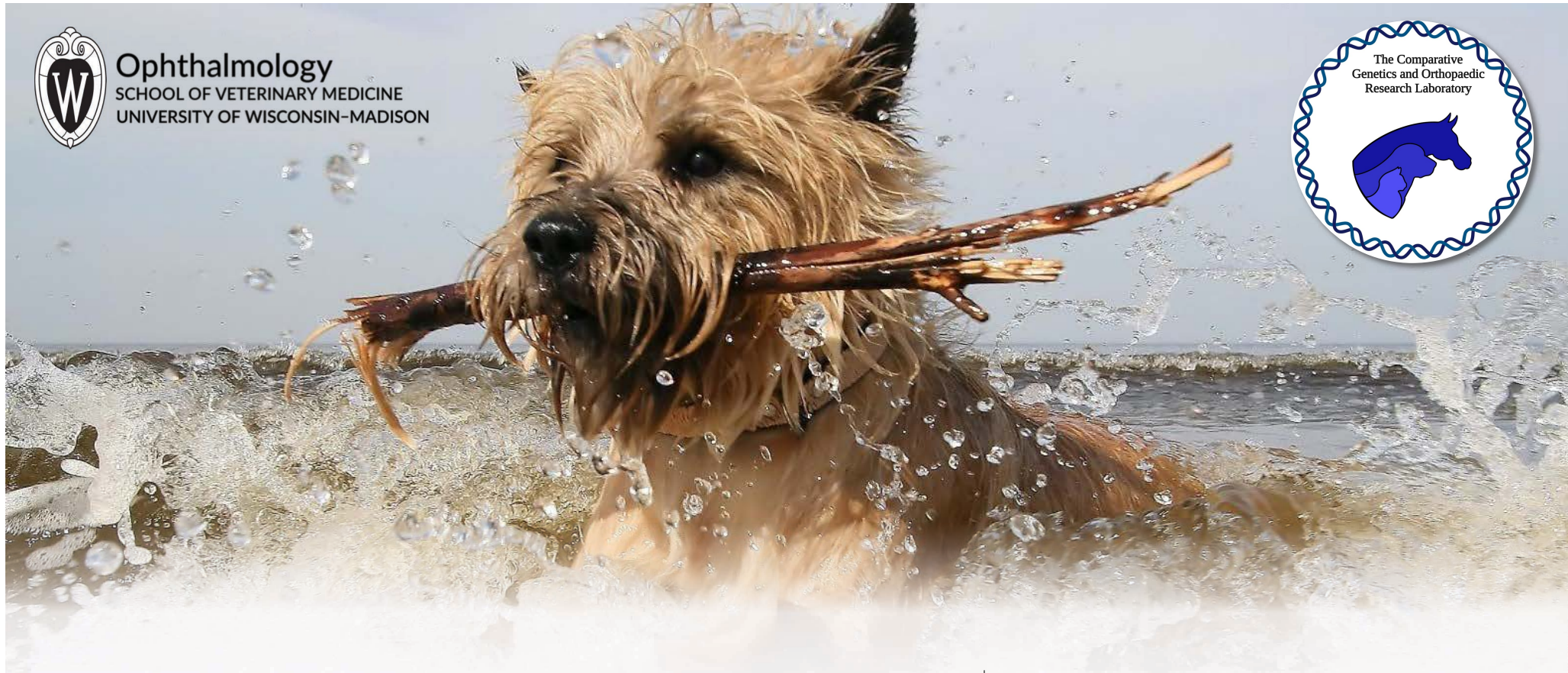




Ophthalmology
SCHOOL OF VETERINARY MEDICINE
UNIVERSITY OF WISCONSIN-MADISON



Ocular Melanosis of Cairn Terriers: What's Next for This Frustrating Problem?

