid bilayers, involving e.g. pore formation or more subtle catalytic mechanisms. We demonstrate here a new structural principle for the folding and self-assembly of membrane proteins, based on electrostatic interactions. In these so-called “charge zippers”, long ladders of salt bridges form between amphiphilic transmembrane segments, running all the way across the lipid bilayer. The role of this functionally important structural motif will be illustrated for two case studies with pharmaceutical and biotechnological relevance: the biofilm-inducing peptide TisB [1], which enables the controlled passage of protons across bacterial membranes; and the Twin-arginine translocase [2], which drives the export of fully folded proteins through a pore with variable diameter.

References:

[1] Steinbrecher, T., S. Prock, J. Reichert, P. Wadhwani, B. Zimpfer, J. Bürck, M. Berditsch, M. Elstner, A.S. Ulrich (2012) *Biophys. J.*, 103:1460-1469

[2] Walther T.H., C. Gottselig, S.L. Grage, M. Wolf, A.V. Vargiu, M.J. Klein, S. Vollmer, S. Prock, M. Hartmann, S. Afonin, E. Stockwald, H. Heinzmann, O. Nolandt, W. Wenzel, P. Ruggerone, A.S. Ulrich (2013) Folding and self-assembly of the TatA translocation pore based on a novel charge zipper mechanism, *Cell*, 152: 316–326