A KJELDGAARD LECTURE

Thursday 21 April 2016 at 13:15
1632-201 AIAS auditorium
Same location for the PhD session

Christopher B. Burge
Massachusetts Institute of Technology
USA

Protein-RNA interactions and function of alternative 3' untranslated regions

Many RNA binding proteins (RBPs) bind specific RNA sequence motifs, but only a small fraction (5-10%) of RBP motif instances are occupied in vivo. To determine what additional contextual features discriminate between bound and unbound motifs, we performed a pooled in vitro binding assay using 12,000 mouse intronic RNA sequences with the RBPs MBNL1 and RBFOX2. Surprisingly, the subset of motif instances bound in vitro correlated with evolutionary conservation of alternative splicing and predicted both in vivo binding and developmental regulation. Multiple lines of evidence indicate that the primary context effect that impacts binding in vitro and in vivo is RNA secondary structure. Large-scale combinatorial mutagenesis of unfavorable sequence contexts revealed a consistent pattern whereby mutations or combinations of mutations that increased motif accessibility improved protein binding. Together, our results indicate widespread inhibition of motif binding by local RNA secondary structure and suggest that mutations that alter sequence context commonly impact RBP binding and regulation.

Host: Torben Heick Jensen, Gene Expression and Gene Medicine,
Department of Molecular Biology and Genetics, Aarhus University

The lecture will be followed by a chalk-board session for PhD students

The Kjeldgaard Lecture Series is organised by
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