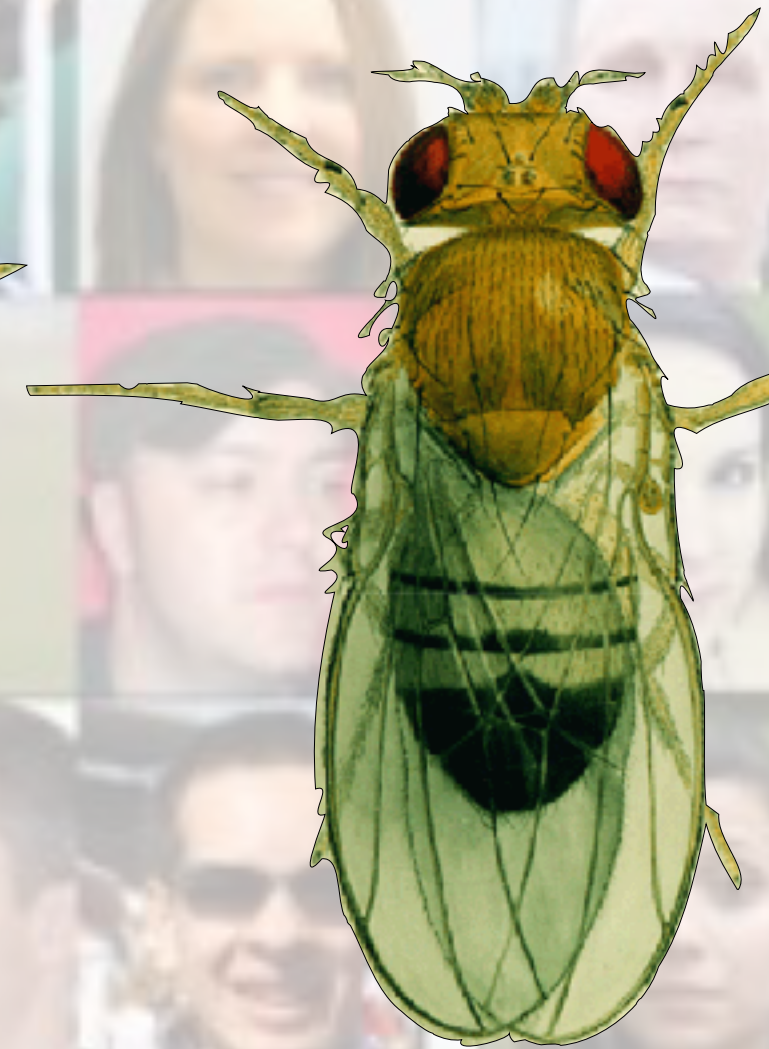


Fruit Flies for Precision Toxicology & Medicine

Brian Oliver, NIH, Bethesda MD, USA



briano@nih.gov



National Institute of
Diabetes and Digestive
and Kidney Diseases



