

Title: Globally optimizing therapeutic combinations against bortezomib-resistant multiple myeloma using a quantitative parabolic optimization platform (QPOP)

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Multiple myeloma is an incurable hematological malignancy that relies on drug combinations as first and secondary lines of treatment. The inclusion of proteosome inhibitors, such as bortezomib, into these drug combination regimens has improved median survival. Resistance to bortezomib, however, is a common occurrence that ultimately contributes to treatment failure. Thus, there remains a need to identify improved drug combinations that may serve as later lines of treatment for improved treatment against bortezomib-resistant multiple myeloma. We have developed the quantitative parabolic optimization platform (QPOP) to optimize drug combinations against bortezomib-resistant multiple myeloma. By mapping phenotypic output data to parabolic response surfaces, QPOP is able to deterministically optimize drug combinations as well as drug dosages. By continuously optimizing in multiple systems of interest, from in vitro to in vivo, drug combinations can be globally optimized for greater efficacy in increasingly complex biological systems. While QPOP does not rely on molecular mechanism modeling or prediction, identified optimal drug combinations can reverse DNA hypermethylation and silencing of tumor suppressors that occurs following acquired bortezomib-resistance in multiple myeloma. Furthermore, this drug combination is broadly effective across a range of primary multiple myeloma patient samples. Beyond bortezomib-resistant multiple myeloma, global optimization of drug combinations by QPOP can serve to improve drug combination design across a range of other cancers and diseases through a continuous optimization process across the entire drug development pipeline.

Biography

Masturah is a fourth year PhD student from National University of Singapore (NUS). Her research interests include identifying optimal drug combinations on different systems of interest across the drug pipeline, where her work on liver cancer was selected as the cover article for the August 2015 JALA biosensing special issue. She has also won best poster presentations for Society for Laboratory and Screening (SLAS) 2016 and NUS Medicine 7th Annual Graduate Scientific Congress (AGSC) 2017.

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