

**BiRC seminar Friday, November 9th, 2012**

Adam Siepel: *Genome-wide inference of natural selection on human transcription factor binding sites*

For decades, it has been hypothesized that gene regulation has played a central role in human evolution, yet much remains unknown about the genome-wide impact of regulatory mutations. Here we use complete genome sequences and genome-wide chromatin immuno-precipitation and sequencing data to demonstrate that natural selection has exerted a profound influence on human transcription factor binding sites since our divergence from chimpanzees 4-6 million years ago. Our analysis is based on a new probabilistic method for characterizing natural selection from collections of short interspersed noncoding elements. We find that binding sites have experienced somewhat weaker selection than protein-coding genes, on average, but that the binding sites of several transcription factors show clear evidence of adaptation. We project that regulatory elements may make larger cumulative contributions than protein-coding genes to both adaptive substitutions and deleterious polymorphisms, which has important implications for human evolution and disease.