

FLATCOATED RETRIEVER TUMOUR SURVEY REPORT 2015

Overview 1990 – 2014

by Dr Jane Dobson read by Debbie Miller

TUMOUR SURVEY

In 1990, due to the concern about the number of Flatcoated Retrievers dying from cancer, an independent enterprise administered by its Trustees, in collaboration with Dr Jane Dobson, Department of Veterinary Medicine, University of Cambridge set up the Tumour Survey.

The Trustees involved past and present:-

Mrs Sheila Godbolt

Mrs Shirley Johnson

Mr Brian Jones

Mrs Debbie Miller

Mr Martin Roe MRCVS

Mrs Betty Roe

Mrs Mary Tanner

The aim was to diagnose and document the type of tumours affecting the breed by offering a free pathology service to owners with the cost of processing being paid for through the tumour survey by donations and fund raising events.

Since its beginnings, we have now received 2,975 submissions. Many of these submissions had more than one sample for processing, making the total number well over 3,000.

These, along with the information collected have been invaluable in understanding the high incidence of histiocytic sarcoma within the breed.

Over the years our work has consisted of:

HEALTH STUDY

In 1996 we recruited 174 dogs into the "Health Study" and we followed their medical and reproductive history for their lifetime, by way of an annual questionnaire. Preliminary analysis of pedigrees strongly suggested the disease was familial. This information formed the basis of a successful grant application by Dr David Sargan & Dr Jane Dobson to CRUK.

GRANTS AWARDED

CRUK – Dr David Sargan / Dr Jesus Aguirre-Hernandez

To study the molecular genetic basis of the histiocytic sarcoma by examining regions of DNA along the whole canine genome.

Petplan Charitable Trust – Dr David Sargan / Dr Jesus Aguirre-Hernandez / Dr Fiona Behan

To use microRNA (miRNA) profiling as a means to gain a better understanding of soft tissue sarcomas and histiocytic sarcomas in particular.

Overall, this study has selected miRNAs that are most significantly associated with particular FCR soft tissue sarcomas. Hopefully, this information will be used to improve the classification and also the accuracy of prognostic forecasting for these tumours in Flatcoated Retrievers. This will allow a more informed consideration of treatment options.

IN-HOUSE FUNDING

Dr Jesus Aguirre-Hernandez

Comparing Dog Leucocyte Antigen (DLA) alleles in affected dogs with histiocytic sarcoma and non-affected dogs.

We hoped there would be a difference between the cases and controls, showing the cases were not able to recognize the tumours prior to them becoming a clinical problem. Unfortunately we found no difference at all between cases and controls in these genes, so we have to discount this theory.

Dr Ola Marcinowska

Characterisation of T lymphocytes in histiocytic sarcomas.

The results revealed splenic HS expressed a significantly higher proportion of naïve T cells than localised HS. A naïve T cell is considered a mature cell that has yet to encounter an antigen. We also found that localised tumours expressed a higher percentage of positive cells to FoxP3, a marker of regulatory T cells. Such cells may inhibit the body's ability to suppress the formation of cancerous cells.

The above work has resulted in several publications in veterinary journals and poster presentations at veterinary congresses internationally. (details at the end of this article)

OTHER STUDIES

Web-based Register of Death for the breed in the UK. This is running successful and Val Jones has reported separately on this.

TO CONCLUDE

The tumour survey has been ongoing for 25 years now and its initial aim to diagnose and document the type of tumours affecting the breed has been achieved. As this has always been administered as an independent enterprise it may be an opportunity to review the survey and consider further work to be performed in collaboration with the breed society.

We thank all owners/breeders for the continued support and valuable contribution to all our studies over the years.

PROPOSAL FOR FURTHER STUDIES

We have previously documented the presence of infiltrating T cells in canine histiocytic sarcomas (Constantino-Casas et al, 2011) and recently demonstrated that a significant proportion of these are regulatory T cells (Marcinowska et al, 2014, abstract). The current proposal is to establish and validate a panel of reagents (antibodies) to allow us to examine T cell profiles (including T-regs) in the peripheral blood and tumour tissue of dogs bearing histiocytic sarcoma and T cell lymphoma by flow cytometry, to document changes in these profiles during the course of treatment and at relapse, and determine whether these correlate with prognosis.

To achieve this we require fresh blood and tissue samples as the tests have to be performed within 24 hours of sample collection.

Once this panel/technique is established and validated it could also be used for other projects to examine T cell profiles in peripheral blood of dogs receiving both conventional and metronomic chemotherapy, as immunomodulation through regulation of T cell function is one proposed mechanism of action for metronomic chemotherapy and in tumour microenvironment studies to determine the nature (T cell vs macrophage) and proportions of infiltrating inflammatory cells in naturally occurring canine tumours.

