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No Evidence for Monoallelic Expression of *Gnas* and Fourteen Other Genes in the Distal Region of Mouse Chromosome 2

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Distal chromosome 2 is one of ten regions of the mouse genome subject to parental imprinting. Maternal duplication/paternal deficiency of distal chromosome 2 leads to hypokinetic mice with long flat-sided bodies and arched backs, which fail to suckle and die within a few hours of birth. The reciprocal type, paternal duplication/matemal deficiency, shows an opposite phenotype: the mice have short square bodies and broad flat backs and are distinctly hyperkinetic [1]. The region is defined by the breakpoints of two reciprocal translocations, T(2;8)2Wa and T(2;16)28H, is estimated to be about 7.5 Mb in size and shows linkage conservation with human chromosome 20q13. We have tested for monoallelic expression of a number of candidate genes that are either likely or known to lie within the distal imprinting region. These included three-*Cebpb*, *E2f1* and *Tcf4*-that express transcription factors, two-*Cyp24* and *Pck1*-that are involved in growth, six-*Acra4*, *Edn3*, *Kcnb1*, *Mc3r*, *Ntsr* and *Ppgb*-where a defect could lead to neurological and probably behavioural problems, three:-*Cd40*, *Plcg1* and *Rcad*-that are doubtful candidates but whose sequence was available for testing their expression and finally, *Gnas*, which is our best candidate because there is clinical and biochemical evidence suggesting that its human homologue, GNAS1, is imprinted. On/off expression of each gene was tested by RT-PCR analysis of RNA extracted from tissues of mice with maternal duplication/paternal deficiency and its reciprocal for the distal region of chromosome 2. None of these genes was monoallelically expressed in the appropriate tissues before and after birth, suggesting that they are not imprinted. Evidence for the imprinting of GNAS1 in humans is based on studies of patients with Albright's hereditary osteodystrophy (AHO) who possess a dysfunctional GNAS1 allele. AHO somatic features together-with resistance to parathyroid hormone and other hormones that act via cAMP occur when the defective allele is inherited from

the mother whereas AHO somatic features alone occur in paternally transmitted cases [2]. If genomic imprinting regulates *Gnas* expression in the mouse, then its effect must be specifically confined to hormone-responsive cells.

REFERENCES

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