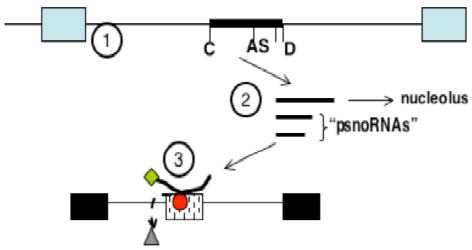
Rotation projects available

The lab studies the molecular basics of the *Prader-Willi Syndrome* and *Spinal Muscular Atrophy*. Based on this basic research, we develop rational therapeutic approaches for these diseases. The projects are funded by the National Institutes of Health and the Muscular Dystrophy Association until 2013 and would therefore be suitable for a ***Ph.D. project***

Prader Willi Syndrome

PWS is the most frequent genetic cause for type II diabetes. It is now clear that the loss of small nucleolar RNAs located in the PWS critical region on Chromosome 15 is the cause of the disease. We showed that these RNAs function in premRNA processing and discovered a new class of non-coding RNAs.

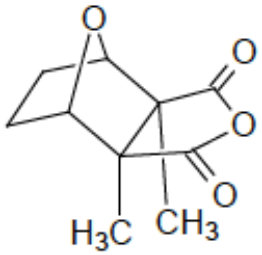


The rotation project would be to identify new target genes for these snoRNAs, determine their processing and analyze their composition. Techniques include RNAse protection analyses, RT-PCR, cell culture, transfection and bioinformatics approaches.

Reference: Kishore, S., and Stamm, S. (2006) The snoRNA HBII-52 regulates alternative splicing of the serotonin receptor 2C. Science **311**, 230-232.

Spinal Muscular Atrophy

Spinal Muscular Atrophy is the most common genetic cause for death of children. The disease could be cured if the alternative splicing pattern of a gene, SMN2 could be altered towards exon 7 inclusion. We demonstrated that tra2-beta1, a constiutive splicing factor promotes inclusion of this exon. We discovered that protein phosphatase 1 binds to tra2-beta1 and regulates its activity. PP1 inhibitors promote exon 7 inclusion. In collaboration with *David Watt*, an organic chemist, we designed a new class of compounds that appear to be non-toxic and promote exon 7 inclusion. The rotation project would analyze new compounds, test their toxicity and mechanism of action. Techniques include RNA mobility shifts, protein purification, RT-PCR, cell culture, transfection, and protein:protein interaction studies.



cantharidin

Reference: Novoyatleva, T., Heinrich, B., Tang, Y., Benderska, N., Butchbach, M. E., Lorson, C. L., Lorson, M. A., Ben-Dov, C., Fehlbaum, P., Bracco, L., Burghes, A. H., Bollen, M., and Stamm, S. (2008) Protein phosphatase 1 binds to the RNA recognition motif of several splicing factors and regulates alternative pre-mRNA processing. Hum Mol Genet, 52-70.