Summary by Debbie Miller

As Dr Jane Dobson has reported the tumour survey has been ongoing for over 25 years now and its initial aim to diagnose and document the type of tumours affecting the breed has been achieved. Following a recent meeting with Jane we have agreed it is time to wind down and close the survey. Now that pathological specimens are no longer needed it makes sense for any future cancer research for the breed to be handled by the Society's Health Committee.

It is therefore apposite that the Trustees now hand the cancer baton over, with this proposal for tissue research to Liz Branscombe – your new Health Co-ordinator. I feel sure Liz will be an ideal incumbent to embrace yet another challenge to her already busy health agenda.

The ground breaking research over two and a half decades would not have been possible without the help and support of all Flatcoat owners who were prepared to submit tumours and blood to Cambridge. And too, without the fund raising which came from many sources, including the hard work of the Litter Co-ordinator, Shirley Johnson, and many a raffle, coffee morning or private donation the scheme would never have been so successful. It shows the care so many had, and still have, for the health of our lovely dogs. On behalf of the Trustees and the survey I thank every one of you.

Not only would I like to acknowledge the Trustees for their support in running the survey I would particularly like to express my appreciation to Val Jones for her time and commitment. Despite the scheme being outside the remit of the Society, we have worked closely in exchanging information as I believe it was the only way forward, as after all, we were working to a common

goal in regards to the health of our Flatcoats.

Importunately I feel too it is appropriate that Dr Jane Dobson is congratulated on her unique achievements for our breed which came about because one caring owner, Sheila Godbolt, who took the initiative to try and help but sadly died herself from the disease she most feared for our Flatcoats – Cancer.

On a personal note I should like to add that I will miss all the calls particularly from many companion owners who have shared their joys, and their fears and concerns of tumours, in this special breed of ours. It has been an honour and a pleasure.

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Publications & Presentations arising from our Studies into Cancer in flat-coated Retrievers.

1. Morris JS., Bostock DE., McInnes EF., Hoather TM., **Dobson JM.** A histopathological survey of neoplasms in flat-coated retrievers: 1990 – 1998. *Veterinary Record* 147: 291 – 295, 2000.
2. Morris JS., McInnes EF., Bostock DE., Hoather TM., **Dobson JM.** Immunohistochemical and Histopathologic features of 14 malignant fibrous histiocytomas from flat-coated retrievers. *Vet Pathol* 39: 473 - 479, 2002.
3. Mellanby RJ., Holloway A., Chantrey J., Herrtage ME & **Dobson JM.** Immune-mediated haemolytic anaemia associated with a sarcoma in a flat-coated retriever [Case Report] *Journal of Small Animal Practice* 45: 21 - 24, 2004
4. **Dobson J.M.** Villiers E., Roulois A., Gould S., Mellor P., Hoather T., Watson P. Histiocytic sarcoma of the spleen in flat-coated retrievers presenting with regenerative anaemia and hypoproteinaemia. *Veterinary Record* 158 (24) 825 – 829, 2006
5. **Dobson J.M.**, Hoather T., McKinley T.J. & Wood J. Mortality in a Cohort of Flat-coated Retrievers in the UK. *Veterinary and Comparative Oncology*, 7 (2) : 115 – 121, 2009
6. Constantino-Casas F., Mayhew D., Hoather T.M. **Dobson J.M.** The presentation and classification of histiocytic sarcomas in the flat-coated retriever. *Veterinary Pathology* May 2011 48: 764-771, first published on October 7, 2010 doi:10.1177/0300985810385153
7. Abbondati E, Del-Pozo J, Hoather T, Constantino-Casas F, Dobson J An immunohistochemical study of the expression of the hypoxia markers Glut-1 and Ca-IX in canine tumors. *Veterinary Pathology* 50(6):1063 – 1069, 2013. E pub 29th April 2013

Presentations

1. Morris JS, Bostock DE., McInnes E., Hoather T., **Dobson JM** . A histopathological survey of cancer in the Flat-coated Retriever. *Clinical Research Abstract*, BSAVA Congress 1999, Congress Synopses p 314.
2. Aguirre_hernandez J., Dobson JM., Hoather T. Sargan D. Inheritance of histiocytic sarcomas in flat-coated retrievers. *BSAVA Congress 2005 Scientific Proceedings* p 634
3. Dobson JM Radiation response of appendicular histiocytic sarcoma in flat-coated retrievers. *ESVONC Spring meeting, Cambridge, March 2007*
4. Marcinowska A, Hoather T, Williams T, Dobson J, Constantino-Casas F Assessment of infiltrating lymphocytes in histiocytic sarcoma of Flat-coated retriever: a comparison of different locations. *ESVONC Congress 2014.*