

CSCB Virtual Seminar Series

Functional precision medicine in acute myeloid leukemia.

Date: 10th May 2021 (Monday)

Time: 12noon-1pm (SGT)

Venue: *via Zoom*

For details, please contact:

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Abstract:

Relapse is the leading cause of treatment failure in acute myeloid leukemia (AML) patients. To identify individualized therapy for AML, we adopted broadly applicable functional approach to precision medicine called “dynamic BH3 profiling” (DBP) and coupled it with RNA-seq and targeted exome sequencing technology. We derived landscapes of pharmacologic sensitivity of 17 patient-derived xenograft (PDX) AML models to a panel of 40 clinically relevant agents, together with genomic and transcriptomic profiles. Aggregated across the panel, drug-induced apoptotic signaling by dynamic BH3 profiling (DBP) by itself could segregate PDXs according to prior treatment status. DBP could accurately predict in vivo efficacy of drugs of widely varying mechanism of action, including a FLT-3 inhibitor, BCL-2 antagonist, SMAC mimetic, and BRD4 inhibitor. After selecting for in vivo acquired resistance to single agent therapies of distinct mechanism a common mechanism of resistance was identified for all – a reduction in mitochondrial apoptotic priming. Reduction in priming was accompanied by broad chemoresistance, even to mechanistically distinct agents. Nonetheless, even in the resistant setting we could use DBP to identify agents with persistent in vivo activity. Such an approach for assigning drugs would be feasible in the human clinical setting.

Speaker:

Dr. Shruti Bhatt

Assistant Professor

Department of Pharmacy, National University of Singapore



Dr. Bhatt joined the department of Pharmacy of NUS as assistant professor in 2020. Her lab focuses on overcoming drug resistance to cancer therapy using functional and genomic approaches. Her lab uses BH3 profiling assay as key technology that measures cancer cells' proximity to apoptosis. Dr. Bhatt led an effort to predict response to leukemia therapy using BH3 profiling during her postdoctoral training in Anthony Letai's lab at Dana-Farber. Dr. Bhatt holds PhD in pharmacology from University of Miami. Dr. Bhatt was recently named as 2021 AACR Nextgen Star.

Host:

Li Shang

Associate Professor

Programme in Cancer & Stem Cell Biology

Duke-NUS Medical School

Singapore

**No registration is required.
All are welcome.**