

Role of Chromosomes in Cancer: Diagnosis and Prognosis
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Cancer occurs when the normal cell cycle control mechanisms become defective, resulting in uncontrollable cellular growth. Within each cell the genome is organized into a series of chromosomes, nature's biological filing cabinets. In human cancer studies, it has been established that almost all forms of human cancer are associated with non-random "shuffling" of the genome in the form of both structural and numerical chromosome rearrangements. Many of these recurrent chromosome aberrations have been significantly associated with specific histopathological or immunological subgroups and also with response to therapy. These associations are now widely used as important diagnostic and prognostic aides during the evaluation of human cancers and have led to improved clinical management of patients. Patients with a good prognosis have been spared unnecessary treatment and, conversely, for cases presenting with a cytogenetic abnormality indicative of a poor prognosis, more intensive treatment has improved the outcome of these patients. The World Health Organization recognizes that genetic abnormalities are one of the most reliable criteria for the classification of tumors and has stressed the importance of further research into this area.

Humans and dogs share a remarkably high level of genetic similarity and both species are exposed to identical environments. However, the extent and identity of chromosome aberrations associated with canine cancers remains largely unknown. This is primarily due to the difficulty in identifying reliably many of the dog chromosomes. We overcame this difficulty by developing a set of chromosome-specific reagents that were used to identify unequivocally each chromosome of the dog. These reagents were also used to contribute to the development of the first integrated canine genome map and to determine the distribution of evolutionarily conserved chromosome segments shared between the human and canine karyotypes. These data allow chromosome aberrations found in dog cancers to be compared directly with the chromosome aberrations associated with corresponding human cancers.

We have already identified a series of recurrent chromosome aberration in canine cancers that are breed and/or tumor-type specific. We are now focusing our attention on such aberrations as a means to ensure that the correlation between chromosome aberrations and clinical manifestation of

canine cancers is thoroughly evaluated. In this way we will be able to develop additional aides for the diagnosis, prognosis and treatment of canine cancers.