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Contributions of Mouse Genetic Studies to Genomic Imprinting

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Maternal and paternal disomies and equivalent duplications for specific chromosome regions can readily be generated in the mouse. Most do not result in abnormality but for 10 regions distributed over 6 chromosomes developmental anomalies ranging from early embryonic lethalities to characteristic phenotypic abnormalities occur. With certain chromosome regions, maternal or paternal duplication leads to different and, in some cases, opposite anomalies so that, in total, 15 different imprinting effects can be distinguished. These observations have provided key evidence on the occurrence of imprinting in mammals.

On the basis of the established homologies between mouse and human chromosomes, it is possible to predict which segments of the human genome are subject to equivalent imprinting. In this regard it is significant that candidate imprinting effects for the two classical examples of imprinting in humans, namely the Prader-Willi and Angelman syndromes, have been found in the mouse.

Current studies are aimed at reducing the size of the imprinting regions with the objective of facilitating identification of the genes involved. Furthermore, the developmental profiles of genes already identified as being subject to imprinting are being determined.

A new approach involves the analysis of a novel mutation that causes growth retardation and cranial abnormalities and which shows the inheritance pattern of an imprinted gene, as originally predicted by Hall (Am J Hum Genet 46: 857, 1990). It is anticipated that the mutation will represent a deletion and will lie within one of the recognised imprinting regions.

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