November 15th, 2022

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Our Team

- **Seth Eaton, VMD, DACVO** | Clinical Assistant Professor, Ophthalmology
- **Peter Muir***, BVSc, MVetClinStud, PhD, DACVS, DECVS, FRCVS | Professor, Orthopedic Surgery
- **Susannah Sample***, DVM, MS, PhD, DACVS | Clinical Assistant Professor, Soft Tissue Surgery
- **Nyah Kohler, BS, Global Health Certificate** | UW SVM Class of 2026
- **Shelby Ale** | UW-Madison Undergraduate Student Assistant
- **Gabi Conidi** | UW-Madison Undergraduate Student Assistant

* *Principal Investigators, Comparative Genetics and Orthopaedic Research Laboratory*



The Comparative Genetics Laboratory at UW

- Multidisciplinary research group led by Drs. Muir and Sample
- Located within the UW-Madison SVM
 - Campus collaborations with the School of Medicine and College of Engineering
- Current research
 - Canine
 - Cruciate ligament rupture
 - Laryngeal paralysis
 - Orthopedic trauma and degenerative joint disease
 - And more ...
 - Equine
 - Degenerative suspensory ligament desmitis (DSLSD)



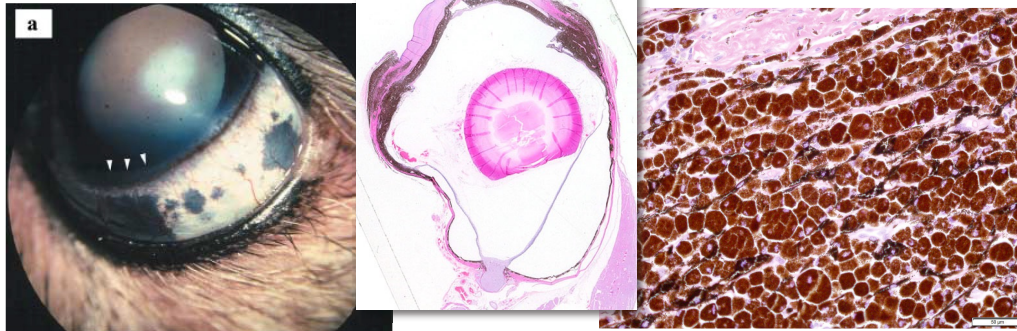
Building on Previous Work ...

- Clinical characterization

- Petersen-Jones, S. M., et al. (2007). "Ocular melanosis in the Cairn Terrier: clinical description and investigation of mode of inheritance." *Veterinary Ophthalmology* 10: 63-69.

- Histologic description

- Petersen-Jones, S. M., et al. (2008). "Ocular melanosis in the Cairn Terrier: histopathological description of the condition, and immunohistological and ultrastructural characterization of the characteristic pigment-laden cells." *Veterinary Ophthalmology* 11(4): 260-268.

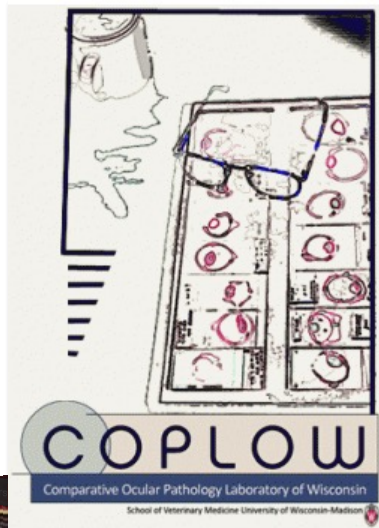


Excluded Genes
ASIP
COMT
GPNMB
GSK3B
LYST
MC1R
MITF
SILV
TYR
TYRP1
TYRP2

Candidate genes were selected because they either had a known involvement in ocular pigmentary disturbances in other species or a role in melanocytes and melano-some development

Winkler, P. A., Bartoe, J. T., Quinones, C. R., Venta, P. J., & Petersen-Jones, S. M. (2013). Exclusion of eleven candidate genes for ocular melanosis in cairn terriers. *Journal of negative results in biomedicine*, 12(1), 1-5.

