MOLECULAR STRUCTURE AND FUNCTION PROGRAM SEMINAR

Dr. Laila Dafik

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Dr. Dafik is a candidate for a staff position in the Molecular Structure & Function Program

In vitro Evolution of Bioactive Small Molecules Using DNA-programmed Combinatorial Chemistry

Abstract: Directed evolution of large combinatorial chemistry libraries is an emerging approach for small-molecule discovery. To advance this field, we developed a DNA-programmed combinatorial chemistry technique that enables selection of drug-like compounds over iterative generations. To discover biologically active small molecules, we apply a purifying selection to a naive DNA-programmed library comprising of 1.1 billion distinct compounds. The composition of the library is then determined by high-throughput sequencing. Given the comprehensive nature of the combinatorial synthesis and the deep sampling enabled by high throughput sequencing, we can observe simultaneous enrichment of different chemical families, increasing our chances of identifying a true hit. Thus far we have identified novel protein ligands and non-peptidic substrates for protein kinases. More broadly, we have performed the first directed evolution of a billion member combinatorial library. We anticipate that our approach will lead to the discovery of novel small-molecule affinity reagents, pharmaceutical lead compounds, imaging probes, and other high-value compounds. This can substantially increase global access to small-molecule reagents and open up new areas of biological inquiry.

Date : Thursday, January 30, 2014
Time : 1:00 - 2:00 pm
Location : Room 02.9330 (Auditorium, 2nd Floor)
SickKids Peter Gilgan Centre for Research and Learning (PGCRL),
686 Bay Street

Host: Dr. P. Lynne Howell

Pizza lunch will be served outside of the Auditorium at 12:30 pm

Note: Please do not enter the Auditorium with food/drinks – thank you.

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