Small RNAs: computational challenges and global role in gene regulation

In recent years, small RNAs have gained enormous attention and have been implicated in many developmental and cellular functions. For example, microRNAs direct the inhibition of target messenger-RNA, whose misregulation can cause cancer. RasiRNAs and piRNAs are thought to silence mobile genetic elements and are ultimately responsible for genome integrity.

In this talk, I will show that a comparative analysis of 12 recently sequenced Drosophila species allows the de-novo discovery of miRNAs with unprecedented accuracy. We found more than 50 novel miRNA genes, many of which we validate experimentally. We also find distinct evolutionary signals for the precise annotation of the start position of mature miRNAs. This allows us to correct the annotation and strand of previously known miRNA genes, sometimes leading to drastic corrections in their target genes. When a precise signal for the miRNA start does not exist, we find that indeed experimental information suggests that multiple starts are used in practice. Similarly, when both strands score highly according to our evolutionary models, we find that indeed a mature product is found from both strands.

I will also present data from large scale sequencing of small RNAs, isolated from different Drosophila protein complexes. Intrestingly, we found that many of these sequences cluster in the genome and fall within regions known to be important for transposon silencing. Sequences from different protein complexes show an intriguing relationship that hints to a possible mechanism for small RNA mediated transposon silencing.