The Comparative Ocular Pathology Laboratory of Wisconsin



- Largest pathology laboratory committed to comparative veterinary ocular pathology worldwide
- ~60,000 cases/submissions in their collection (mostly canine)
- Archived formalin-fixed paraffin-embedded slides
- Extensive and searchable database



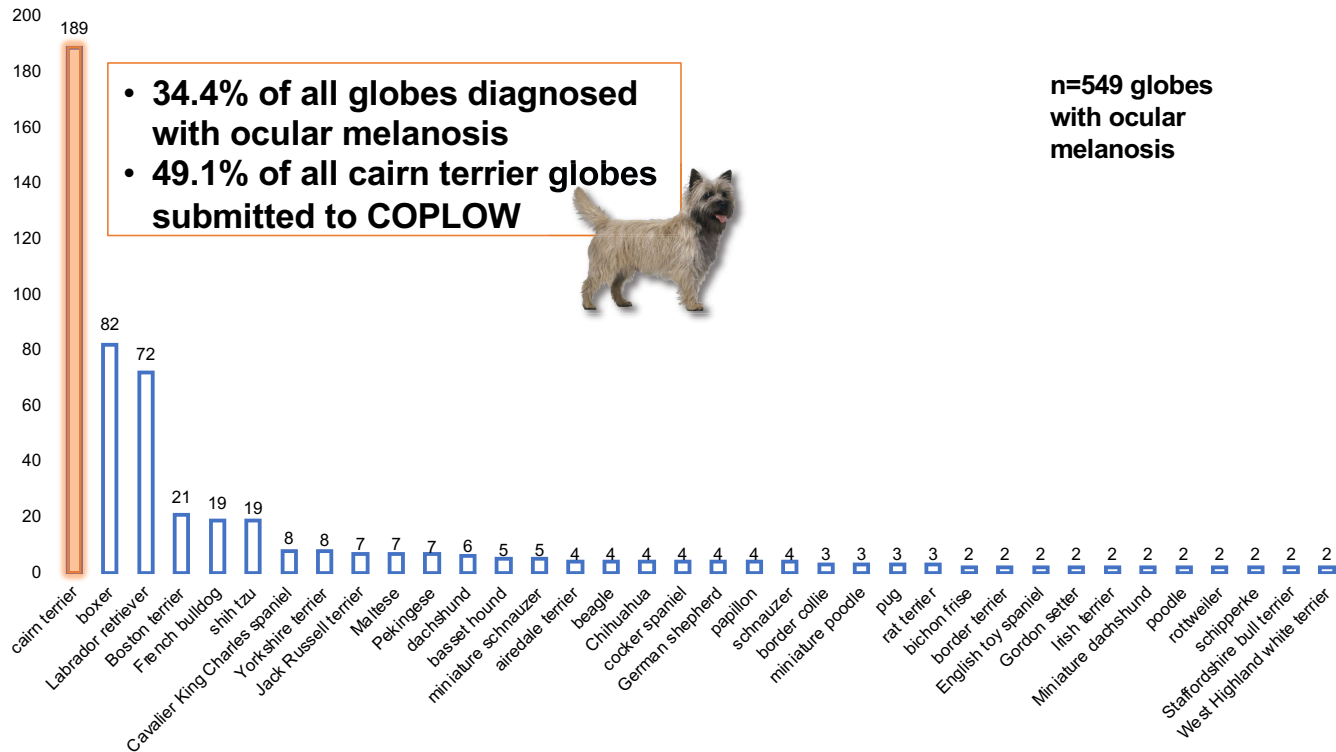
Featured on the Big Ten Network™



COPLOW

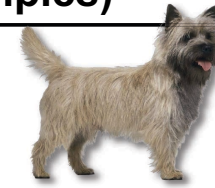
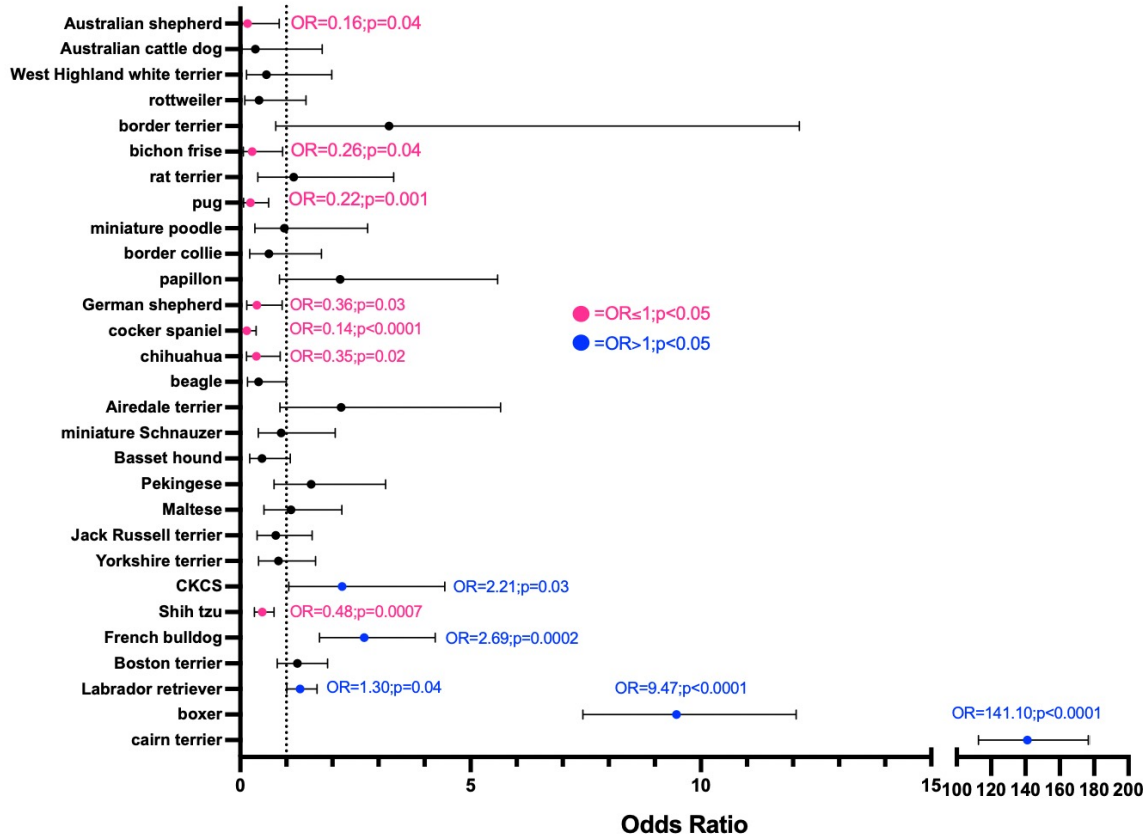
Comparative Ocular Pathology Laboratory of Wisconsin

Raw Numbers of Globes by Breed Histologically Diagnosed with Ocular/Uveal Melanosis (Source: COPLOW Database as of 7/24/22)



