Irmgard Sinning

Ph.D. 1989 Max-Planck-Institute for Biochemistry, FRG. Postdoctoral work at the Max-Planck-Institute for Biophysics, FRG; the Biomedical Center at the University of Uppsala, Sweden. Group leader in Structural Biulogy at EMBL 1994-2000. Since 2000 Professor at BZH, University Heidelberg.
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Membrane proteins and protein targeting to membranes

Previous and Current research

We combine X-ray crystallography, spectroscopy and molecular biology in order to study the mechanism of the proteins of our interest.

A wide range of fundamental biological processes such as energy and information transport across biological membranes is mediated by membrane proteins. However, compared to their importance our knowledge about the three-dimensional structure of these proteins is very limited. This is mainly due to difficulties in obtaining well-ordered three-dimensional (3D) crystals from these proteins and/or problems with the expression. Current projects with membrane proteins include a number of transport proteins from bacteria and yeast and G-protein coupled receptors. Our strategies include the use of monoclonal antibodies for co-crystallization.

Coming from membranes, we got interested in how proteins are targeted to membranes, and in how they are inserted in or translocated across membranes. In mammalians targeting of secretory proteins to the ER membrane is a rather well characterized process. It involves the signal recognition particle (SRP, a complex of a 7S RNA and six polypeptides ranging from 9 to 72 kDa) and the SRP receptor. In procaryotes several pathways for protein targeting exist which meet at the same translocon. In *E. coli*., SRP consists of only one protein (Ffh, p48) and a 4.5 S RNA. SRP and the SRP receptor are multidomain proteins that contain a conserved GTP binding domain. We have determined the structures of several SRP GTPases and we could show that the kinetics of nucleotide binding are very different from other GTPases. This implies that the regulation of SRP GTPases is different from the classical molecular switch model. We have started to assemble larger complexes of SRP and its receptor form a number of different sources (including Archaebacteria and the plant chloroplast) with the aim of structure determination and kinetic characterization.
As far as manpower allows, we are open for collaborations concerning the structure determination of proteins with interesting mechanisms.

Future projects and goals

We continue our efforts with membrane proteins, putting more emphasis on expression strategies, especially for G-protein coupled receptors.
For the SRP project we continue with the structure determination of other SRP components, especially concentrating on larger complexes from differenct sources. The aim is to understand how SRP GTPases regulate the transport of nascent proteins to the membrane and subsequent translocation or insertion into the membrane.

Interesting projects for predoctoral students:

- Structure determination of SRP/SRP receptor complexes and related proteins
- Structure of the phosphate uptake system in yeast

Selected publications

Crystal structure of the NG-domain of the signal-recognition particle receptor FtsY. Montoya, G., Svensson, C., Luirink, J. & Sinning, I.(1997) Nature 385,365-368.
The signal recognition particle receptor of E. coli (FtsY) has a nucleotide exchange factor built into the GTPase domsin. Moser, C., Mol, O., Goody, R.S. & Sinning, I. (1997) PNAS 94, 11339-11344.
Anionic phospholipids are involved in membrane association of the Signal Recognition Particle receptor FtsY and stimulate its GTPase activity. de Leeuw, E., te Kaat, K., Moser, C., Menestrina, G., Demel, R., de Kruijff, B., Luirink, J. & Sinning, I. (2000) EMBO J. 19, 531-541.
A spectroscopic method for observing the domain movement of the Rieske iron sulphur protein. Brugna, M., Rodgers, S., Schricker, A., Montoya, G., Kazmeier, M., Nitschke, W. & Sinning, I. (2000) PNAS 97, 2069-2074.
The crystal structure of the conserved GTPase of SRP54 from the archaeon Acidianus ambivalens and its comparison with related structures suggests a model for the SRP/SR receptor complex. Montoya, G., te Kaat, K., Moll, R., Schäfer, G. & Sinning, I. (2000) Structure Fold. Des. 8, 515-525.