Donnelly Centre
for Cellular + Biomolecular Research
UNIVERSITY OF TORONTO

UNIVERSITY OF TORONTO

Special Seminar

"HT-SELEX studies of transcription factor binding specificities"

2016 Charles H. Best
Postdoctoral Fellowship Awardee

Arttu Jolma

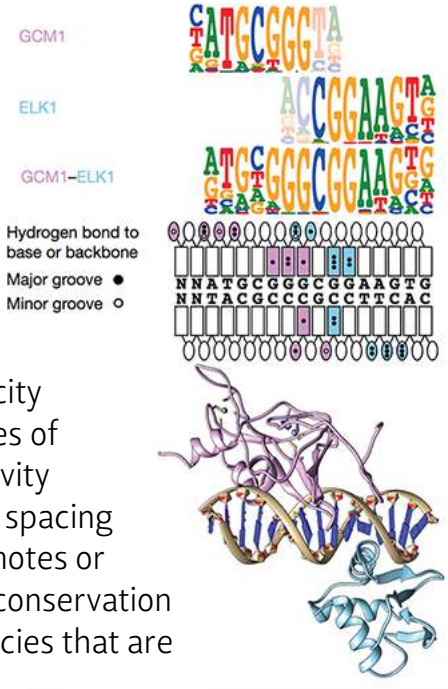
Department of Biosciences and Nutrition
(BioNut), H2
Karolinska Institutet
Stockholm, Sweden

Tuesday, December 15, 2015, 11:00 am
Donnelly Centre Red Seminar Room

Abstract:

Human genome codes for 1200-2000 sequence specific transcription factors (TFs). Each TF has its inherent target specificity, it binds to a range of similar sequences that can be ranked based on their relative binding strengths. TFs can bind either as monomers or as homo- or heterodimeric complexes and their binding to the DNA can be affected by methylation of the CpG dinucleotides.

We have developed several types of high throughput systematic evolution of ligands by exponential enrichment (HT-SELEX) assays and used these to analyze the binding specificities of large numbers of human, mouse and Drosophila melanogaster TFs. TF specificities have been analyzed in context of individual TFs using regular and CpG methylated selection ligands (HT-SELEX and methyl HT-SELEX) and as cooperatively binding heterodimeric complexes using consecutive affinity-purification based assay (CAP-SELEX).



The main results of our systematic analyses are the large TF binding specificity model datasets but additionally they have shed light to the general properties of the TF-DNA interactions revealing also: i) common DNA-mediated cooperativity occurring when multiple TFs bind to target sites that are situated in specific spacing and orientation relative to each other, ii) the way that CpG methylation promotes or inhibits the binding of certain TFs to their target sites, and iii) the extent of conservation of the TF DNA binding specificities between human and Drosophila, two species that are separated by over 600 million years of evolution.

Host: Dr. Timothy Hughes