Cancer Science Institute of Singapore

SEMINAR ANNOUNCEMENT

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Biophysics in the Cell - CETSA to Guide Preclinical Drug Development

Date: Monday, 9 Jan 2017
Time: 10.30am – 11.30am
Venue: LT35, Level 1, CeTM (MD6) (14 Medical Drive, S117599)
Host: Prof Daniel Tenen

Abstract:

A key step of the action of most drugs is their binding (engagement) of the target protein(s). However, limitations in the available methods for directly accessing this critical step have added uncertainties in many stages of drug development. We have developed a generic method for evaluating drug binding to target proteins in cells and tissues (Martinez Molina, 2013). The technique is based on the physical phenomenon of ligand-induced thermal stabilization of target proteins; the method is therefore called the cellular thermal shift assay (CETSA). The technique allows for the first time to directly measure the biophysical interactions between a drug and protein target in non- engineered cells and tissues. We show that using CETSA a range of critical factors for drug development can be addressed at the target engagement level, including drug transport and activation, off-target effects, drug resistance as well as drug distribution in cells, patient and animal tissues. CETSA has also been shown to be a stringent strategy for library screen for target engagement (Almqvist, 2016). Using quantitative mass-spectrometry, proteome-wide CETSA has been established which allows for off-target effects as well as downstream biochemistry to be discovered (Savitsk, 2014). Together the data supports that CETSA is likely to become a valuable tool for biomedical research and drug development in the future.

Biography:

Pär Nordlund is a structural biologist now working in the area of molecular and cellular cancer research. At the Karolinska Institute he funded the Swedish node of the Structural Genomics Consortia that solved 140 human protein structures during the period 2005-2010. His groups have developed expertise in membrane protein structural biology and did in 2007 solve the first structure of a human integral membrane protein. He is also the inventor of the Cellular Thermal Shift Assay, which has emerged as a valuable tool for studies of drug action in cells and tissues. He is a member of the Nobel Assembly and the Swedish Academy of Science, as well as a reviewing editor for Science Magazine. He is the co-funder of the biotech companies Sprint Bioscience, Pelago Bioscience and Evitra Proteoma.