SMART BioSyM Seminar

Short-Term Expansion of Breast Circulating Cancer Cells Predicts Response to Anti-Cancer Therapy

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19th October 2015, Monday
4pm – 5pm
SMART Enterprise Wing Level 5,
Perseverance Rooms 1 & 2

Purpose
Circulating tumor cells (CTCs) are considered as surrogate markers for prognosticating and evaluating patient treatment responses. This study assessed the ability to predict breast cancer patient responses to neo-adjuvant therapy using a new short-term culture method for CTCs.

Method
Here, 226 blood samples from 92 patients with breast cancer, including patients with newly diagnosed or metastatic refractory cancer, and 16 blood samples from healthy subjects were cultured in laser-ablated microwells. Clusters containing an increasing number of cytokeratin-positive (CK+) cells appeared after 2 weeks, while most blood cells disappeared with time.

Results
Cultures were heterogeneous and exhibited two distinct sub-populations of cells: 'Small' (≤ 25 μm; high nuclear/cytoplasmic ratio; CD45-) cells, comprising CTCs, and 'Large' (> 25 μm; low nuclear/cytoplasmic ratio; CD68+ or CD56+) cells, corresponding to macrophage and natural killer-like cells. The Small cell fraction also showed copy number increases in six target genes (FGFR1, Myc, CCND1, HER2, TOP2A and ZNF217) associated with breast cancer. These expanded CTCs exhibited different proportions of epithelial–mesenchymal phenotypes and were transferable for further expansion as spheroids in serum-free suspension or 3D cultures. Cluster formation was affected by the presence and duration of systemic therapy, and its persistence may reflect therapeutic resistance.

Discussion
This novel and advanced method estimates CTC clonal heterogeneity and can predict, within a relatively short time frame, patient responses to therapy.

Dr. Khoo is currently a research associate in BioSystems and Micromechanics Inter-Disciplinary Research Group of Singapore-MIT Alliance for Research and Technology (SMART). She received her Ph.D. from the Mechanobiology Institute, NUS Graduate School (NGS) in 2015, working on the design and characterisation of a microwell-based assay for the culture of primary human cancer cells isolated from blood of patients (i.e. circulating tumor cells (CTCs)). Prior to her graduate studies, she had been involved in various bioengineering and translational projects under both A*STAR and Nanyang Technological University (NTU), where she did her undergraduate studies in Biomedical Sciences. Her current research focuses on the development of microfluidic devices and microassays for application in various biological studies, including cancer.