WINN FELINE FOUNDATION
For the Health and Well-being of All Cats

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PRECISION MEDICINE GENOMICS FOR CATS (CONTINUED)

PROJECT STUDY: Precision medicine genomics for cats (continued)

Principal Investigator: Leslie Lyons PhD; University of Missouri-Columbia

Interim progress report summary, MT19-001

The overall focus of our research is to discover DNA variants causing traits and diseases in domestic cats and their breeds. The overall goal is to eradicate genetic diseases from cat populations using genetic testing that will inform owners and breeders of the status of their animals so they can use proper breeding practices to eliminate diseases or produce desired traits.

More recently, because genome sequencing has become affordable, a complete DNA profile of an animal can be produced by whole genome (WGS) or whole exome sequencing (WES). This advance now allows Precision Medicine to be feasible in animal health care, i.e., using an animal's DNA profile to make informed and targeted decisions for treatment. For Precision Medicine to be feasible in the clinic, the process of DNA sequencing and data analyses must be rapid so that targeted treatments deduced from the identified DNA mutations can be implemented within the normal course of treatment for a health condition. This grant is focused on improving the pipelines/workflows that lead to rapid whole genome, DNA profiling of cats, not only to identify the mutations, but to make Precision Medicine feasible.

The specific aims of this project are to develop rapid and efficient workflows for whole exome sequencing (WES) and structural variant (SV) annotation in cats as an asset for the research community and to identify disease causing variants in projects initiated by the Lyons Laboratory. The workflow for the whole exome sequencing has been completed and has been successfully implemented to identify disease mutations in cats.

The Lyons Laboratory identified a causal variant for neuronal ceroid lipofuscinosis in the gene *CLN6* (published), a second mutation for polycystic kidney disease in the gene *PKD2*, and re-identified a Greek cat with a mutation in *SLCA3A1* causing cystinuria (publication submitted).

Two papers are in preparation with UC Davis (Dr. Karen Vernau) on hypothyroidism and with the University of Bristol for pycnodysostosis. Four additional candidate variants are under investigation for Vitamin D deficiency in a Singapura, a type of Ehlers-Danlos syndrome in a Japanese domestic shorthair with colleagues in Japan, as well as a candidate mutation for atrichia in the Peterbald and candidates for mediastinal lymphoma in Orientals. Additional variants for other diseases will be examined after the next analysis of the 99 Lives exome dataset with the newly submitted cat exomes to be submitted Fall 2020.

At least 5 variants have been validated and will be published. Four additional variants are under investigation. Thus, at least 4 publications are expected. Therefore, the Laboratory considers the project 100% successful but still hope to prove additional DNA variants leading to additional publications. SV analyses will be conducted with the next iteration of the data from the 99 Lives project.

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