**Models for human health:
all are wrong, many are useful**

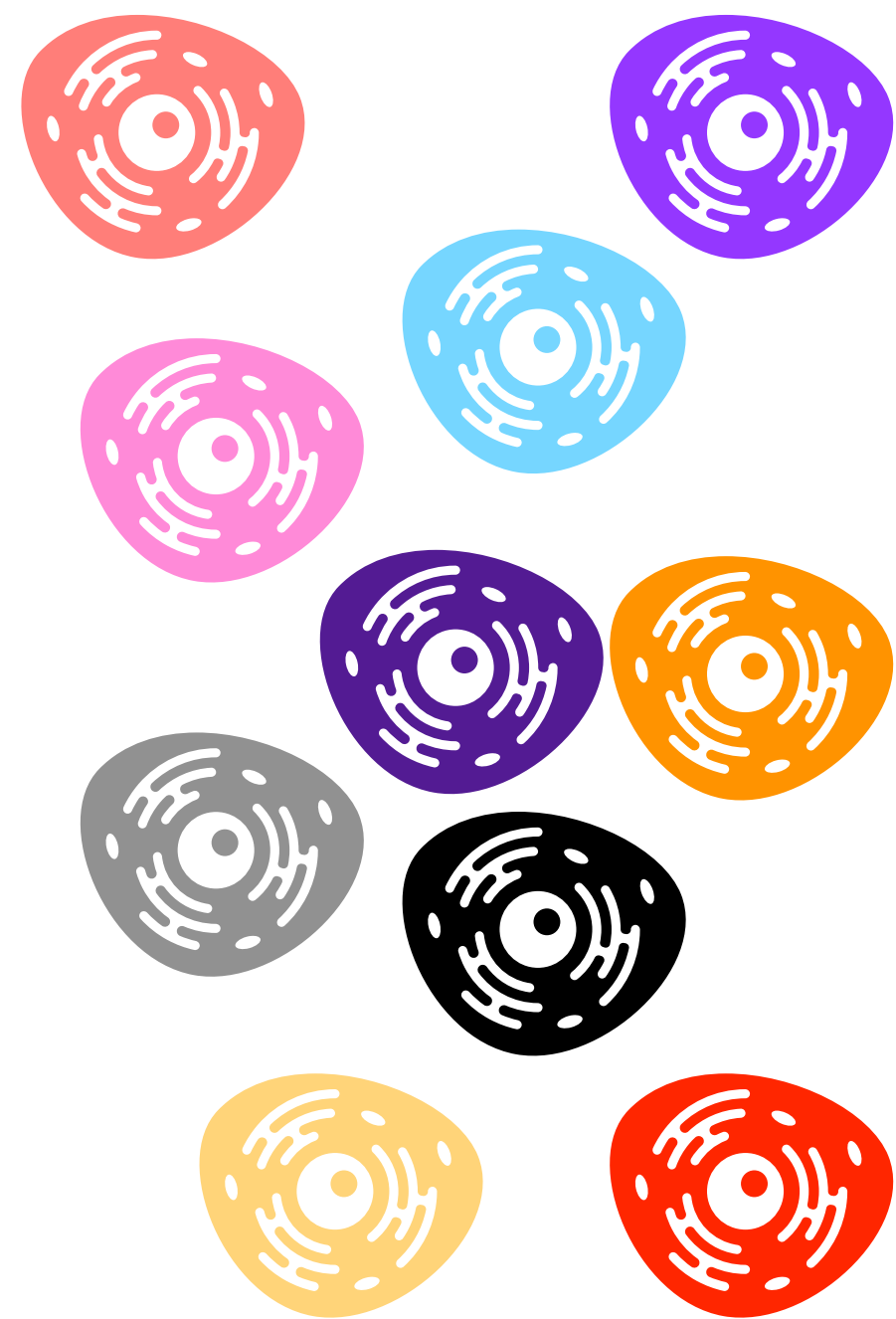
Genotypic Similarity

Argument for human iPS, organoids, & cell chips

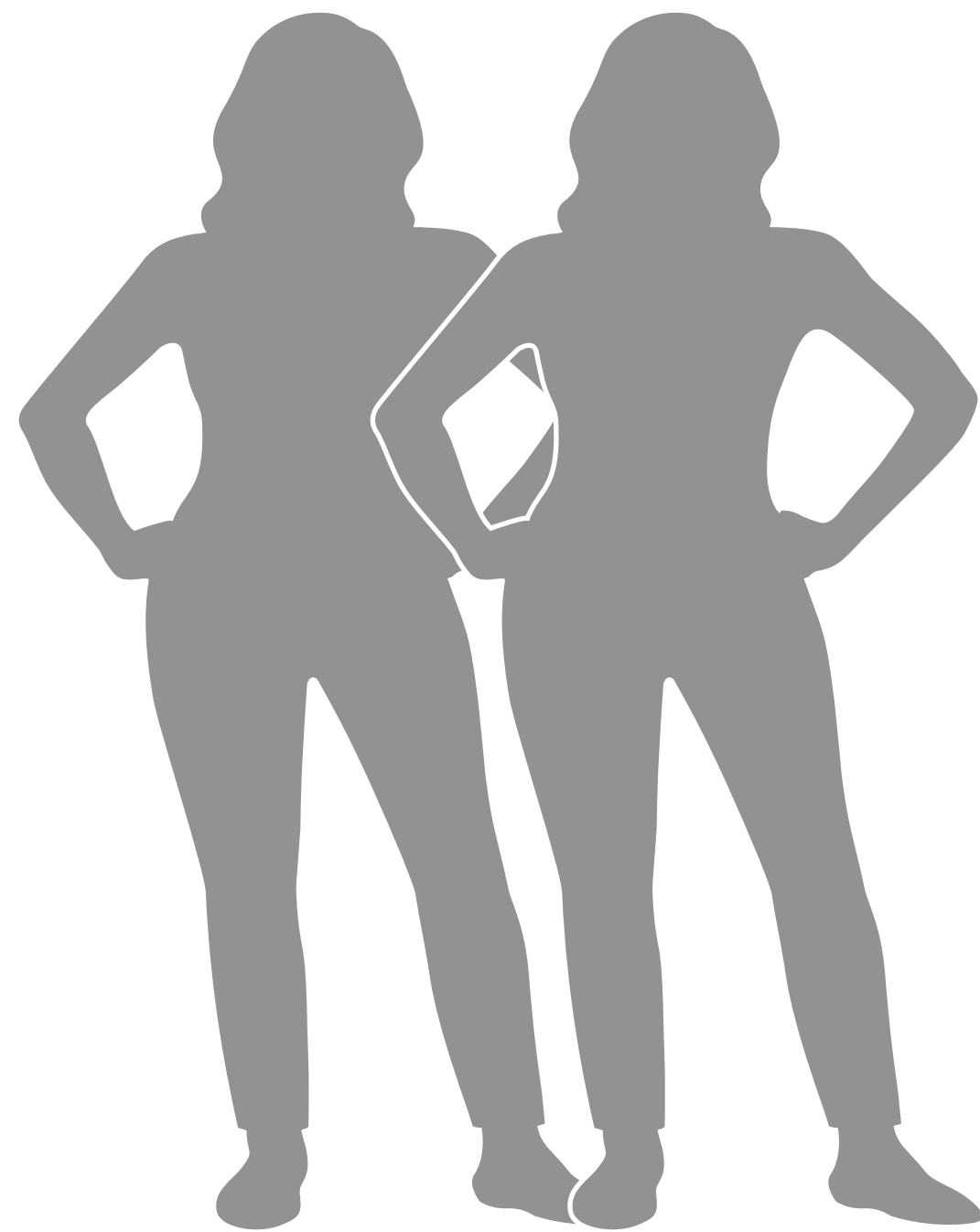
High

Low

