The 106th iCeMS SEMINAR

Thu 05 Apr 2012
16:00-18:00

Venue: 2nd floor Seminar Room (#A207) Main Building
iCeMS Complex 1, Kyoto University

<Part 1: 16:00–17:00>

"Analyzing the Haemolysin Secretion Machinery of E. coli"

Prof. Dr. Lutz Schmitt
Institute of Biochemistry,
Heinrich Heine University Düsseldorf, Germany

<Part 2: 17:00–18:00>

"Treatment of Leukemia and Lymphoma with Recombinant Immunotoxin Moxetumomab Pasudotox: Successes and Challenges"

Prof. Dr. Ira Pastan
National Cancer Institute,
National Institutes of Health (NIH), USA

Contact: iCeMS Ueda Lab at ueda-g@icems.kyoto-u.ac.jp
Hosted by: iCeMS (Institute for Integrated Cell-Material Sciences), Kyoto University
Co-hosted by: Center for Frontier Medicine, Global COE Program, Kyoto University

The 106th iCeMS SEMINAR

Abstracts for April 5 iCeMS Seminar

Prof. Dr. Lutz Schmitt <*16:00–17:00*>

In Gram-negative bacteria, Type 1 secretion systems (T1SS) export their cognate substrates in a single step directly from the cytosol to the extracellular medium without the formation of periplasmic substrate intermediates. T1SS facilitate the secretion of structurally and functionally distinct proteins, which include hemophores (HasA), adenylate cyclases, lipases, proteases and pore-forming toxins such as haemolysin A (HlyA). The 110 kDa HlyA is a member of the repeats in toxin (RTX) protein family as it contains glycine rich nonapeptide repeats in the C-terminal domain, which are the hallmark of substrtaes of T1SS.

One of the best-studied T1SS is the haemolysin (Hly) secretion system of Escherichia coli. The Hly translocator consists of the inner membrane protein HlyB, which is an ATP binding cassette (ABC) transporter, the membrane fusion protein HlyD, which are both anchored in the inner membrane and the outer membrane protein TolC and. The interaction of HlyA with HlyB and HlyD triggers recruitment of TolC, thereby creating a continuous, but transient channel-tunnel from the cytosol directly into the extracellular medium.

Here, I will summarize our recent progress concerning the molecular analysis of the HlyA secretion machinery, in particular the ABC transporter HlyB and present a model that tries to covers various aspects of recognition and secretion in this T1SS.

Prof. Dr. Ira Pastan <*17:00–18:00*>

Moxetumomab pasudotox (HA22) is a recombinant immunotoxin containing the Fv portion of an antibody to CD22 with a portion of Pseudomoans exotoxin A. This agent binds to CD22 on B cell malignancies and after endocytosis, inactivates elongation factor 2 leading to protein synthesis arrest and cell death. We have been carrying out clinical trials with this agent in patients with leukemia and lymphoma, who no longer respond to standard therapies. In drug resistant Hairy Cell Leukemia the agent has a very high response rate with over 60% of patients obtaining a complete and long lasting remission (CR). In pediatric ALL, the agent is also active, although the CR rate is lower with about 25% of children receiving a CR. Using ALL cell lines we have identified several mechanisms of resistance to the immunotoxin .

Contact: iCeMS Ueda Lab at ueda-g@icems.kyoto-u.ac.jp
Hosted by: iCeMS (Institute for Integrated Cell-Material Sciences), Kyoto University
Co-hosted by: Center for Frontier Medicine, Global COE Program, Kyoto University