**Genetic and functional analysis of neuronatin in mice with maternal or paternal duplication of distal Chr 2.**

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**Abstract**

Functional differences between parental genomes are due to differential expression of parental alleles of imprinted genes. **Neuronatin** (Nnat) is a recently identified paternally expressed imprinted gene that is initially expressed in the rhombomeres and pituitary gland and later more widely in the central and peripheral nervous system mainly in postmitotic and differentiating neuroepithelial cells. Nnat maps to distal chromosome (Chr) 2, which contains an imprinting region that causes morphological abnormalities and early neonatal lethality. More detailed mapping analysis of Nnat showed that it is located between the T26H and T2Wa translocation breakpoints which is, surprisingly, proximal to the reported imprinting region between the T2Wa and T28H translocation breakpoints, suggesting that there may be two distinct imprinting regions on distal chromosome 2. To investigate the potential role of Nnat, we compared normal embryos with those which were PatDp.dist2.T26H (paternal duplication/maternal deficiency of chromosome 2 distal to the translocation breakpoint T26H) and MatDp.dist2.T26H. Expression of Nnat was detected in the PatDp.dist2.T26H embryos, where both copies of Nnat are paternally inherited, and normal embryos but no expression was detected in the MatDp.dist2.T26H embryos with the two maternally inherited copies. The differential expression of Nnat was supported by DNA methylation analysis with the paternally inherited alleles being unmethylated and the maternal alleles fully methylated. Although experimental embryos appeared grossly similar phenotypically in the structures where expression of Nnat was detected, differences in folding of the cerebellum were observed in neonates, and other more subtle developmental or behavioral effects due to gain or loss of Nnat cannot be ruled out.