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## THE SMALL NUCLEOLAR RNAs AND THEIR POTENTIAL ROLE IN PWS

Alexander Hüttenhofer, M.D., Ph.D.

Innsbruck Biocentre, Division of Genomics and RNomics, Medical University Innsbruck, Innsbruck, Austria

In our quest to identify novel non-coding RNAs (ncRNAs) in model organisms (an approach for which we coined the term RNomics), we have identified three brain-specific ncRNAs, designated as HBII-13, HBII-52 and HBII-85 from a mouse brain cDNA library. We have isolated the human orthologs of the three ncRNAs and mapped them between the *SNRPN* and *UBE3A* genes on chromosome 15q11-q13. The region containing the three ncRNA genes has been implicated in the etiology of the Prader-Willi syndrome. Two of the ncRNA genes, HBII-52 and HBII-85, are encoded in tandemly repeated arrays of 47 or 27 units, respectively. Interestingly, these RNAs were absent from a PWS patient cortex and from a PWS mouse model, demonstrating their paternal imprinting status and pointing to their potential role in the etiology of PWS. By a bioinformatical approach, we were able to identify three additional ncRNA genes within the same locus, designated as HBII-436, HBII-438A and HBII-438B, which are also subject to imprinting and are predominately expressed in the brain.

Due to conserved sequence and structure motifs, the six ncRNAs can be assigned to the class of small nucleolar RNAs (snoRNAs). This class of RNA molecules has previously been shown to target ribosomal RNAs by a short antisense element located within snoRNAs. By this mechanism, ribosomal RNAs are targeted for modification at the site of complementarity to snoRNAs. All six brain-specific snoRNAs from the PWS region lack complementarity to ribosomal RNAs. In one case, the HBII-52 snoRNA, we could show a potential interaction with a brain-specific mRNA, the serotonin receptor mRNA 5-HT<sub>2c</sub> at a site where the mRNA is regulated by alternative splicing and editing. We could demonstrate that the HBII-52 snoRNA is able to regulate gene expression of the serotonin receptor 5-HT<sub>2c</sub> by modification of the mRNA. This implies novel biological function for this class of ncRNAs and points to their potential role in the etiology of PWS.