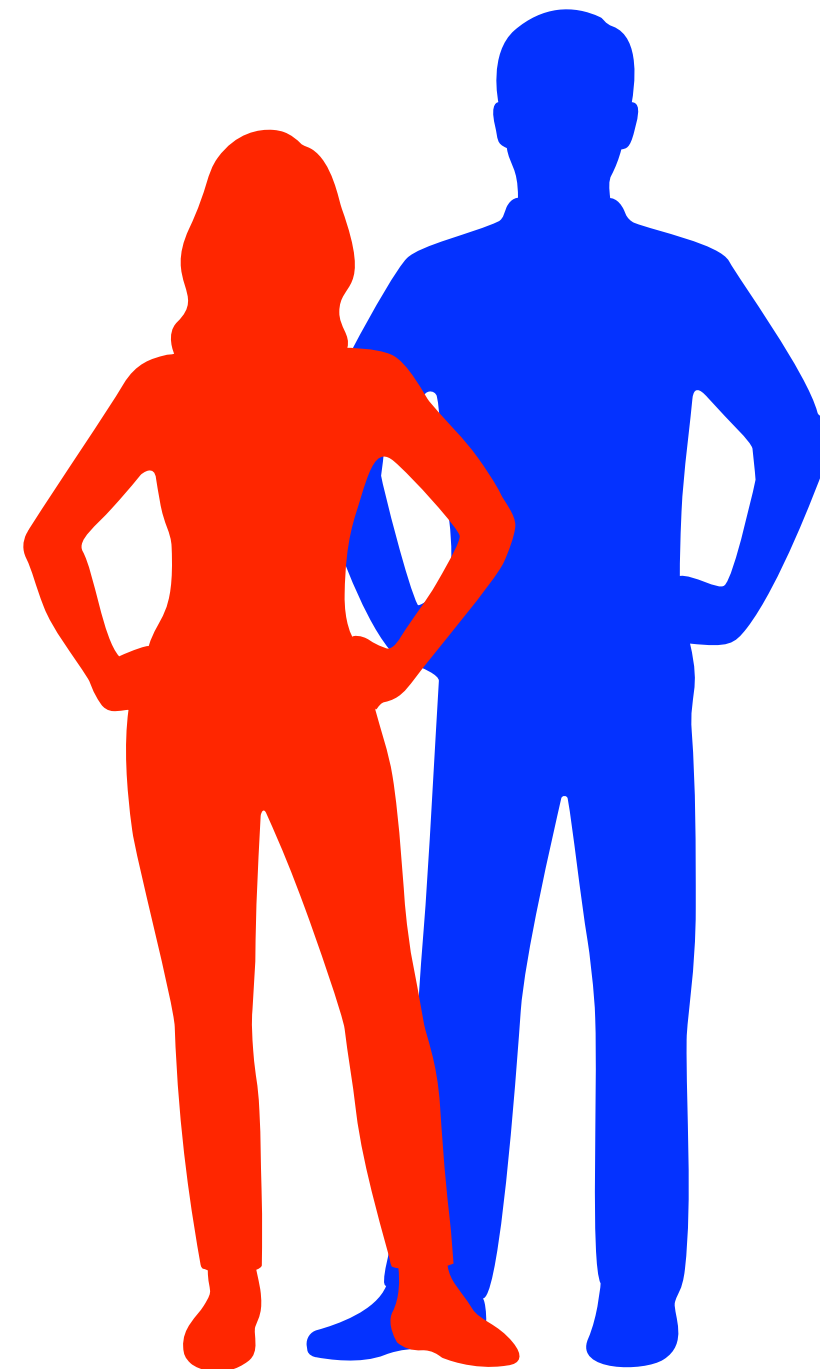
Cell type



Twins



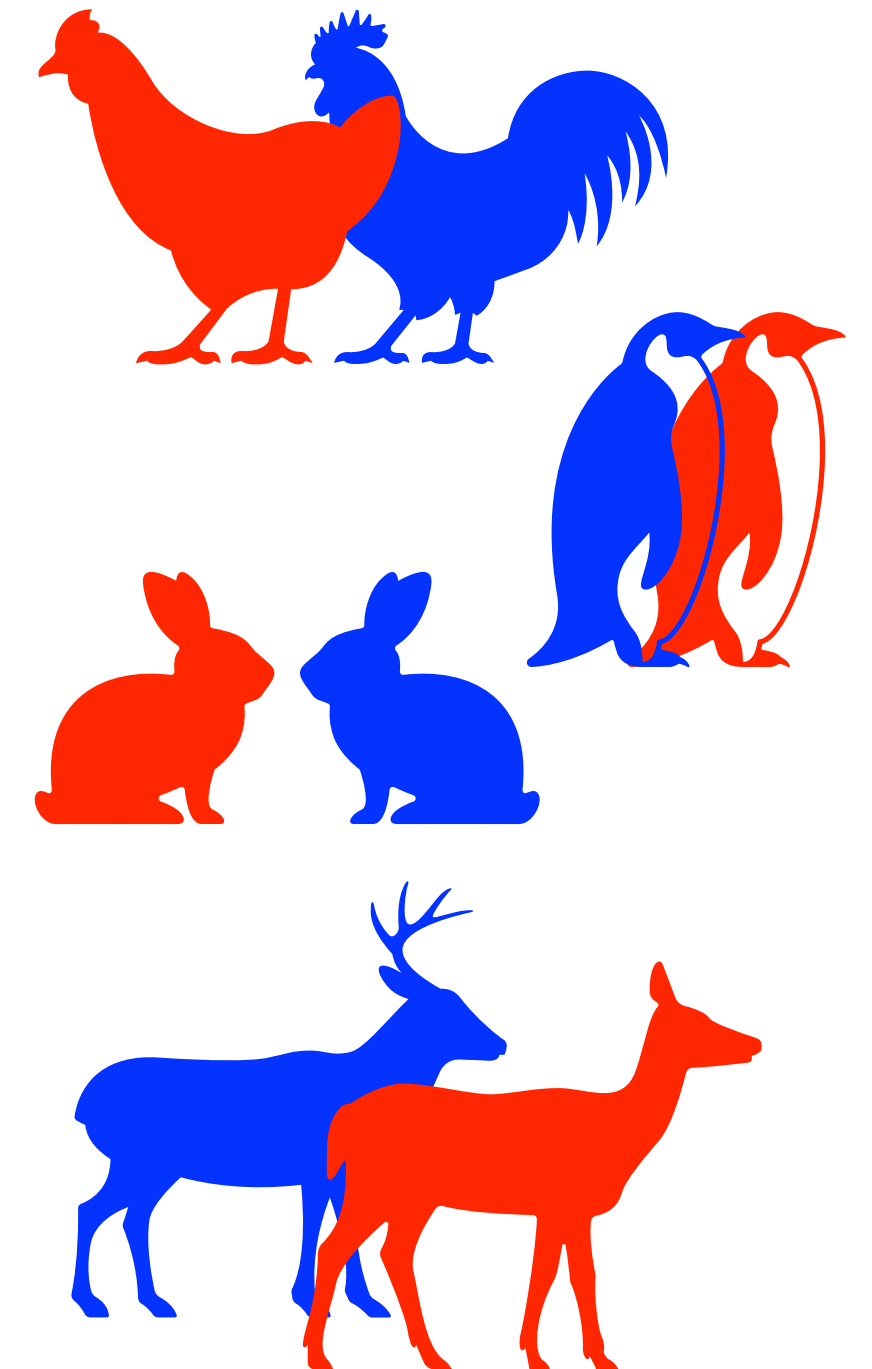
Sex



Population



Species

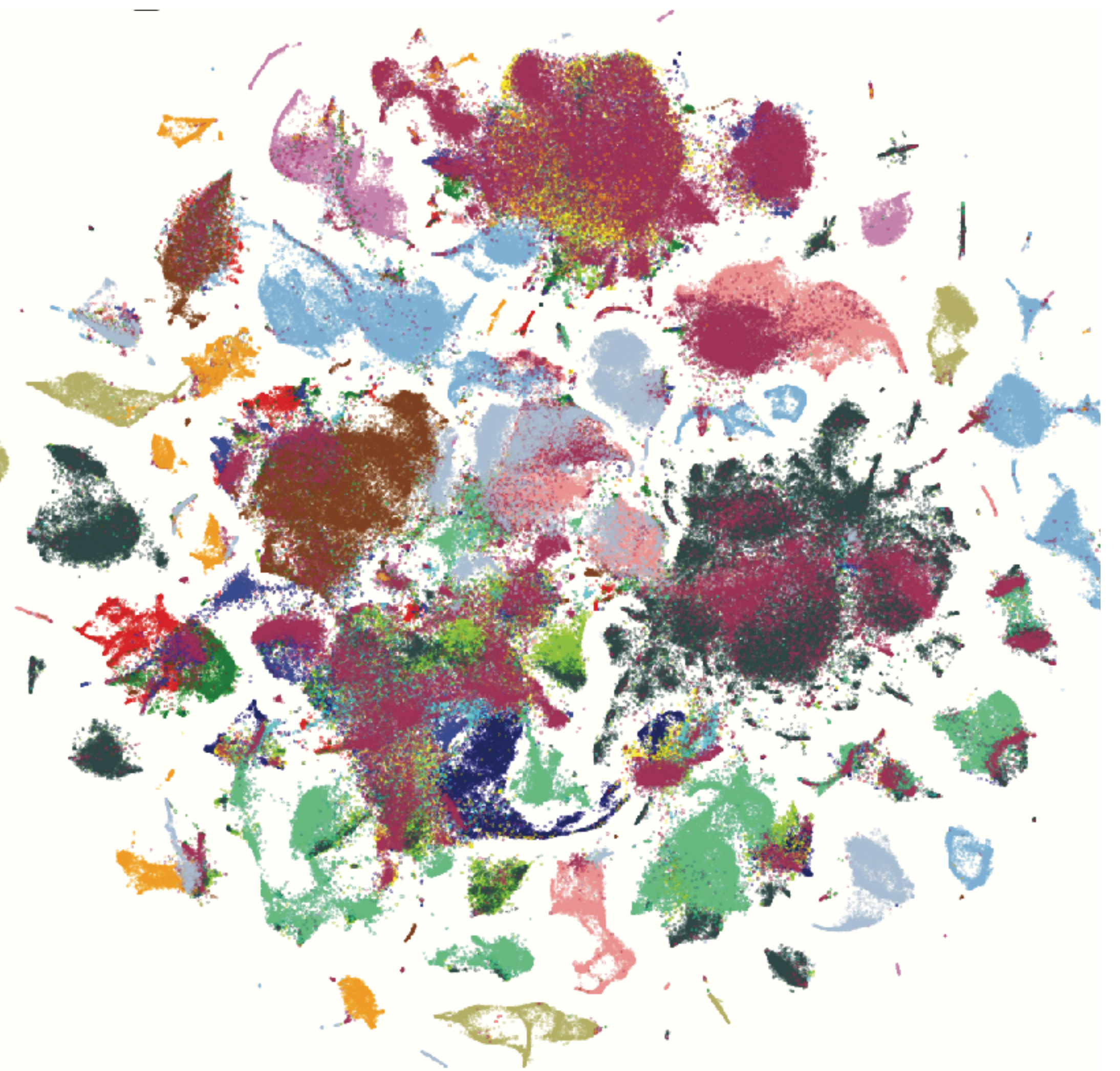
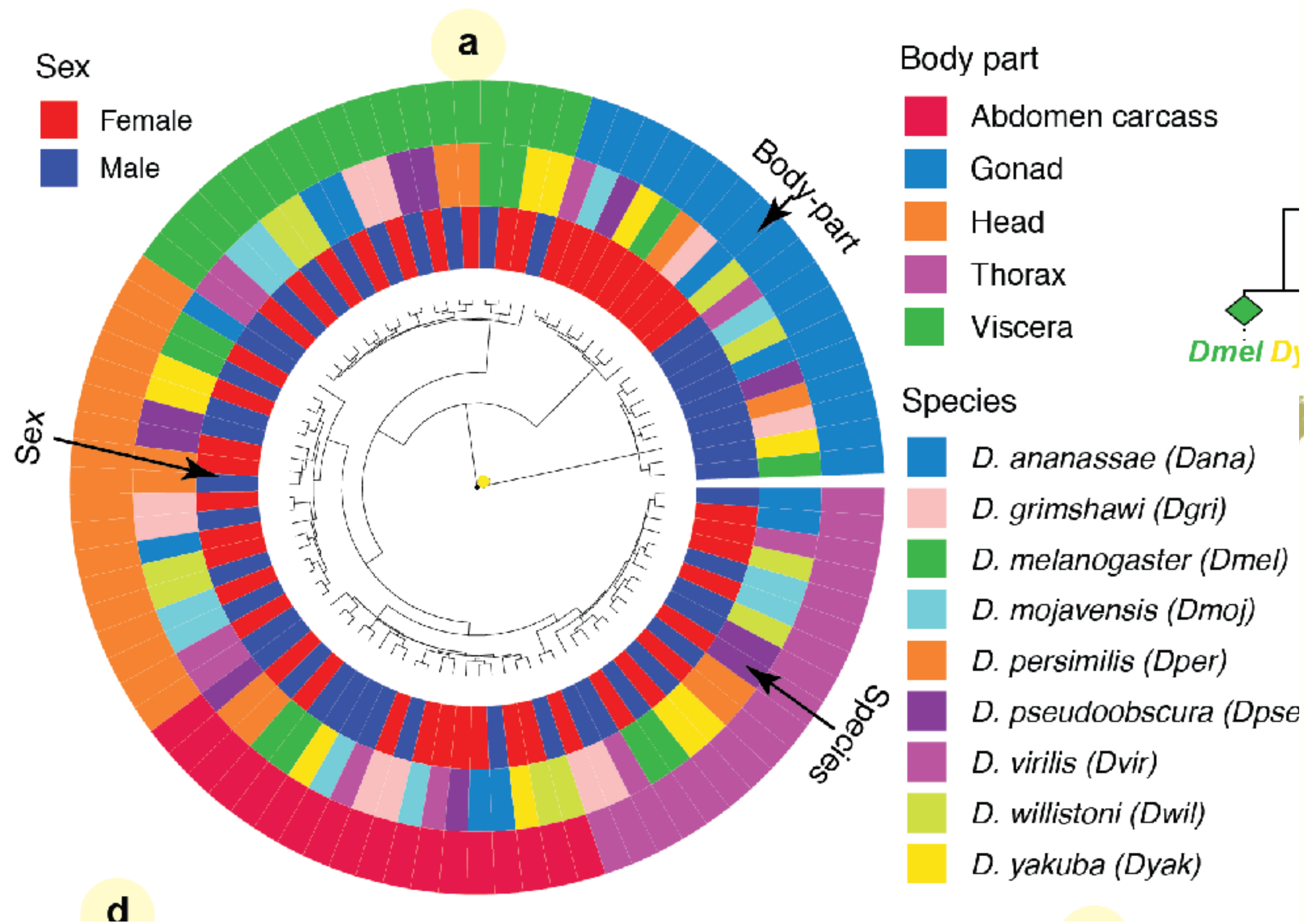


