NUS National University of Singapore | NUS Centre for Cancer Research
Yong Loo Lin School of Medicine

N2CR Thematic Seminar
Precision Cancer Medicine

Date: Monday, 17 October 2022
Time: 5 - 6 pm
Host: A/Prof Edward Chow
Venue: Zoom

Click or scan the QR code to join!



Dr. Ma Jun

Elaine Lim Hsuen Group
Associate Consultant
National Cancer Centre Singapore

Metastatic Triple-Negative Taxane-Resistant/Refractory Breast Cancer: Investigating the Role of Bexarotene in Inducing Susceptibility to Chemotherapy by Differentiating Cancer Cells from a Mesenchymal-Like to an Epithelial-Like Phenotype (BEXMET)

Abstract

Triple-negative breast cancer (TNBC) is biologically aggressive and has limited systemic treatment options, often compounded by treatment resistance, hence conferring an overall poorer prognosis. Cell state transitions, e.g. epithelial-to-mesenchymal transition (EMT) and mesenchymal-to-epithelial transition (MET), influence the functional behaviour of cancer cells, such as proliferation, invasiveness, metastatic potential and resistance to chemotherapy. Our preliminary studies revealed Bexarotene (retinoid) as a potent MET inducer, verified in TNBC cells in vitro and in animal models, rendering greater chemotherapy sensitivity. BEXMET is a target validation clinical study that is open for recruitment at National Cancer Centre Singapore, where taxane-resistant/refractory TNBC patients are exposed to Bexarotene and assessed for susceptibility to Capecitabine via transcriptome and immunohistochemical analysis of serial tumour tissue biopsies.

Biosketch

Dr. Ma Jun graduated from Monash University, Melbourne with M.B.B.S(Hons) and completed her specialty training in Medical Oncology at National Cancer Centre Singapore (NCCS). She currently specializes in breast cancer. Her key areas of interests are breast cancer in young women, and supportive care needs in breast cancer. Dr. Ma is currently involved in setting up a Young Women (YOWO) with Breast Cancer programme at NCCS, focusing on supporting their unique needs and offering streamlined multi-disciplinary patient-centred care.



Lee E Hui Clarissa

Alan Prem Kumar Group
PhD Student
Department of Pharmacology
National University of Singapore

Characterization of a Lyn Kinase-specific Inhibitor in Immune Activation and Targeted Immunotherapy of Aggressive Breast Cancer

Abstract

SFKs have been attractive targets for anti-cancer therapy, however, clinical trials of pan-SFK inhibitors concluded with lack of clinical benefit for TNBC patients. The clinical failures of pan-SFK inhibitors were associated with a lack of correlation between Src kinase and SFK sensitivity, and increased liver metastasis. Src-family kinase, Lyn, is highly expressed in TNBC and correlates with reduced overall survival. Knockdown experiments involving Lyn or Src kinases demonstrated Lyn-depleted TNBC cells functionally and phenotypically resembled pan-SFK inhibitor-treated cells, suggesting that Lyn kinase, is the more biologically relevant target. To explore this further, we developed a novel Lyn-selective small-molecule inhibitor, CHL-4, and demonstrated its anti-cancer properties in several TNBC lines and animal models. Interestingly, we also show CHL-4-mediated Lyn kinase inhibition resulted in differential expression of genes involved in the regulation of inflammatory response and immune activation, suggesting that Lyn suppresses immune cell activation to promote tumor immune evasion. Moreover, patients with advanced breast cancer expressing high levels of Lyn exhibited poorer response to a combination treatment of Durvalumab (anti PD-L1) and Bevacizumab compared to those with low Lyn expression.

Biosketch

Clarissa obtained her Bachelor's degree by completing her Honors project and thesis with Professor Ding Jeak Ling. The focus of her undergraduate research was to delineate the roles of the evolutionarily conserved transcription factors T-bet and Eomes in regulating natural killer cell function against non-small cell lung cancer. As a PhD student in Dr Alan Prem Kumar's group, her focus is to understand Lyn's biology and immunoreactive effects of CHL-4, which hold significant potential in developing strategies that could complement existing therapeutic modalities in TNBC.