PG Research Day 2019 – Impact Statement
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Genetics of Breed Susceptibility to Canine Diabetes Mellitus and Insulinoma: From One Extreme to the Other

Diabetes mellitus (DM) affects approximately 1 in 300 dogs in the UK[1,2], with prevalence reported to be even higher in other countries[3]. The mechanisms leading to hyperglycaemia are poorly understood, although a number of disease processes are thought to be involved[4]. Currently, the only effective treatment for canine DM is daily insulin injections, to control clinical signs. As well as the risk of insulin-induced hypoglycaemia, management of the condition places a huge financial and lifestyle burden on dog owners. This project is investigating the genetic causes of canine DM, to understand why it occurs more frequently in some breeds than others. By carrying out whole genome sequencing (WGS) analysis of breeds at high risk of developing the disease (e.g. Samoyed) and those at extremely low risk (e.g. Boxer), the aim is to identify genetic factors that make some dogs more likely to become diabetic. Understanding these factors will offer insights into disease aetiology and provide the potential for development of novel diagnostic and treatment strategies. The project will concurrently investigate why certain breeds (e.g. Boxer) that are resistant to canine DM, are at high risk of malignant β-cell transformation, leading to insulinoma.

An immediate benefit of the research will be an increased understanding of the pathogenesis of canine DM and insulinoma. This has inherent value by allowing the veterinary profession, researchers and dog owners to better understand these conditions. It will also improve the design of future studies of canine DM, by allowing sub-grouping of diabetic patients according to disease aetiology and reducing the error caused by inclusion of phenocopies. The research will be disseminated by publication in veterinary journals and presentation at conferences such as ECVIM[a] and ICCFGG[b]. Additionally, a collaborative group of experts, the Canine Diabetes Genetics Partnership (CDGP), was set up at the start of the project, to provide a broad range of specialist input and ensure increased visibility of the work. The recently-created CDGP website and social media channels will be used to communicate research outcomes to the wider society and provide a fantastic opportunity for public engagement. Examples include communication with breed groups (e.g. the Samoyed foundation, who have already provided financial support for the project) and attendance at breed shows.

The sharing of the new WGS datasets with the international research community will be of economic benefit, by reducing sequencing costs in future studies of other canine diseases. The data will contribute to publicly accessible archives of canine genomic data, maximising the benefits to canine health. Furthermore, findings may offer insight into the genetics of human DM, unlocking potential translational benefits in human medicine, where DM is of enormous social and economic burden[5].

The project aims to identify disease pathways and molecular targets that could lead to novel diagnostic and treatment options. This will be assisted by the project partnership with the pharmaceutical company, Dechra Veterinary Products, who recognise the potential commercial benefit of the project. Possible developments include preventative strategies or a personalised medicine approach to treatment. Advancement in this area will improve canine health and welfare, as well as reducing the negative impact of DM and insulinoma on owners of affected dogs.

Abbreviations
[a] European Congress of Veterinary Internal Medicine
[b] International Conference on Canine and Feline Genetics and Genomics

References

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[3] Fracassi, F. *et al.* Breed Distribution of Canine Diabetes Mellitus in Italy. *Vet. Res. Commun.* **28,** 339–342 (2004)

[4] Catchpole, B. *et al.* Canine diabetes mellitus: can old dogs teach us new tricks? *Diabetologia* **48,** 1948–1956 (2005)

[5] Cho, N. H. *et al.* IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res. Clin. Pract.* **138,** 271–281 (2018)