Body Parts

~100 million yrs divergence
Similar Expression

Single Cells

0 yrs divergence
Different Expression



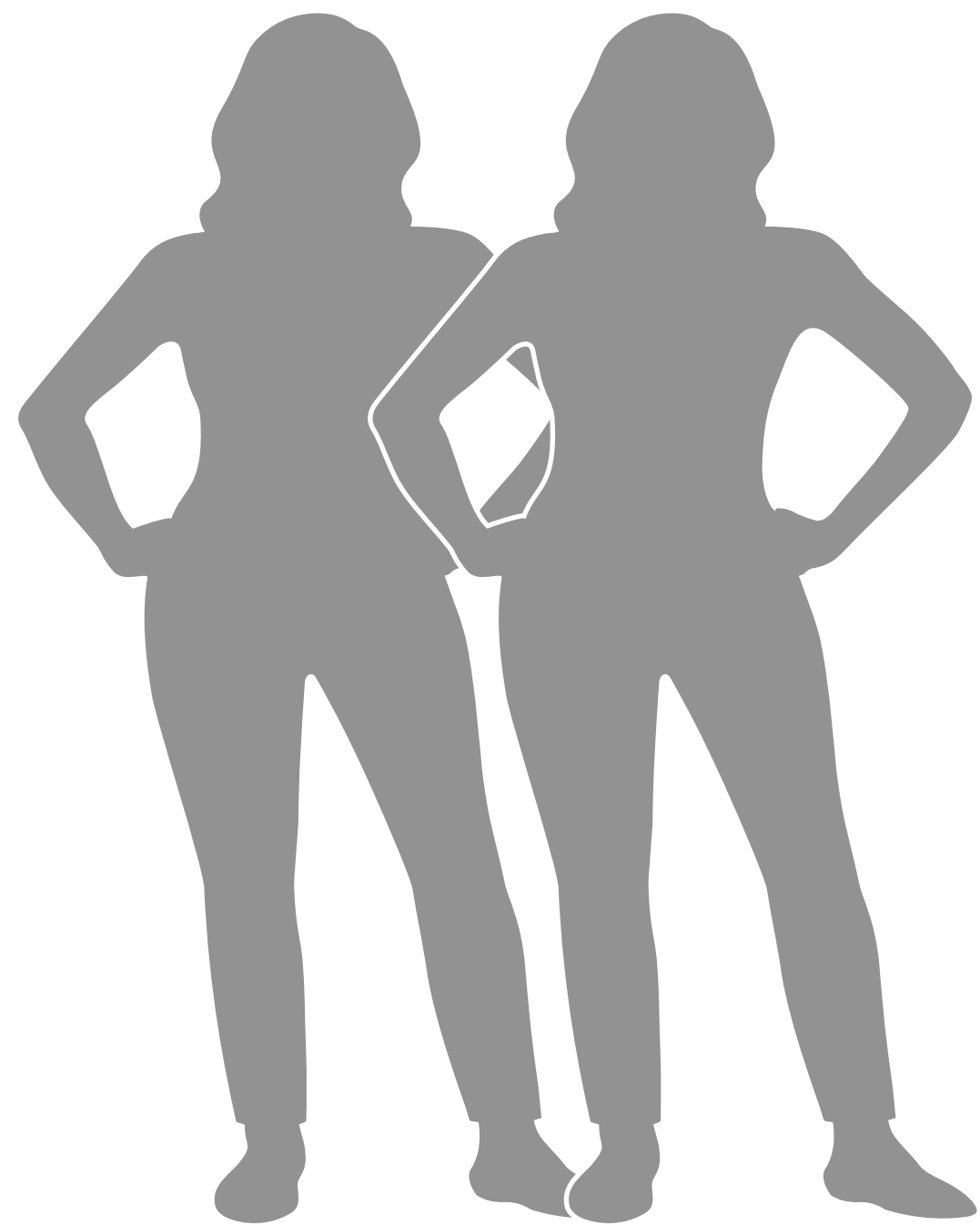
Gene Expression Similarity

Argument for complex whole organisms

High

Low

