



# WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

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637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • [www.winnfelinefoundation.org](http://www.winnfelinefoundation.org)

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## PRECISION MEDICINE GENOMICS FOR CATS

**PROJECT STUDY:** Precision medicine genomics for cats.

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

*Final report summary, MT18-009; MTW18-009*

The 99 Lives Cat Genome Sequencing Initiative is a project that combines genetic information from domestic cats from all over the world. As of end of summer 2019, the project will have genome sequences from over 225 domestic cats. Researchers usually submit whole genome DNA sequence from a diseased cat. This DNA sequence gets processed by the Lyons laboratory and the resulting variant call file (VCF) is accessible to participating researchers. The objective this project was to develop automated workflows that can process and combine these data efficiently, which has been successfully completed. With this workflow, researcher participants can then more easily find DNA changes that likely cause the diseases in their submitted cat. The analysis of these cat genetic data is complex but similar to techniques used in human genetics.

Recently, there was a major improvement in the reference assembly of the DNA in cat chromosomes, making assembly version 9.0 one of the best genetic references of all species. The genetic data from the 99 Lives project (~195 domestic cats) was compared to this new reference to identify DNA differences between a study cat and the reference. These DNA differences were then compared to other databases to help determine if newly identified DNA variants are “good variants” for genetic diversity, or “bad variants” that cause disease. The project has been successful, the Lyons laboratory has updated the genetic data to the new reference and has shared the results (VCF file) with the research community.

Since the project has had early success, an even larger dataset is now being processed for the research community, including > 225 cats. Also, over 250 cats may be processed to help develop a new high-density DNA array for cat research studies. **The Lyons laboratory has contributed ~50% of the cats in the 99 Lives project and has successfully identified DNA mutations for two different forms of methemoglobinemia, dwarfism in the “Munchkin” cat breed, Chediak-Higashi Syndrome and a cranial developmental abnormality in Oriental cats that causes hydrocephalus.** Two of these studies have been submitted for publication and two manuscripts are in preparation. They have also hosted external investigators at MU to support their data analyses. Most recently, a member of the cat HCM Consortium has been using our software for variant discovery in a variety of cats with cardiac disease. Additional funding will be requested to continue the support of the 99 Lives research effort.

*Summary prepared for Winn Feline Foundation © 2020*

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The Winn Feline Foundation is a non-profit organization [501(c)(3)] established by The Cat Fancier's Association.

Member Combined Federal Campaign #10321

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## Publications:

Clinical, metabolic, and genetic characterization of hereditary methemoglobinemia caused by cytochrome b5 reductase deficiency in cats. J.A. Jaffey,<sup>a,\*</sup> N.S. Reading,<sup>b-d</sup> U Giger,<sup>e</sup> O., Abdulmalik,<sup>h</sup> R.M. Buckley,<sup>f</sup> S. Johnstone,<sup>g</sup> L.A. Lyons<sup>f</sup> and the 99 Lives Cat Genome Consortium *Description of two variants for methemoglobinemia* [J Vet Intern Med.](#) 2019 Oct 25. doi: 10.1111/jvim.15637. [Epub ahead of print]

[Assisted reproduction mediated resurrection of a feline model for Chediak-Higashi syndrome caused by a large duplication in LYST.](#) Buckley RM, Grahn RA, Gandolfi B, Herrick JR, Kittleson MD, Bateman HL, Newsom J, Swanson WF, Prieur DJ, Lyons LA. *Sci Rep.* 2020 Jan 9;10(1):64. doi: 10.1038/s41598-019-56896-9.

A new domestic cat genome assembly empowers feline genomic medicine. Reuben M. Buckley<sup>1</sup>, Wesley A. Brashear<sup>2</sup>, Brian W. Davis<sup>2</sup>, Fabiana H. G. Farias<sup>3</sup>, Tina Graves<sup>3</sup>, LaDeana W. Hillier<sup>3</sup>, Milinn Kremitzki<sup>3</sup>, K. Kuroki<sup>4</sup>, Gang Li<sup>2</sup>, Rondo Middleton<sup>5</sup>, Patrick Minx<sup>3</sup>, Chad Tomlinson<sup>3</sup>, Leslie A. Lyons<sup>1</sup>, William J. Murphy<sup>2</sup>, Wesley C. Warren<sup>5,6</sup> and the 99 Lives Consortium. (Accepted – PLoS Genetics). *Description of dwarfism variant*

A deletion of *GDF7* is associated with feline forebrain commissural malformation concurrent with ventriculomegaly and interhemispheric cysts. Yoshihiko Yu<sup>1,2,\*</sup>, Reuben M. Buckley<sup>1,\*</sup>, Erica K. Creighton<sup>1,\*</sup>, Leslie A. Lyons<sup>1,†</sup>, 99 Lives Consortium. (Accepted - Genes).

[Neuronal Ceroid Lipofuscinosis in a Domestic Cat Associated with a DNA Sequence Variant That Creates a Premature Stop Codon in \*CLN6\*.](#) Katz ML, Buckley RM, Biegen V, O'Brien DP, Johnson GC, Warren WC, Lyons LA. Katz ML, et al. G3 (Bethesda). 2020 Jun 9:g3.401407.2020. doi: 10.1534/g3.120.401407. Online ahead of print. G3 (Bethesda). 2020.PMID: 32518081

## Presentations:

Plant and Animal Genetics, January 2019

Advances in Canine and Feline Genetics and Genomics, Bern, Switzerland, April 2019

International Society of Animal Genetics, Lleida, Spain, July 2019

World Cat Congress, Cape Town, South Africa, July 2019

American Society of Human Genetics, Houston, Texas, October 2019

## Requests for Winn Feline Foundation Assistance:

**Future efforts for Precision Medicine in cats will be focusing on random bred cats that make up over 90% of the cat population in the USA. We need general practice and feline specialists to become aware of the 99 Lives project and help provide new and interesting heritable disease presentations for future genome sequencing efforts. Thus, we need to spread the word of our success to the lay public and primary care veterinarians and specialists.**

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