Lymphoma (lymphosarcoma) represents the third most common canine neoplasm, and is generally regarded as closely related to forms of human non-Hodgkin’s lymphoma (NHL). Human NHL demonstrates a range of both generalised and subtype-specific, non-random chromosome abnormalities. A number of these aberrations have been correlated with disease progression and response to therapy, aiding the accurate diagnosis, prognosis and appropriate therapy selection for each subtype of human NHL.

At present, the prognosis for canine lymphoma is generally guarded, although a proportion of cases is highly responsive to appropriate chemotherapy. A greater understanding of the underlying mechanisms of dog lymphoma, particularly subtype-specific characteristics, is therefore required. As with human NHL, there is evidence to suggest that dog lymphomas of B-cell origin display fewer chromosome aberrations, and are more responsive to chemotherapy, than those of T-cell origin. Previous cytogenetic studies of dog lymphoma were severely limited by difficulties in accurate chromosome identification and characterisation of aberrant karyotypes; however, we have now made major advances in the development of molecular cytogenetic techniques and resources for the dog that allow these limitations to be largely overcome. Our group is performing an ongoing cytogenetic analysis of dog lymphomas in order to identify consistent chromosome aberrations, to correlate these with the clinical course of the disease, and in turn to enable differentiation of specific lymphoma subtypes. Through our dog-human comparative genomics studies, we aim to determine whether there is an evolutionary link between the genetic basis of lymphoma in these two species, as well as generating additional prognostic indicators that may influence the decision to treat the animal, and the form that treatment takes.

We are performing both direct and indirect techniques for cancer cell karyotype analysis on naive canine lymphoma cases. Each case receives diagnostic histological evaluation and immunophenotyping using CD79a and CD3 markers. Comparative genomic hybridisation (CGH) analysis is performed to detect unbalanced chromosome aberrations, resulting from gain or loss of chromosome material in the tumour as compared to a clinically normal reference individual. Direct study of cancer cell karyotypes is performed by short-term culture of fresh lymphoma tissue to generate metaphase chromosomes. Our panels of chromosome-specific paint probes and single locus probes are then used to characterise chromosome translocations, and to further examine the genomic imbalances detected by CGH analysis. Aberrations detected in each case studied are then correlated in the first instance with the immunophenotyping data, towards more detailed subclassification of this heterogeneous cancer.

To further advance the human-dog comparative genome map, we have also isolated and chromosomally assigned the dog orthologues of 20 proto-oncogenes and tumour suppressor genes that are implicated in common human cancers. This expanding panel of markers is being used to identify and characterise both balanced and unbalanced chromosome aberrations in tumour cells, further aiding the correlation of canine and human cancers at the molecular level. The approaches used in our ongoing study will be demonstrated by describing our studies of one particularly unusual lymphoma case. A nine year old entire male collie x retriever-cross presented with an enlarged prescapular lymph node and a mass under the left mandibular region. A diagnosis of lymphoma was confirmed by histological evaluation of fixed tissue sections, and immunophenotyping demonstrated that 95% of tumour cells expressed both CD3 and CD79a cell markers, indicating B- and T-cell co-expression. Co-expression is extremely rare in human lymphoma, and to our knowledge has not been described in the dog. CGH analysis detected loss of dog chromosomes 11, 30 and 38, and gain of chromosome 36, which was supported by direct analysis of tumour metaphases using chromosome specific probes representing each of these four chromosomes. No recurrent chromosome translocations were detected.