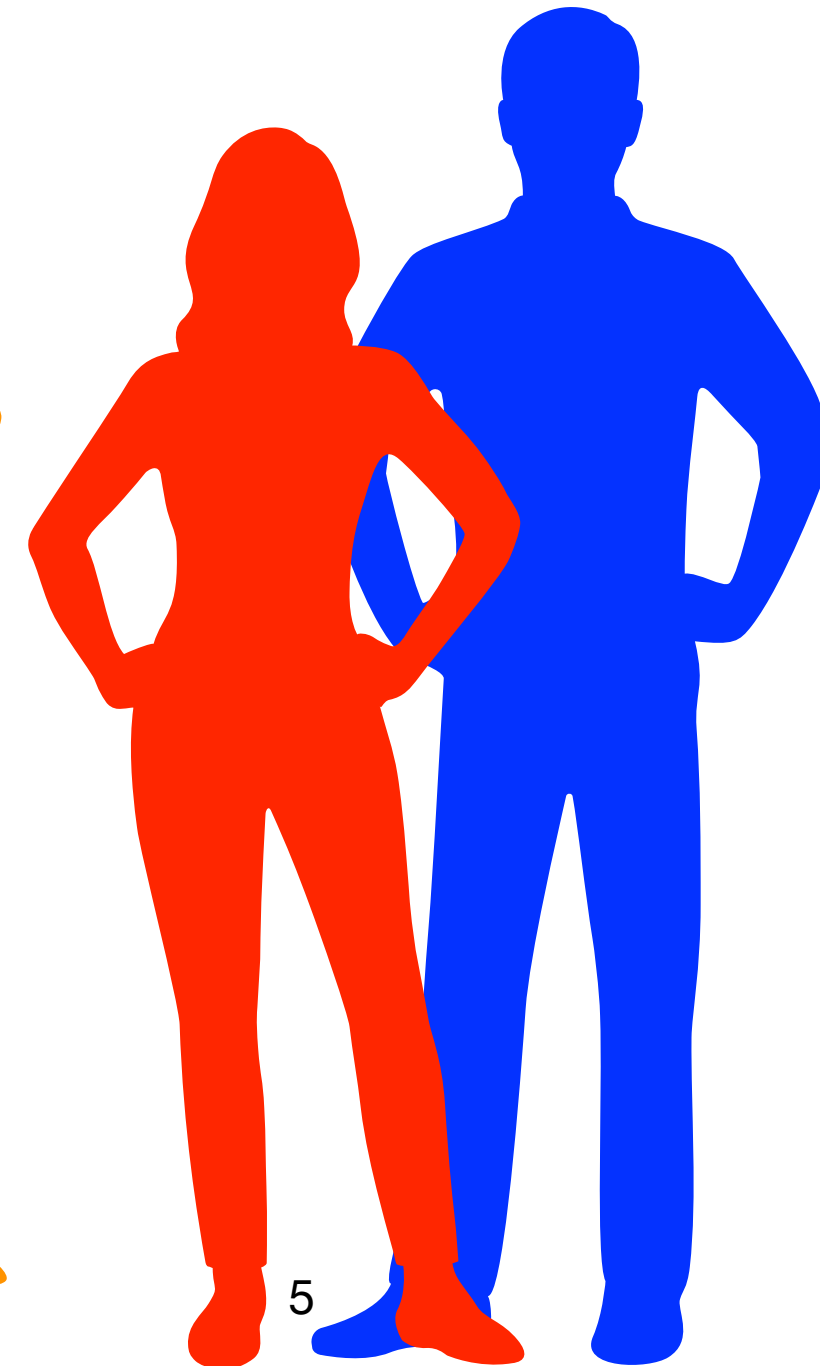
Twins



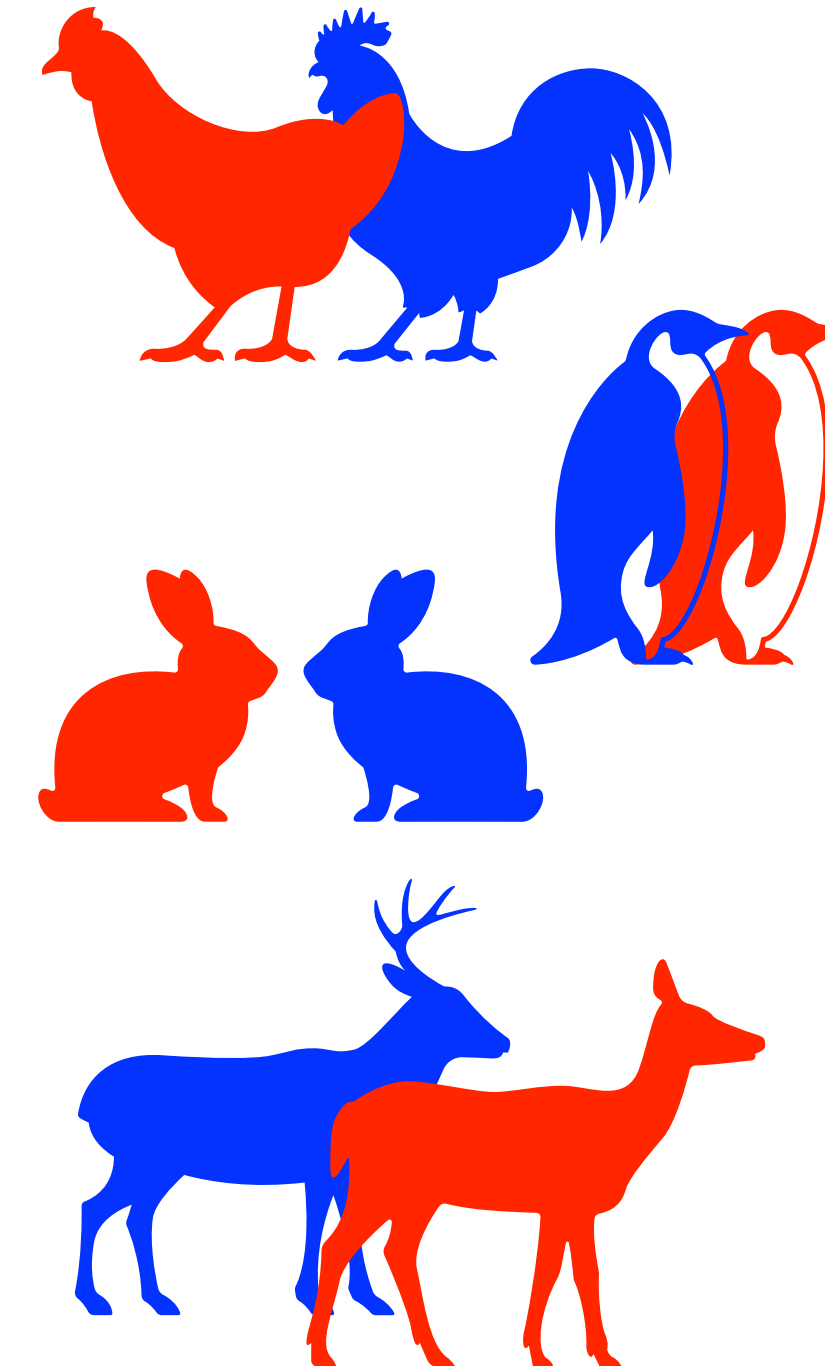
Population



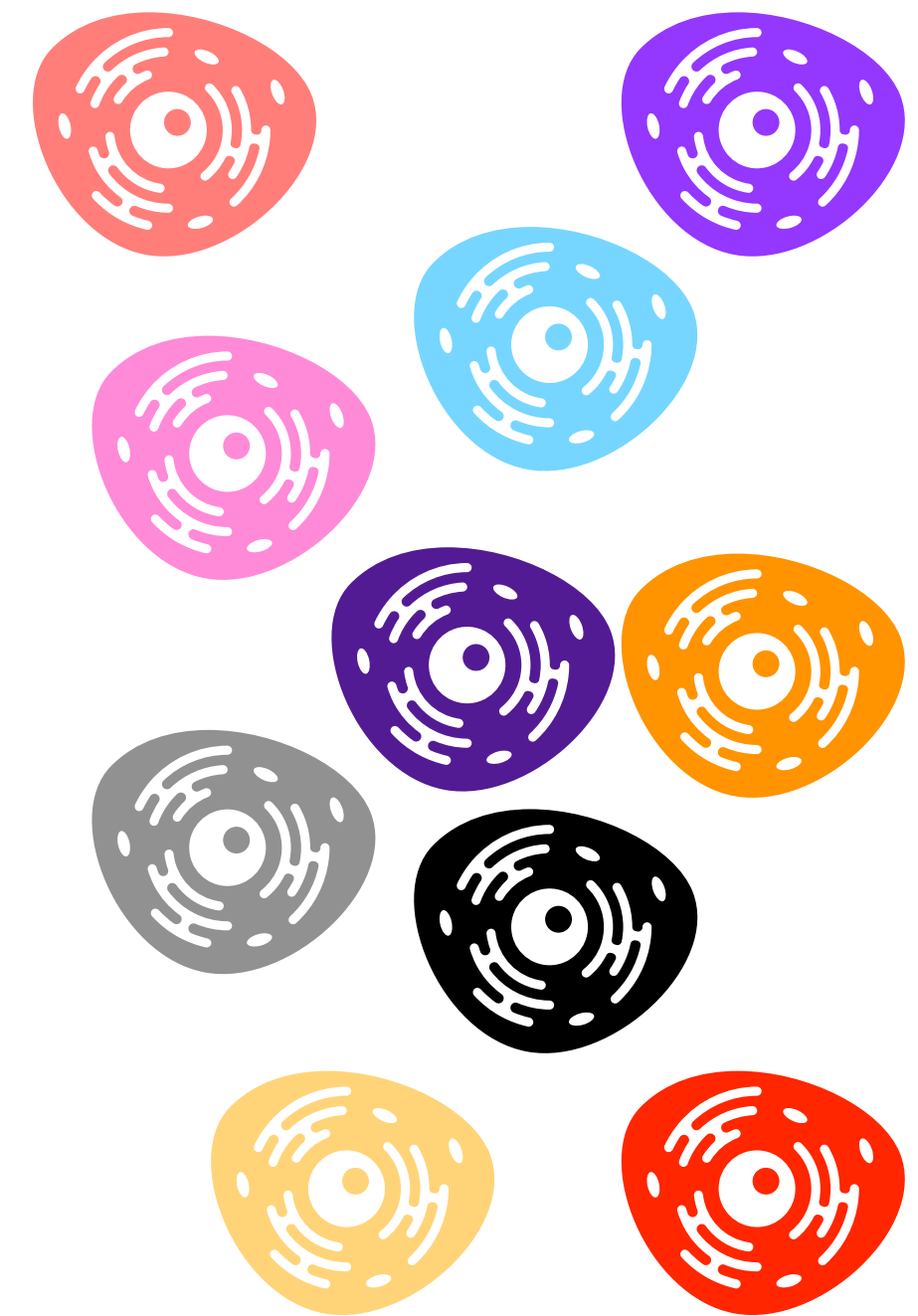
Sex



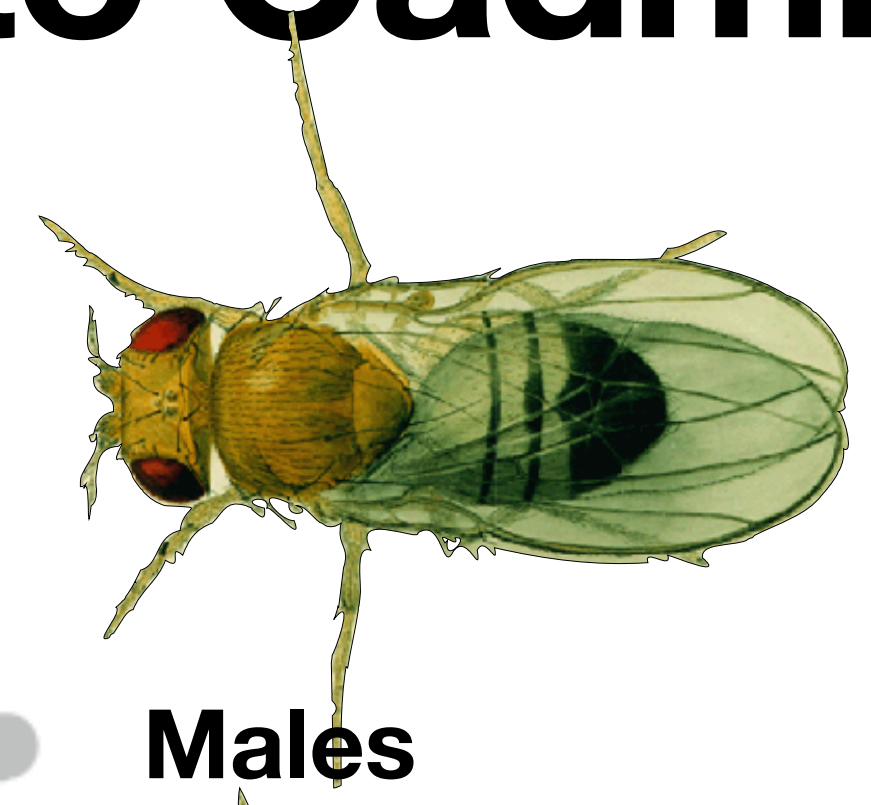
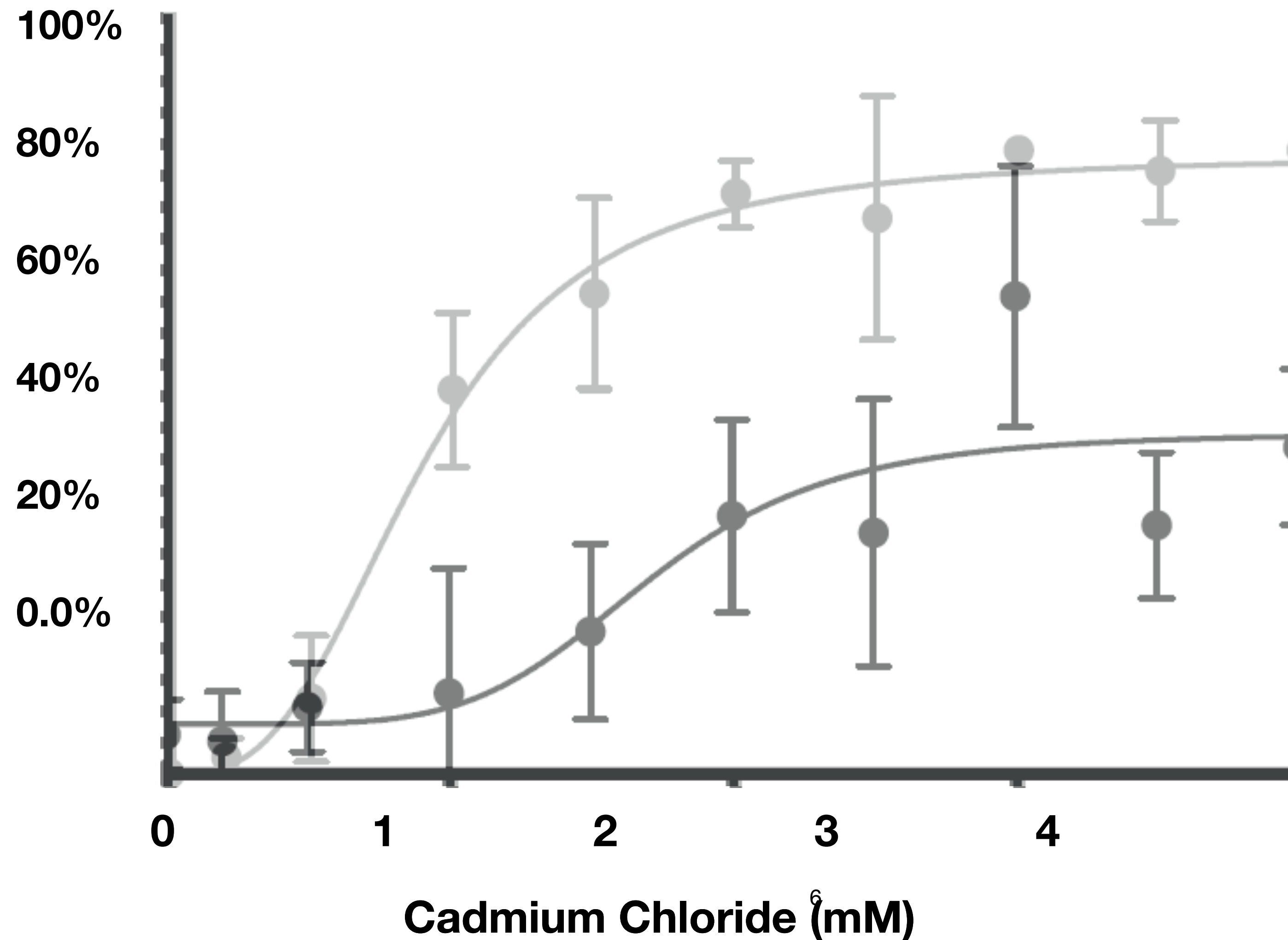
Species



