ABSTRACTS

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GENOMIC IMPRINTING IN CANINE

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For the vast majority of mammalian genes, maternally- and paternally-derived alleles behave identically and are either expressed or repressed, regardless of whether they were inherited from egg or sperm. For imprinted genes however, this is not the case. The alleles of imprinted genes are epigenetically modified in a parent-of-origin-specific manner and, as a consequence, maternally- and paternally-derived alleles behave differently (1). Typically one allele is expressed while the other is silent. Although relatively few in number, imprinted genes are the focus of intensive study since they have important roles in embryonic development. Abnormal expression of imprinted genes results in growth disorders and is implicated in several clinical conditions. The epigenetic modifications associated with imprinted genes (their ‘imprints’) are susceptible to environmental influences, and it appears that these modifications can be dysregulated by the manipulations and/or culture conditions involved in processes such as in vitro fertilization and somatic cell nuclear transfer. Thus aberrant expression of imprinted genes may limit the success of such procedures. Most studies of imprinted genes have been performed in rodents or primates, with limited studies in other mammals such as bovine and opossum. We have recently demonstrated the existence of imprinted genes in the canine, by showing that the canine IGF2 receptor gene (IGF2R) is monoallelically expressed, with predominant expression of the maternally-derived allele and repression of the paternally-inherited allele (2). Our study indicated that the imprinted canine IGF2R was different in important respects from the imprinted murine ortholog and resembled the imprinted opossum IGF2R. These findings indicate the comparative value of studying genomic imprinting in the canine. We have now extended our study to the examination of two additional canine genes: the gene coding for the foetal mitogen IGF2, and a gene called H19 that gives rise to a non-coding RNA. Both genes have important roles in prenatal growth of mammals. Using umbilical cord cDNA, we have shown that both genes are expressed monoallelically in the canine: IGF2 is expressed from the paternally-derived allele, while the maternally-derived H19 allele is expressed. IGF2 and H19 are neighboring genes in all placental mammals studied to date. Typically, monoallelic expression of the two genes is regulated by an imprint control region (ICR) between the two that functions as an insulator. The ICR contains a CpG island that is methylated during spermatogenesis but not during oogenesis, and is consequently referred to as a differentially methylated region (DMR). In its unmethylated state (maternally-derived allele), the ICR has insulator function and allows expression of H19, but not of IGF2. Methylation of the ICR prevents insulator function and allows expression of the paternally-derived IGF2 allele. We are now examining the methylation status of a CpG island located between the canine IGF2 and H19 genes, using the bisulfite sequencing approach. Preliminary results indicate differential methylation of this region in genomic DNA derived from umbilical cord. Analysis of genomic DNA from canine semen indicates that this methylation is generated during spermatogenesis. Our ultimate goal is to characterize all imprinted genes in the canine, and to understand how they contribute to canine reproduction, development and disease. Such knowledge will be vital for optimising the success of most reproductive strategies in canines.

References