TECHNISCHE UNIVERSITÄT WIEN

Prof. Sebastian Springer

DPhil (*Oxon*), Dipl.-Biochem.

Biochemistry and Cell Biology

Constructor University Bremen
Germany

CONSTRUCTOR UNIVERSITY

Tuesday, January 23rd 2024, 14:00 s.t.

Clusters of peptide-free MHC class I molecules at the cell surface

Abstract: Major histocompatibility complex (MHC) class I proteins are transmembrane receptors that bind intracellular peptides and present them at the cell surface to the T cell receptors of cytotoxic T cells; they are also ligands of Natural Killer cell receptors. But once peptide and the invariant light chain beta-2 microglobulin have dissociated, the ‚free' MHC class I heavy chain remains at the cell surface and was previously thought to be rapidly endocytosed and degraded. We now demonstrate that free MHC class I heavy chains have a residence time of hours at the cell surface, and that they form non-covalent clusters that may include other proteins. I will show evidence that heavy chain clustering inhibits endocytosis, and speculate on their biological role.

Sebastian Springer is a biochemist by training. He worked with Stefan Jentsch in Tübingen on the E3 ligases of the ubiquitin system and protein degradation, with Alain Townsend in Oxford for his PhD on MHC class I antigen presentation, and then as a postdoctoral fellow with Randy Schekman in Berkeley on COPII vesicle trafficking and cargo recruitment. Since 2001, he has had his own group at Jacobs University Bremen, Germany, where he is now a full professor of Biochemistry and Cell Biology.

MHC class I proteins present intracellular antigen to cytotoxic T lymphocytes. These proteins are in the focus of research of the Springer lab. Using methods from cell biology, such as flow cytometry, pulse-chase assays and microscopy, we investigate their folding and quality control, their intracellular transport, and their endocytosis from the cell surface, asking especially how the different forms (peptide-bound, empty, unfolded) are recognized by the cell and handled differentially. We also investigate how viruses influence the trafficking of class I (and other proteins) to escape the immune response.

Using methods from biochemistry and biophysics, such as protein thermal denaturation, fluorescence spectroscopy, crystal structure analysis (in cooperation), and molecular dynamics simulations (in cooperation), we investigate peptide binding to class I proteins, the conformational change between the empty and the peptide-bound state, and the catalysis of peptide exchange by cellular and artificial factors. This work has led to conformationally stable empty MHC class I proteins, which are useful as diagnostic reagents for tumor immunotherapy.

Getreidemarkt 9, Building BD, Seminar Room 02C

All interested colleagues are welcome to this seminar lecture
(45 min. presentation followed by discussion)

Biophysics
Institute of Applied Physics
IAP