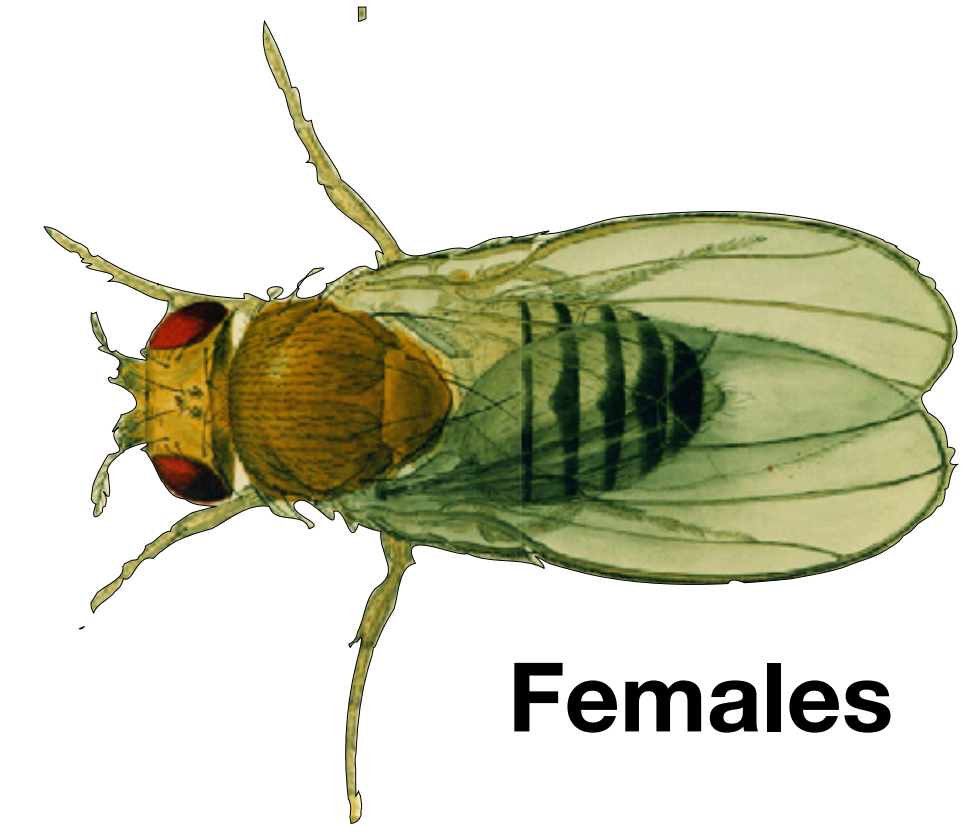
Cell type



Females are strikingly resistant to Cadmium

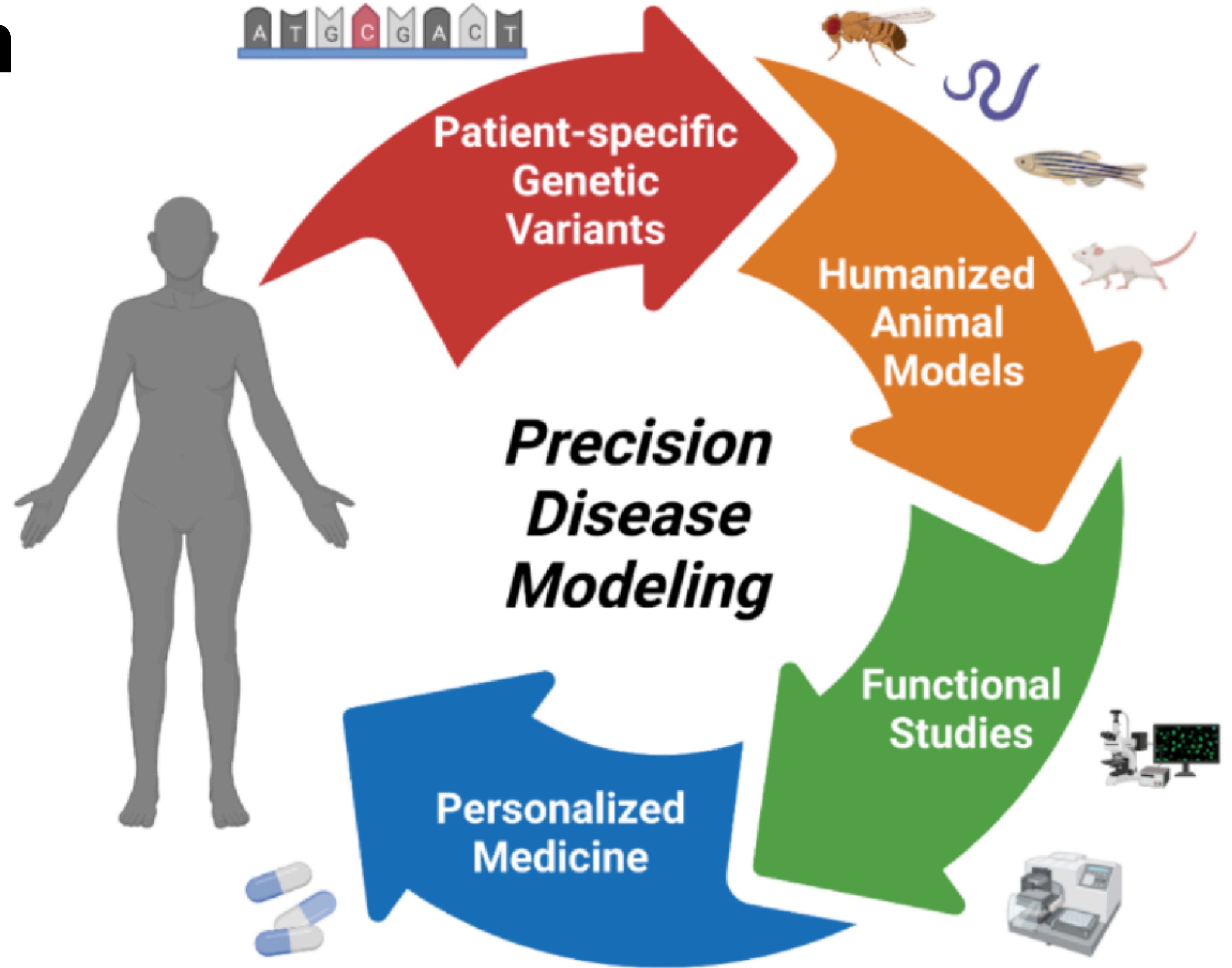


Males

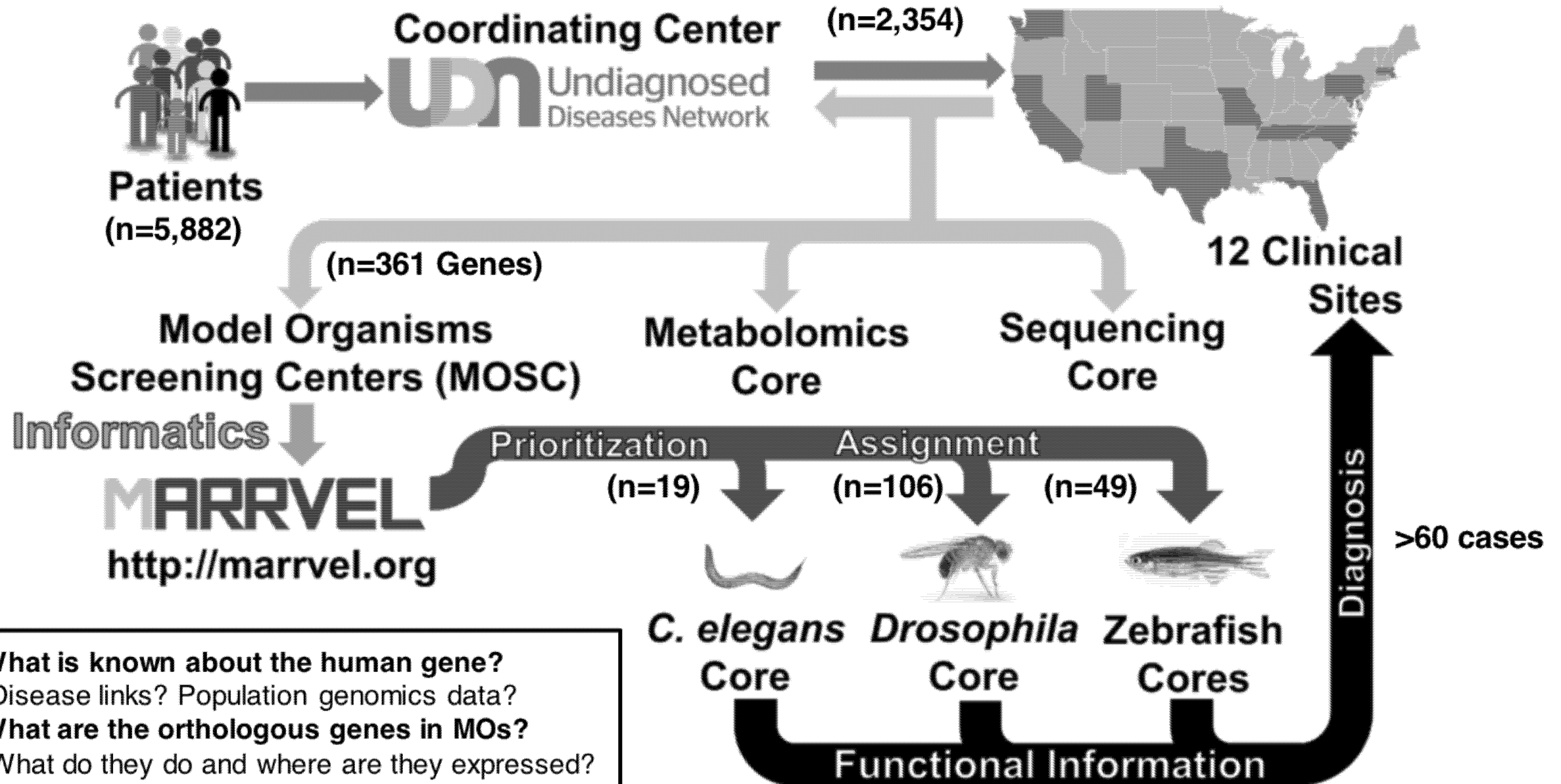


Females

Model Organism Avatars for individuals



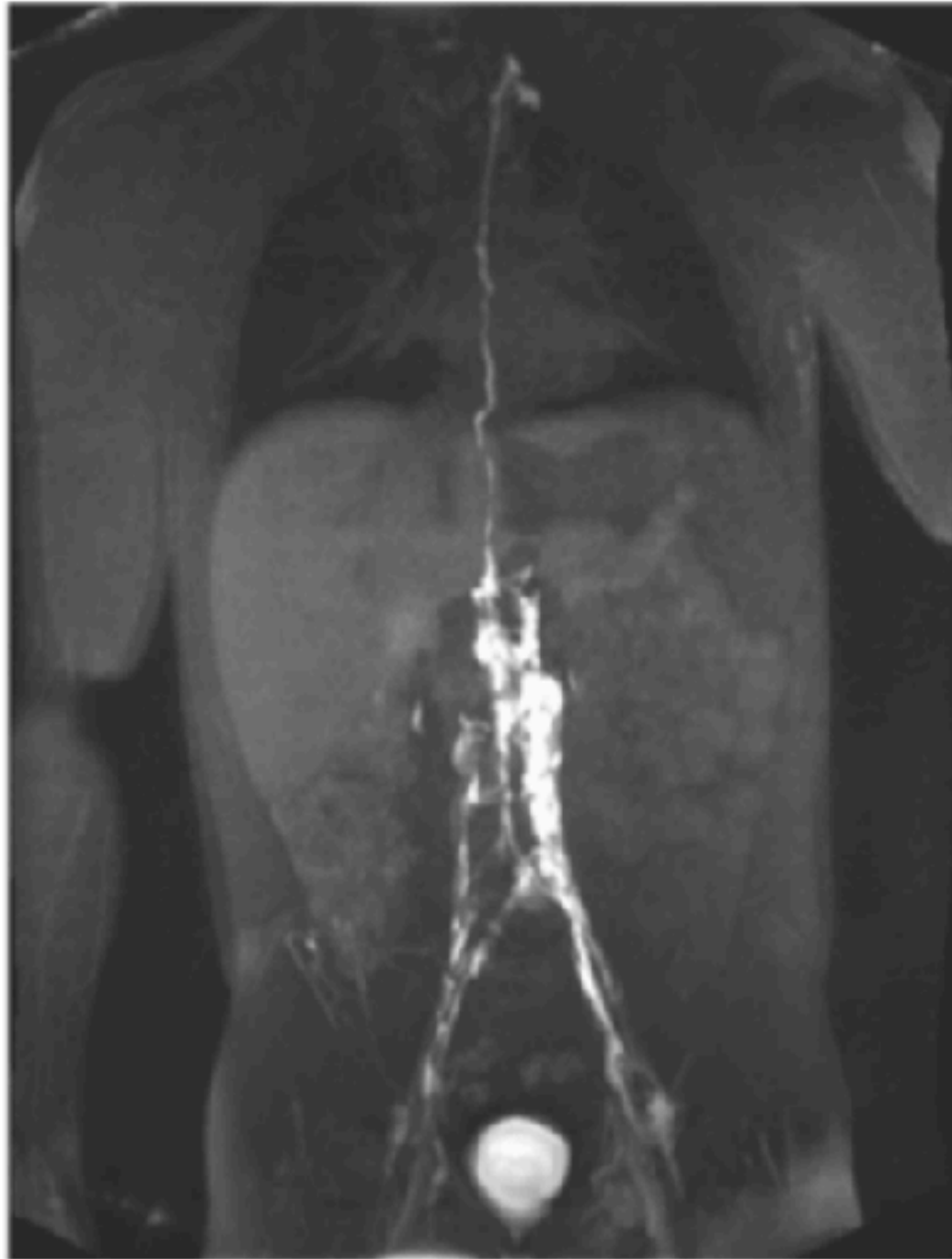
