

Title: Multi-protein Dynamic Combinatorial Chemistry: A Novel Strategy of Drug Design

Name: Mohua Das
National University of Singapore, Singapore

Dynamic combinatorial chemistry (DCC) is a powerful supramolecular approach for discovering ligands for biomolecules. It is currently of tremendous chemical and biological interest. To date, most, if not all, biologically-templated DCC employ only a single biomolecule in directing the self-assembly process, which severely limits the scope and potential of DCC.
Herein, we explored the concept of multi-protein DCC, where two or more target proteins could be used concurrently in the same dynamic system. We envisaged that this will greatly multiply the power and efficiency of DCC. However, such a multi-protein system is extremely challenging to analyse, in part due to the constantly changing nature of dynamic self-assembly. Consequently, to date, there is no report of method suitable for studying multiprotein templated DCC.
To overcome this challenge, we developed a novel multi-protein detection strategy which combines the discriminatory power of zwitterionic 'thermal tag' with the sensitivity of differential scanning fluorimetry. This strategy is also remarkably sensitive and could differentiate the binding of ligands to different proteins, including structurally-similar subfamily members, which are otherwise challenging to discriminate.When used in combination with DCC, we were able to achieve simultaneous evolution of ligands against several proteins. This led to the concurrent discovery of subfamily-selective probes against two clinically-important epigenetic enzymes, FTO and ALKBH3.
To our knowledge, this study represents not only the first report of multi-protein DSF assay, but also a new strategy for probing dynamic chemical system, which hopefully will further our understanding of self-assembly dynamics, and inspire new applications for DCC-based approaches.

Biography

Mohua had started her research career with a Masters in Natural Product Chemistry from the National Insitute of Pharmaceutical Education and Research (NIPER, India). The dissertation work in Masters led to her first publication in a peer-reviewed journal *Organic Letters*, in 2015. She has also received the University Gold Medal for being the best student of the batch in the same year. She is currently pursuing her PhD from the National University of Singapore and already published her first-author paper within three years of her PhD journey.

Presenting author details
Full name: Mohua Das
Contact number: (65)86571469
Twitter account: @d_mohua
Linked In account: https://www.linkedin.com/in/mohua-das-27680174/
Session name/ number: Day 1 or Day 2
Category: Oral presentation