



University
of Basel

Department
Biozentrum



Swiss Institute of
Bioinformatics

BIOZENTRUM

The Center for
Molecular Life Sciences

Basel Computational Biology Seminar

Julian König

IMB Mainz, Germany

“Genomic views of splicing regulation”

Alternative splicing generates distinct mRNA isoforms and is crucial for proteome diversity in eukaryotes. The RNA-binding protein (RBP) U2AF2 is central to splicing decisions, as it recognizes 3' splice sites and recruits the spliceosome. We establish 'in vitro iCLIP' experiments, in which recombinant RBPs are incubated with long transcripts, to study how U2AF2 recognizes RNA sequences and how this is modulated by trans-acting RBPs. We measure U2AF2 affinities at hundreds of binding sites, and compare in vitro and in vivo binding landscapes by mathematical modeling. We find that trans-acting RBPs extensively regulate U2AF2 binding in vivo, including enhanced recruitment to 3' splice sites and clearance of introns. Using machine learning, we identify and experimentally validate novel trans-acting RBPs (including FUBP1, BRUNOL6 and PCBP1) that modulate U2AF2 binding and affect splicing outcomes. Our study offers a blueprint for the high-throughput characterization of in vitro mRNP assembly and in vivo splicing regulation.

Date: **Monday, May 6th, 2019**

Time: **16:00 h**

Room: **Pharmazentrum HS2**

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