UCLA Chemistry & Biochemistry

Biochemistry Seminar Series

Midstream Presentations – Spring 2019

Maeve Nagle

Wollman Group

"Multiplexed Decoding of the Dynamics of Fractional Killing"

ABSTRACT. When tumor cells are exposed to a chemotherapy, some cells are killed while others survive. This fractional killing selects for drug resistance in tumors over time. Currently, drug resistance is a major roadblock to effective eradication of cancers. Further understanding the processes that lead to drug resistance is crucial in developing new targeted therapies to treat cancer. Recent studies have shown that heterogenous gene expression plays a role in this fraction of cells entering a resistant state. Cells that stochastically express high levels of certain genes are more likely to be able to survive a dose of chemotherapy. Current methods to explore the cell states that lead to drug resistance are time-consuming, costly, and scale poorly. We have developed a method called BITS (Barcode-associated Intronic Tagging of endogenous genes in a Scalable Manner). This new technique combines generic and multiplexable CRISPR tagging of endogenous genes with RNA barcodes that allow for the identification of distinct tagged cells in a pooled assay. With BITS, we can use live-cell imaging of thousands of cells to track the dynamic changes in abundance and localization of key proteins and determine their contribution to drug resistance. BITS offers an inexpensive, fast approach to studying cellular heterogeneity and response to chemotherapies.

Wonhyeuk Jung

Loo Group

"Native mass spectrometry analysis of membrane proteins"

Abstract. In most genomes, 20–30% of all genes encode membrane proteins and they represent more than 60% of potential drug targets. However, less than 3% of solved protein structure deposited in the protein database represents membrane protein structures that have at least one transmembrane region. The dearth of structural information of membrane proteins stems from unique challenges associated with them. Membrane proteins are hard to express in large quantity, are highly hydrophobic, and are often flexible and unstable which makes them difficult to crystallize. Thus, complementary methods to gain structural insights about membrane proteins are needed.

In this talk, how native mass spectrometry (MS) can be used for structural investigation of membrane proteins will be discussed. Native MS holds several advantages for membrane protein analysis in that the technique requires a minimal amount of protein, is not restricted by the protein size and that there is no ensemble-averaging involved, which enables direct observation of co-populated conformations.

The current progress of native MS application on AqpZ, a homotetrameric *E. coli* water channel that mediates rapid entry or exit of water in response to abrupt changes in osmolarity, will be presented. Also, how native MS can be combined with top-down technique, in which protein of interest is fragmented to gain further structural information, will be introduced.

Friday, May 24, 2019

3440 Molecular Sciences

3:30 p.m.

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