One each of the following breeds: American bulldog, Australian cattle dog, Australian shepherd, blue heeler, Bouvier des Flandres, bullmastiff, Catahoula leopard dog, Celi, curly coated retriever, English bulldog, English cocker spaniel, English pointer, English toy, fox terrier, Norwegian terrier, Norwich terrier, old English sheep dog, pit bull, pit bull terrier, pointer, Pomeranian, redbone coonhound, Saint Bernard, Scottish terrier, Shetland sheep dog, shiba inu, silky terrier, spitz, springer spaniel, standard schnauzer, Welsh terrier, wirehaired terrier,

Odds Ratio (OR) For Histologic Diagnosis of Ocular Melanosis By Breed Relative to Overall COPLOW Canine Population (n=53,057 samples)



High Risk



Moderate Risk



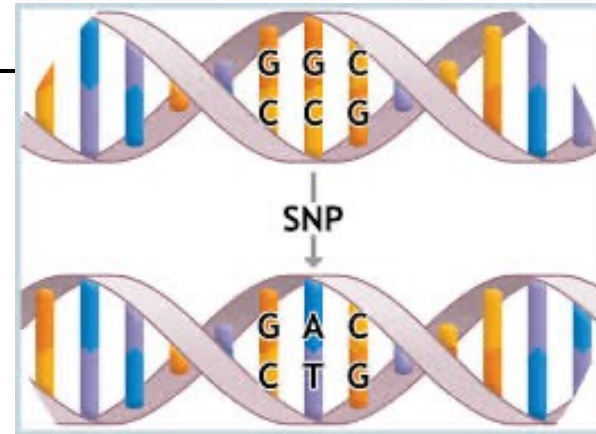
Low Risk



"No Risk"

