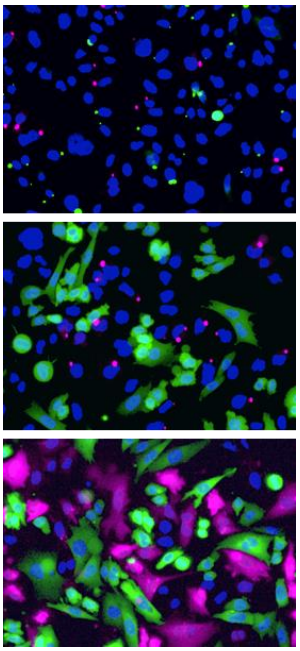
Biomedical Sciences Institutes
A*STAR

p53 Laboratory Seminar Announcement

- All Are Welcome -



Speakers:

Dr Taku Watanabe
Group Leader
Drug Discovery Technology Development,
Life Science Translational Research,
Medical & Biological Laboratories, Co. Ltd.
Nagano, Japan

Dr Chris Brown
Research Scientist
p53 Laboratory
*A*STAR*

Title : **Monitoring Protein:Protein Interactions through the use of MBL Technology (FLUOPPI)**

Date : **21 February 2018 (Wednesday)**

Time : **3pm – 4pm**

Venue: **Creation Theatrette, Matrix Level 4, Biopolis**

Host : **Prof Sir David Lane**
Chief Scientist, A*STAR & Director, p53Lab

Abstract:

Protein-protein interactions (PPIs) are attractive but challenging targets for traditional small molecule drug discovery. Many PPIs are characterized by large and disperse interactions sites and the use of larger molecule weight molecules (e.g. miniproteins, peptides, antibodies) to targets these interactions are increasingly attractive. A large proportion of protein-proteins considered to be medically important (e.g myc:MAX, p53:Mdm2) lie within the nucleus and cytoplasm of the cell. However these modalities suffer from poor cell permeability and are proteolytic; issues making them poor modalities to address intracellular targets. As a result these areas have become key areas for research into transforming these molecules into potential therapeutic candidates. In collaboration with MBL, we have sought to address these issues with the development of a live cell based protein-protein interaction assay to allow successful engagement of the target within the cell to be measured, which should allow the development of novel techniques to deliver these molecules into the cell.

Using FLUOPPI technology from MBL (FLUOPPI) and the p53 pathway as an example, we have developed a protein: protein interaction assay that can simultaneously monitor the interaction of p53 with both Mdm2 and Mdm4 in live cells. We have also demonstrated that the assay can measure the disruption of both Mdm2 and Mdm4 interactions with small molecules and stapled peptides. In addition we have also confirmed that the application of lipid formulation improves the efficiency of stapled peptide delivery into the cell. More importantly, on top of quantitating PPI disruption, the assay can also monitor cell toxicity, ensuring that any decrease in the PPI engagement signal is not the result of indiscriminate cell cytotoxic effects. The application of FLUOPPI to the discovery of novel inhibitors against PPIs should accelerate their identification.

About Medical & Biological Laboratories, Japan:

One of the leaders in the Japanese clinical diagnostics market for over 30 years, MBL's mission is to offer novel diagnostic reagents to meet the healthcare needs of patients, not only for prevalent diseases but also orphan and intractable diseases. Founded in 1969 as a specialist antibody production company, they now provide clinical diagnostics and research reagents for protein and genetic analysis, as well as biomarker development, companion diagnostics and regenerative medicine. They have a clinical (*in vitro*) diagnostics products business arm, and a life science translational research (LSTR) arm that seeks to collaborate with academic and pharmaceutical companies to lay the foundation for future clinical diagnostics. Their research area is broad, spanning across immunology, molecular biology and epigenetics. MBL is now a consolidated subsidiary of JSR Corporation with global business operations in the United States, Europe, and China.