

Analysis of Differentially Expressed Genes in Spontaneously Occurring Canine Melanoma

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Abstract : Introduction: Human and canine melanoma have common clinical, histologic characteristics making dogs a good model for comparative oncology. The identification of specific genes and a better understanding of the genetic landscape, signaling pathways, and tumor-microenvironmental interactions involved in the cancer onset and progression is essential for the development of therapeutic strategies against this tumor in both species. In the present study, the differential expression of genes in spontaneously occurring canine melanoma and in paired normal tissue was investigated by targeted RNAseq. Material and Methods: Total RNA was extracted from 17 canine malignant melanoma (CMM) samples and from five paired normal tissues stored in RNA-later. In order to capture the greater genetic variability, gene expression analysis was carried out using two panels (Qiagen): Human Immuno-Oncology (HIO) and Mouse-Immuno-Oncology (MIO) and the miSeq platform (Illumina). These kits allow the detection of the expression profile of 990 genes involved in the immune response against tumors in humans and mice. The data were analyzed through the CLCbio Genomics Workbench (Qiagen) software using the *Canis lupus familiaris* genome as a reference. Data analysis were carried out both comparing the biologic group (tumoral vs. healthy tissues) and comparing neoplastic tissue vs. paired healthy tissue; a Fold Change greater than two and a p-value less than 0.05 were set as the threshold to select interesting genes. Results and Discussion: Using HIO 63, down-regulated genes were detected; 13 of those were also down-regulated comparing neoplastic sample vs. paired healthy tissue. Eighteen genes were up-regulated, 14 of those were also down-regulated comparing neoplastic sample vs. paired healthy tissue. Using the MIO, 35 down regulated-genes were detected; only four of these were down-regulated, also comparing neoplastic sample vs. paired healthy tissue. Twelve genes were up-regulated in both types of analysis. Considering the two kits, the greatest variation in Fold Change was in up-regulated genes. Dogs displayed a greater genetic homology with humans than mice; moreover, the results have shown that the two kits are able to detect different genes. Most of these genes have specific cellular functions or belong to some enzymatic categories; some have already been described to be correlated to human melanoma and confirm the validity of the dog as a model for the study of molecular aspects of human melanoma.

Keywords : animal model, canine melanoma, gene expression, spontaneous tumors, targeted RNAseq

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