2019 年 10 月 30 日
Oct. 30, 2019

大学院学生各位
To All Graduate Students

2019 年度 基盤医学特論 開講通知
Information on Special Lecture Tokuron FY2019

日時: 2019 年 12 月 3 日(火)17:00～18:30(質疑応答含む)
Time and Date : Tue, Dec. 3, 2019, 17:00～18:30

場所: 基礎医学研究棟 1 階会議室 1
Room : Conference Room 1 on the first floor, Building for Medical Research

使用言語: 英語 **Language:** English

17:00–17:45
Title : Discovering Biomarkers of Extreme Resistance in High-Risk Breast Cancer
Teaching Staff: Dr. Amrita Basu
(Assistant Professor, University of California, San Francisco)

(Abstract)

Amrita Basu[1], Denise Wolf[1], Christina Yau[1], Laura Esserman[1], Laura v' antVeer[1]
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Approximately seventy percent of breast cancer patients with extensive residual cancer burden after neoadjuvant therapy die within 4 years of treatment. These patients have lots of residual disease post treatment and are extremely resistant to therapy. There is currently very little understanding of the biomarker landscape that contributes to their resistance, but a need to recognize these 'super non-responders' early is critical so there is opportunity to tailor their treatment and potentially change or add to their therapeutic regimen early on. Our goal was to develop a predictive model that can identify co-present markers of resistance in the pre-treatment stage of breast cancer. In cancer, differences in module activity potentially represent the heterogeneity of phenotypes important in carcinogenesis, progression, or treatment response. To find gene expression modules active in breast cancer subpopulations, we applied methodology developed in prior studies to identify co-regulated modules, or groups of genes with highly correlated expression patterns, predictive of response in high-risk women with breast cancer who are part of the I-SPY clinical trial. Per drug, we identified genes with bimodal expression to ultimately define multiple modules of genes that are uniquely co-regulated. Functionally, these modules reflect angiogenesis, immune signaling, histone modification, extracellular matrix (ECM) and stroma, and cell proliferation. We also stratified our population based on patient outcomes, receptor subtype, and tumor volume to identify additional markers of that are reflective of signaling biology. Overall, our findings provide a high-level functional view of breast cancer that complements the "cancer hallmarks" and may form the basis for improved predictors and targeted therapies for those likely to achieve poor outcomes.

17:45–18:30
Title : Five-dimensional mass spectrometry to investigate epigenetics epidemiology
Teaching Staff: Dr. Simone Sidoli
(Assistant Professor, Albert Einstein College of Medicine)

(Abstract)

Chromatin is the control panel of the cell. Modifications, interactions and compaction of DNA and chromatin associated proteins modulate gene expression, epigenetics inheritance and cryptic transcription of non-coding regions. During aging, viral infection and many types of cancer, the compaction of chromatin is reduced, demonstrated by DNA hypomethylation and overall increase of histone acetylations. In other words, increase in chromatin entropy is today recognized as cause and effect of a multitude of conditions of reduced cell fitness. Our lab develops and applies technology to investigate unexplored aspects of chromatin. We optimize methods based on mass spectrometry to identify mechanisms leading to aberrant chromatin unfolding. Specifically, we want to determine "context-dependent" roles of histone marks depending on (i) how accessible they are on chromatin, (ii) what other marks they co-exist with and (iii) what is their effect on protein recruitment and DNA readout. This allows us to identify chromatin markers that play a fundamental role in chromatin aberrant states, and eventually target their readers for therapy.
We work also on increasing robustness, throughput and accuracy of our methods for diagnostics. Histones are the most abundant and heterogeneous (i.e. modified) protein family in the cell, so they have high potential to be used as biomarkers. We use ultra-fast injection methods in mass spectrometry to quantify histone and nucleic acid modifications at the rate of >1,000 samples per day. Our methods are now being combined with automated sample preparation and clustering tools for live identifications.

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