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Novel epigenetic markers of chromosome instability in canine solid tumors

One of the most prominent characteristics of solid tumors is the highly abnormal chromosome complement induced by widespread aneuploidy and complex non-reciprocal translocations. Comparative oncology studies have identified major similarities between human and canine tumors, including histologic appearance, tumor genetics and the presence of chromosome instability. However, the mechanisms of chromosome instability are not known. Here, we use the power of mouse genetics in combination with epigenetic and genome wide analysis to search for highly conserved pathways amongst different species. We aim to evaluate target genes and proteins important in cancer biology and determine their potential use as markers of chromosome instability in pre-clinical models. Polycomb repressive proteins are chromatin-remodeling factors essential for stem-cell viability and function. Both a reduction in polycomb protein levels as well as their overexpression may induce malignant neoplastic transformation. Our results indicate that loss of Polycomb proteins in mouse cells induce severe chromosome instability in the form of complex chromosomal rearrangements including deletions, translocations and chromosome fusions. Such chromosome defects are associated with abnormal centromere and telomere function. Notably, Polycomb proteins exhibit a striking >60 fold overexpression in human ovarian cancer cell lines. In addition, transcriptional profiling of canine mammary gland carcinoma cells revealed a significant ($p<0.05$) overexpression of Polycomb transcript levels as well as DNA repair enzymes compared with normal canine mammary gland epithelial cells. Collectively, our results suggest that Polycomb proteins are at the crossroads between DNA repair and pathways that signal the presence of chromosome instability in mammalian cells. Importantly, abnormal activation of DNA repair enzymes in canine mammary tumors is a conserved mechanism associated with severe chromosome instability.

Biography

Rabindranath De La Fuente was graduated with Doctor of Veterinary Medicine degree from the National Autonomous University of Mexico (UNAM) and completed MSc and PhD degrees in Biomedical Sciences at the Ontario Veterinary College, University of Guelph in Ontario, Canada. Following a Post-doctoral training at the Jackson Laboratory in Bar Harbor, Maine, he established a research program in Mammalian Epigenetics. He is currently an Associate Professor at the University of Georgia, College of Veterinary Medicine. He has published more than 30 papers in reputed peer-reviewed journals and currently serves as an Editorial Board Member of *Molecular Human Reproduction* (Oxford, UK).

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