Current workflow of the UDN and MOSC



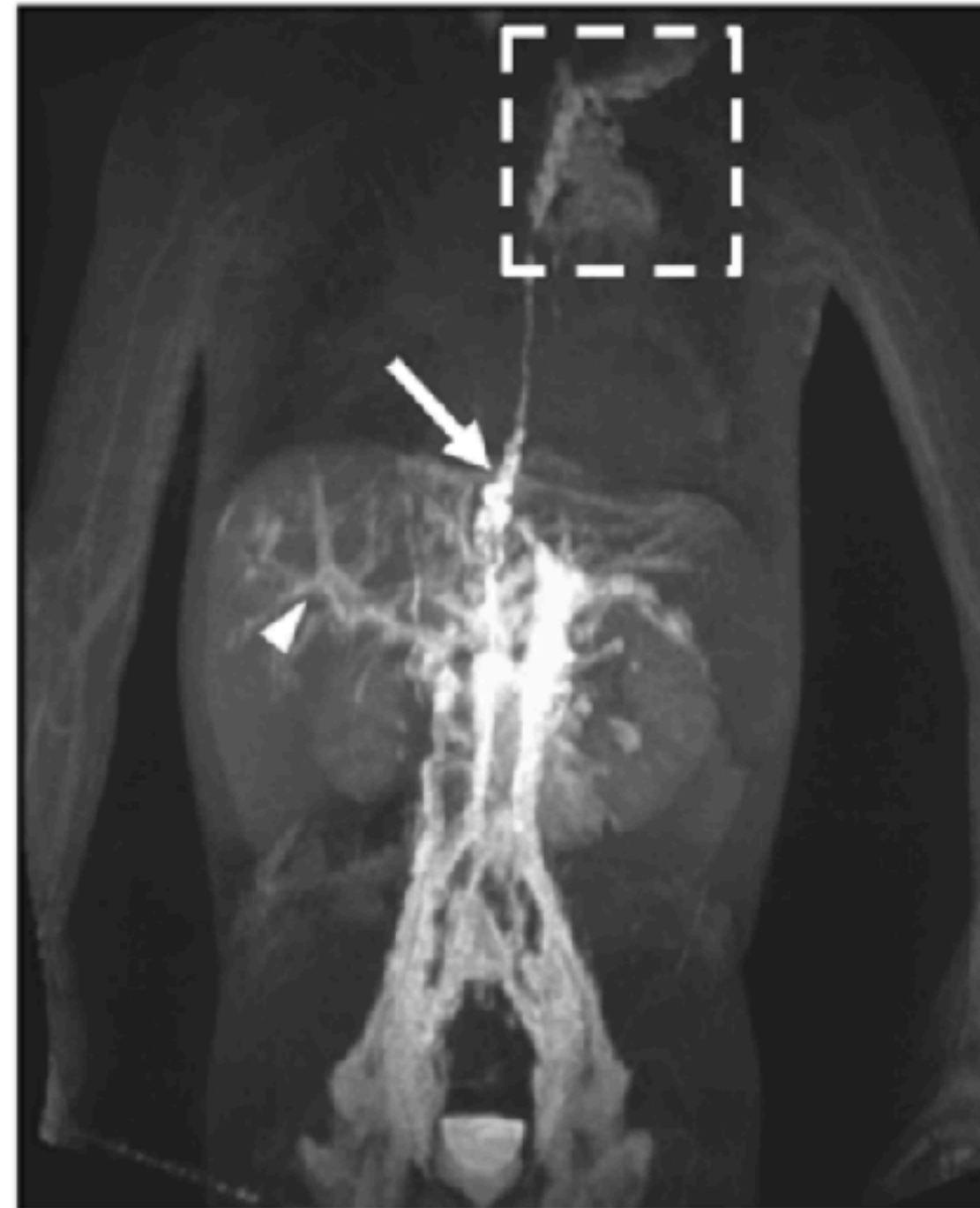
- ✓ What is known about the human gene?
Disease links? Population genomics data?
- ✓ What are the orthologous genes in MOs?
What do they do and where are they expressed?
- ✓ Are the variants of interest likely damaging?