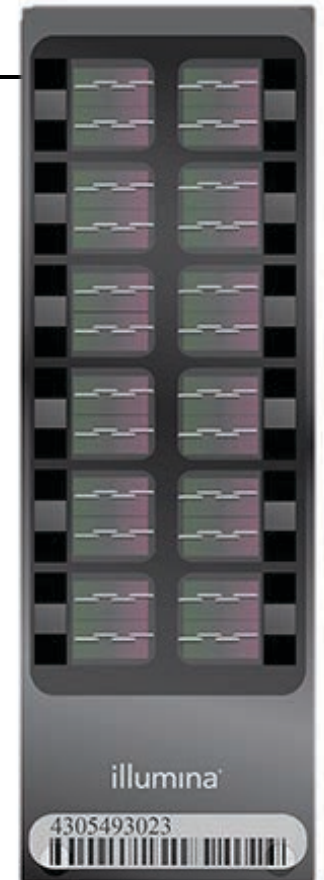
Our Project

- Genome-wide association study (GWAS)
 - Search for many small variations (SNPs) in canine genome
 - Better than candidate gene studies for complex, polygenic diseases

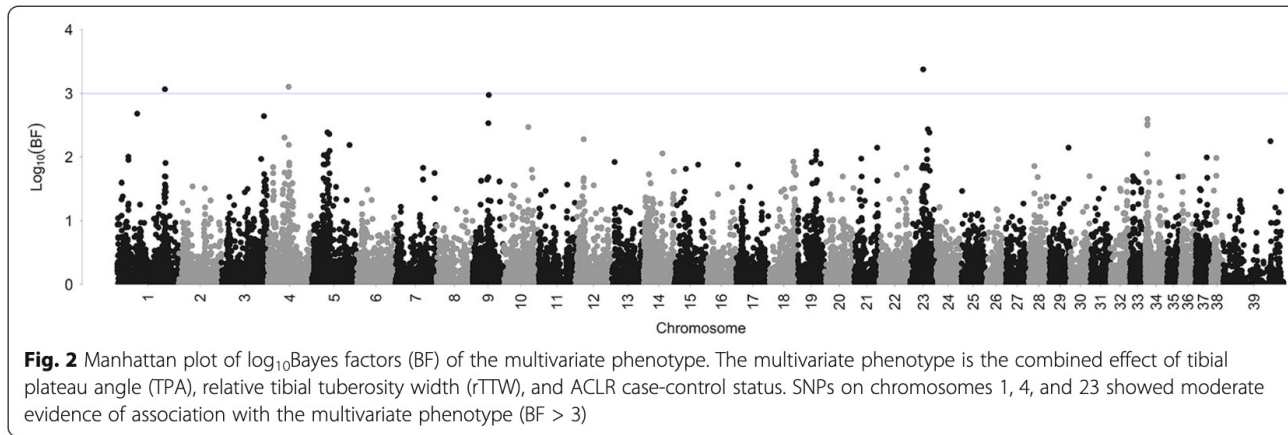


Society for Mucosal Immunology

172,115 genome locations



Baker, Lauren A., et al.
"Multivariate genome-wide association analysis identifies novel and relevant variants associated with anterior cruciate ligament rupture risk in the dog model." *BMC genetics* 19.1 (2018): 1-10.



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Our Project



- Breed categorical genome-wide association study (GWAS) according to phenotypic risk level
 - Seeking to identify novel contributory candidate genetic variants
- Consider whole-genome sequencing of severely-affected individual cairns
- Movement toward development of a genetic risk test or prediction model



High Risk



Moderate Risk



Low Risk



"No Risk"

What Is Needed from Cairn Terrier Owners?



We are seeking (1) pedigreed cairn terriers affected by any stage of ocular melanosis and (2) unaffected pedigreed cairn terriers ≥ 12 years of age

1. Owners enroll by contacting the CGL. For affected dogs, medical records may be requested detailing the ocular melanosis diagnosis. Photographs of the eyes will likely be requested, particularly for unaffected control dogs. Pedigree information will also be requested.
2. The Lab issues a consent form, questionnaire, and saliva swab (with instructions for sample collection). The dog owner sends the sample and all other materials back to the Lab.

There are no significant risks associated with the sample collection.

There is no cost to the owner.

Our study is approved by the University of Wisconsin-Madison Institutional Animal Care & Use Committee (IACUC)

Questions?



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