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"Coming here, you will discover yourself, discovering others"
Romanian Prader-Willi Association

ASOCIACIÓN MADRILEÑA
PARA EL SÍNDROME DE
PRADER-WILLI



CANDIDATE GENES FOR PRADER-WILLI SYNDROME

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The proximal long arm of human chromosome 15 (15q11-q13) contains a cluster of imprinted genes which are under the control of a bipartite imprinting centre. *MKRN3*, *MAGEL2*, *NDN*, *SNURF-SNRPN* and several snoRNA genes are expressed from the paternal chromosome only. In 2000, we identified an intronless gene (*C15orf2*) between *NDN* and *SNURF-SNRPN*, which encodes an 1156-amino-acid protein of unknown function. By Northern blot analysis we had found that *C15orf2* is exclusively expressed in testis. Biallelic expression of *C15orf2* in adult testis correlated with the absence of methylation of a 250 bp CpG island. *C15orf2* appears to be primate-specific and under strong positive selection. Recently, we have identified two novel genes (*prader-willi region non-protein-coding RNA 1 and 2*; *PWRN1* and *PWRN2*) between *NDN* and *C15orf2*. By data base search we found five partially duplicated copies, of which only one copy each appears to be active. *PWRN2* is only expressed in testis and biallelic. *PWRN1* transcripts are most abundant in testis, but present in other tissues, also. It is biallelically expressed in testis and kidney, but monoallelically in fetal brain. Methylation analysis of a CpG island 15 kb upstream of exon 1 showed absence of methylation in spermatozoa, but methylated and unmethylated alleles in fetal brain. Reinvestigation of *C15orf2* revealed that this gene is also expressed in fetal brain and that expression in this tissue is monoallelic.

Each of the above mentioned genes may play a role in PWS. There is no evidence that a mutation in a single gene causes the full phenotype of PWS. Atypical deletions in humans as well as mouse models may help to elucidate the contribution of each of these genes to PWS.