Precision Medicine

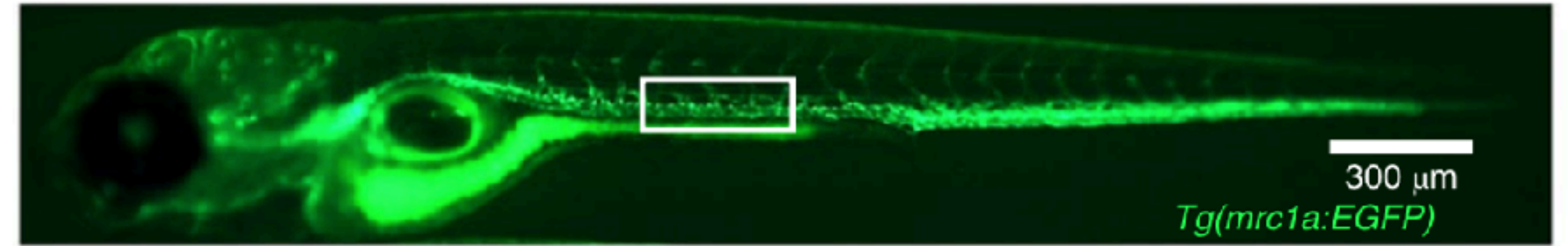
Healthy lymphatic system



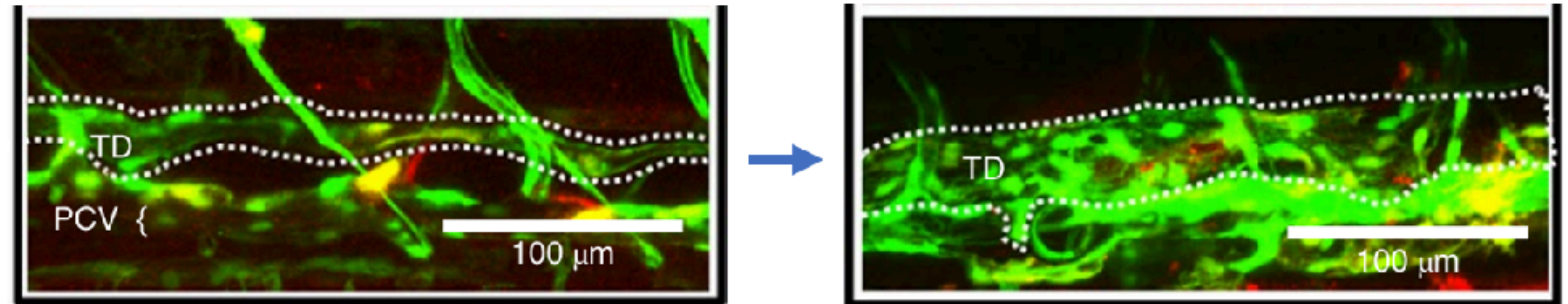
Overgrowth in patient with mutation



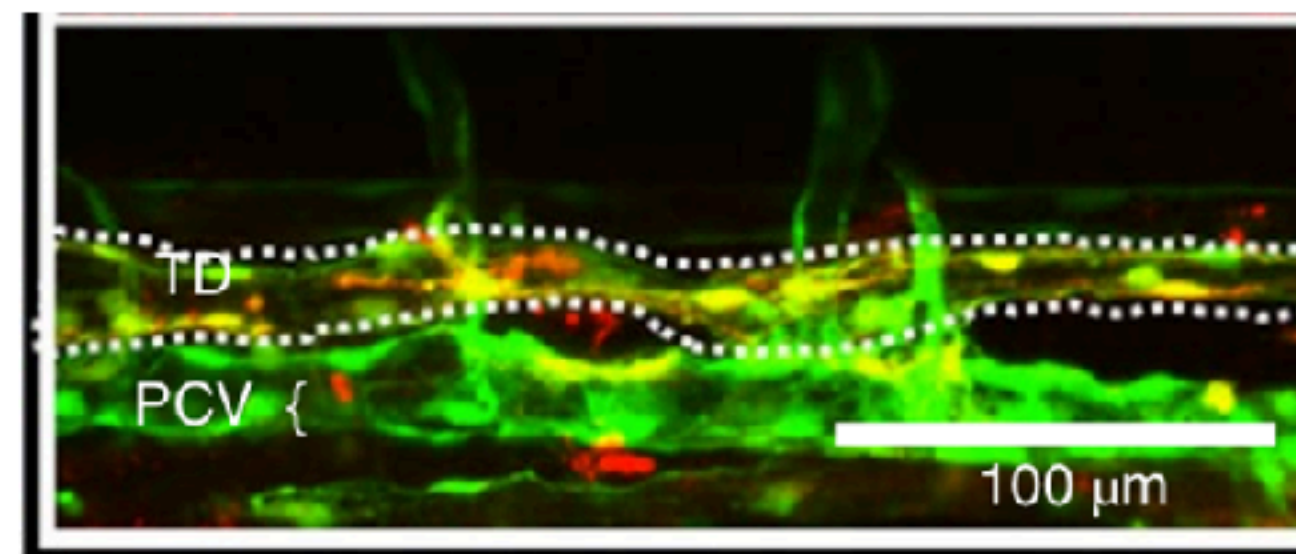
Zebrafish with labeled lymphatic (developed at NIH!)



Introduction of patient mutation into zebrafish causes similar overgrowth



Drug screen with FDA-approved drugs on zebrafish with patient mutation identified that Cobimetinib reduced overgrowth



Cobimetinib given to patient, who is now a healthy, happy teenager



From Jeffery Ferrall

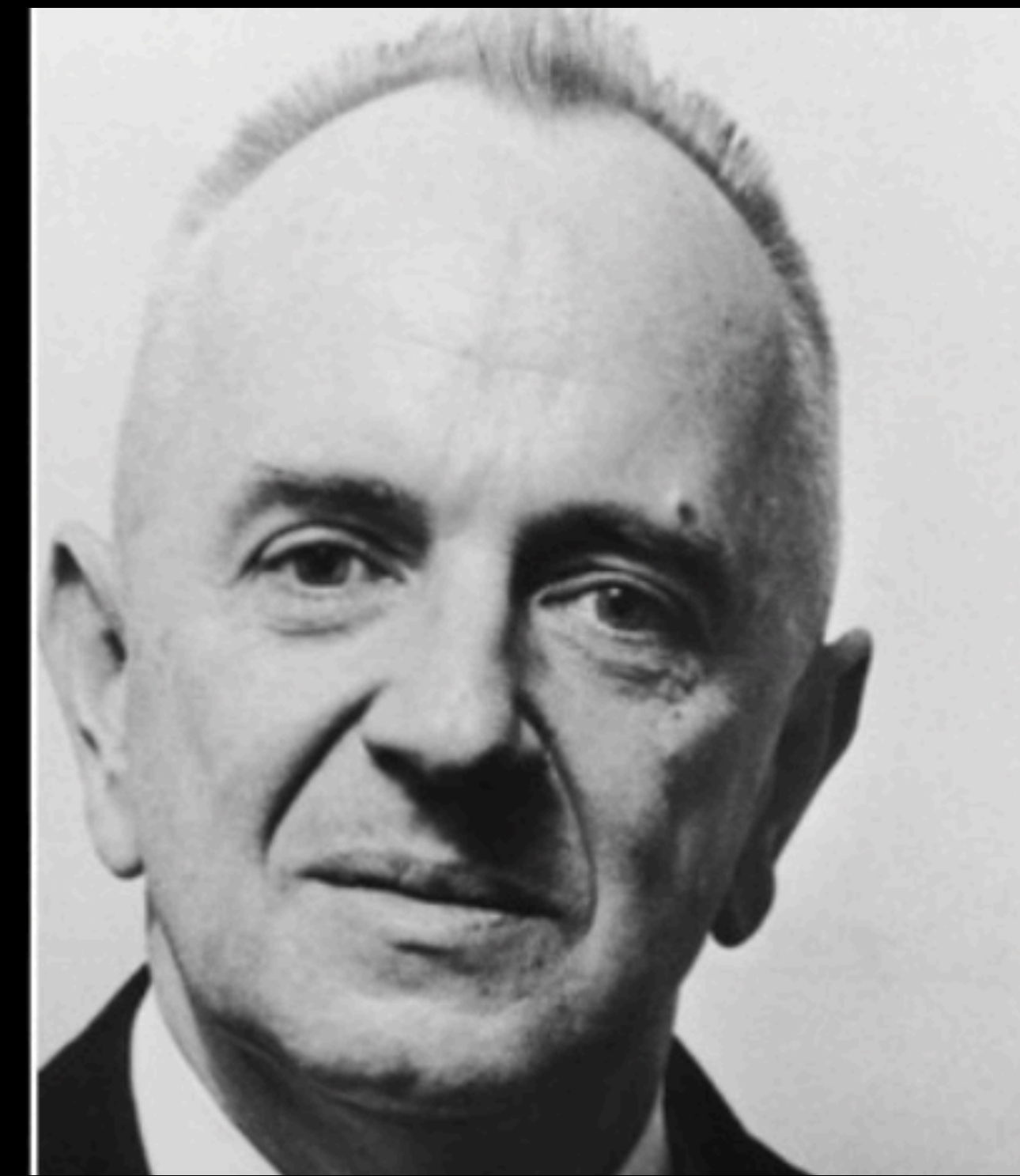
LETTERS

<https://doi.org/10.1038/s41591-019-0179-2>

nature
medicine

ARAF recurrent mutation causes central conducting lymphatic anomaly treatable with a MEK inhibitor

Dong Li¹, Michael E. March¹, Alvaro Gutierrez-Uzquiza^{1,2}, Charly Kao¹, Christoph Seiler², Erin Pinto², Leticia S. Matsuoka¹, Mark R. Battig¹, Elizabeth J. Bhoj¹, Tara L. Wenger⁴, Lifeng Tian¹, Nora Robinson¹, Tiancheng Wang¹, Yichuan Liu¹, Brant M. Weinstein², Matthew Swift⁶, Hyun Min Jung⁵, Courtney N. Kaminski¹, Rosetta Chiavacci¹, Jonathan A. Perkins⁷, Michael A. Levine^{8,9}, Patrick M. A. Sleiman^{1,9}, Patricia J. Hicks⁹, Janet T. Strausbaugh⁸, Jean B. Belasco^{9,10}, Yoav Dori^{3,9} and Hakon Hakonarson^{1,9,11*}



Nothing in biology makes sense
except in the light of evolution.

— *Theodosius Dobzhansky* —

