Indian Institute of Technology Delhi

DEPARTMENT OF BIOCHEMICAL ENGINEERING & BIOTECHNOLOGY

2016-17 Seminar Series

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Using whole genome sequencing to diagnose resistant bacterial infections

Prof. Philip W Fowler

Nuffield Department of Medicine
University of Oxford, Oxford, UK

http://sbcb.bioch.ox.ac.uk/formermembers/fowler.php

The discovery of antibiotics was one of humanity's greatest achievements in the twentieth century, however, the evolution of antibiotic resistance by pathogens now threatens many advances of modern medicine. There is an urgent need for improved diagnostic tools so that resistant infections can be identified and treated appropriately. Analysis of whole-genome sequence data generated on affordable high-throughput platforms has the potential to allow resistant infections to be more rapidly and cheaply diagnosed in the clinic than conventional culture based approaches. A key limitation of this approach is that it cannot identify rare or previously unseen mutations. Here we provide proof-of-principle that a well-established class of methods from computational chemistry, alchemical free energy methods, can successfully predict the resistance phenotype of a series of mutations in *Staphylococcus aureus* dihydrofolate reductase identified by whole-genome sequencing of patient infections. I shall demonstrate that not only can the method predict which mutations cause resistance (and which do not), but also that the minimum inhibitory concentration of trimethoprim for each mutation can be predicted with reasonable accuracy. Having established that the approach has the potential to be successful, I shall discuss how this and similar approaches will be used in a major international collaboration, CRyPTIC, that was launched in March 2016 and is funded by the Gates Foundation, the Wellcome Trust and the Newton Fund. The goal of this project is to collect 100,000 *M. tuberculosis* samples from across Africa, Asia, Europe and the Americas. Each sample will have both its drug susceptibility profile established and its whole genome sequenced.

All are welcome

Seminar will be held in DBEB SEMINAR ROOM at Block I, Room 223 at 4 PM
For additional information, contact Seminar coordinator D. Sundar at sundar@dbeb.iitd.ac.in