A black and white photograph of a Saguaro cactus in a desert landscape. The cactus is the central focus, with several arms reaching upwards. The background shows a vast desert plain with low mountains in the distance under a sky filled with dramatic, layered clouds. The overall mood is stark and atmospheric.

Numbers and Neurons:
**Initial Bioinformatic Analysis of the McKnight
Collaborative Data**

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Potential Genomic Mechanisms of Cognitive Aging [in rodents]

What does it mean (genomically) when you identify an animal who outperforms age-matched peer animals on a specific task?

- Their DNA includes a variant that gives them a competitive advantage on the task? (unlikely)
- The brain circuit participating in the task existed at an “advantageous state” prior to the measurement of task performance? (Experience driven and transcriptionally manifest? Stochastic?)
- The brain circuit participating in that task responded differently than age-matched peer animals?

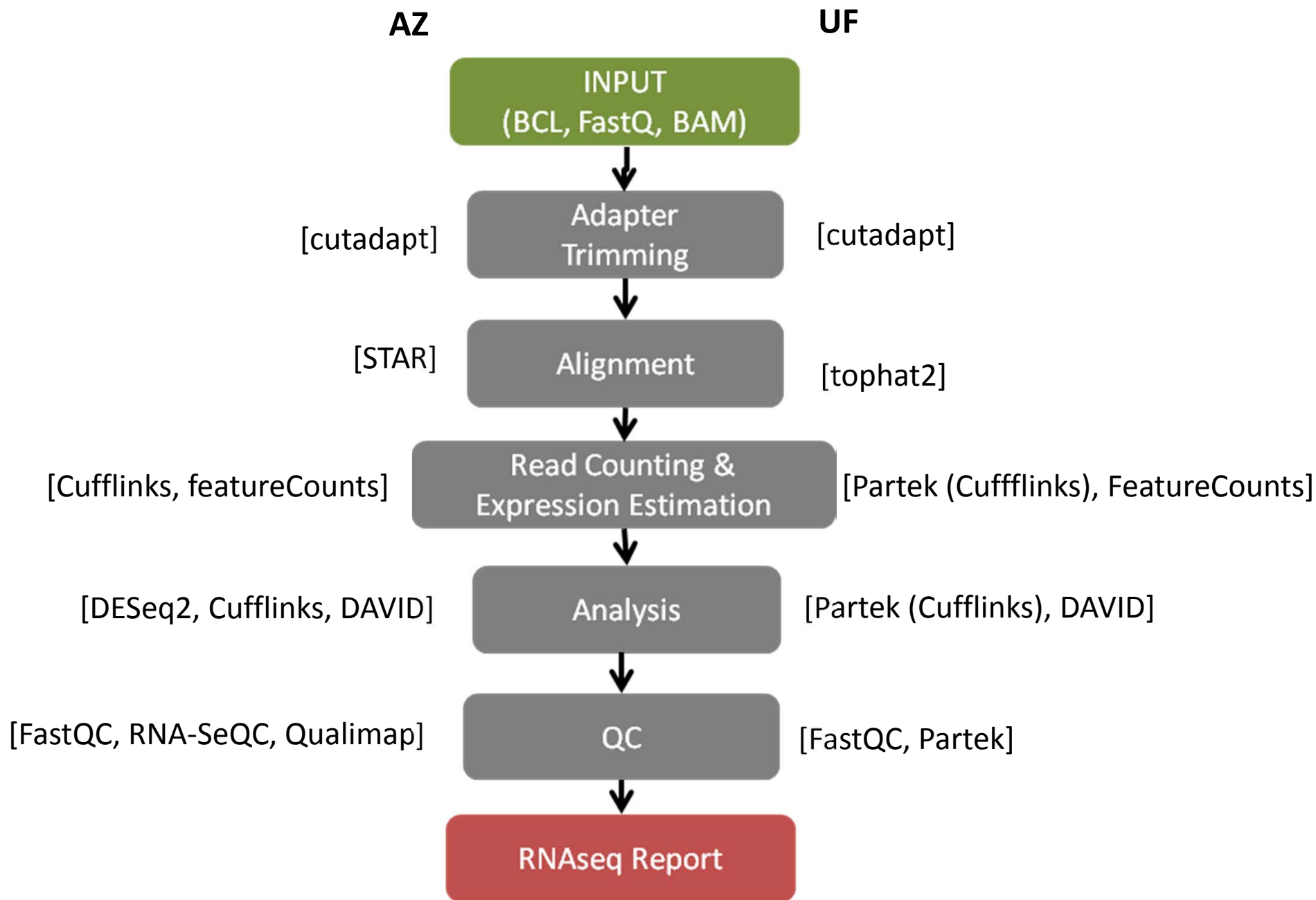
Brief Study Overview - AZ

Samples	Young	Old Good	Old Bad
CA1	3	2	2
CA3	3	2	2
DG	3	2	2
Amygdala*	1	1	1

*Amygdala data was dropped due to lack of replicates

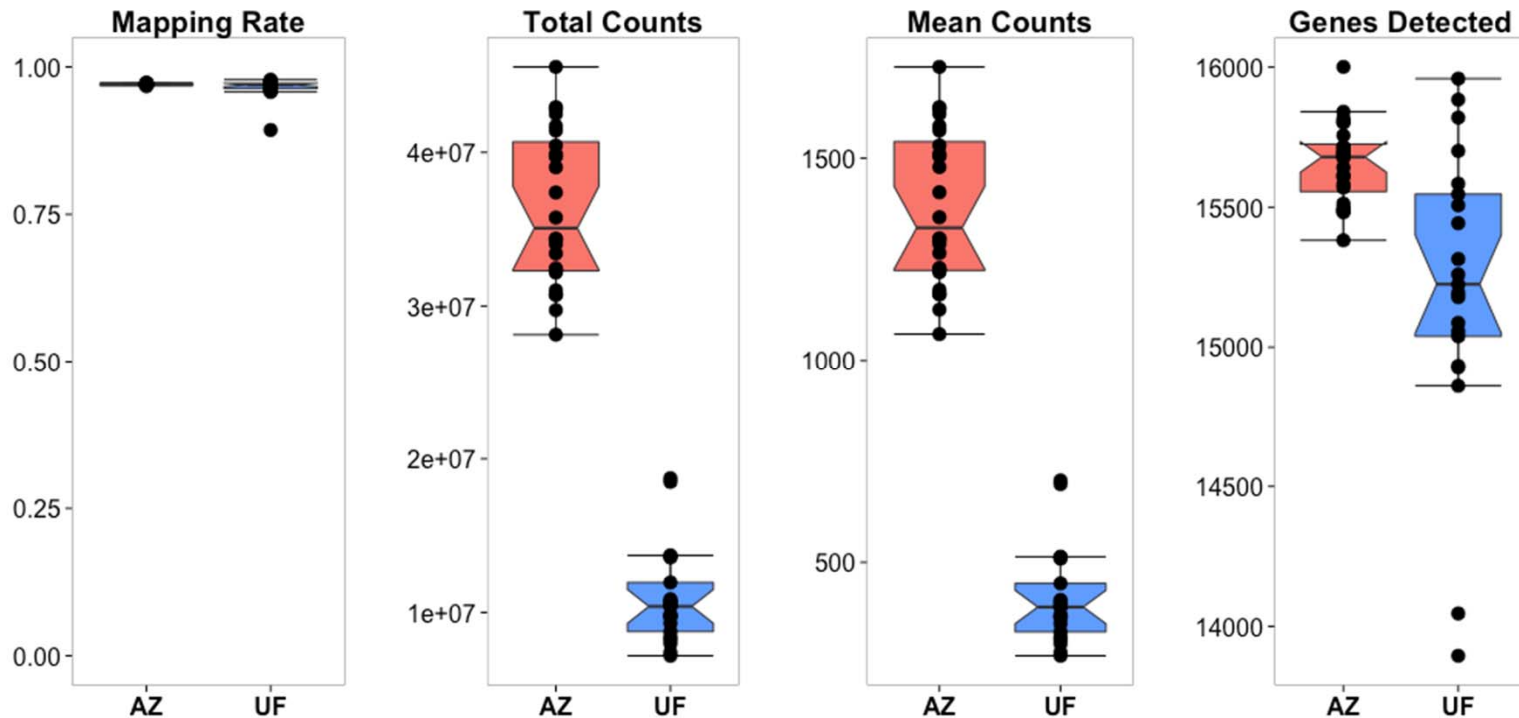
- RNA sequencing was performed using 250ng of total RNA.
- Sequencing libraries were prepared with Illumina's Truseq mRNA Sample Preparation Kit following the manufacturer's protocol.
- The final library pool (N=24 samples) was sequenced by 50bp paired-end sequencing on 7 lanes of a HiSeq2500.

Informatics Pipeline Comparison – AZ and UF

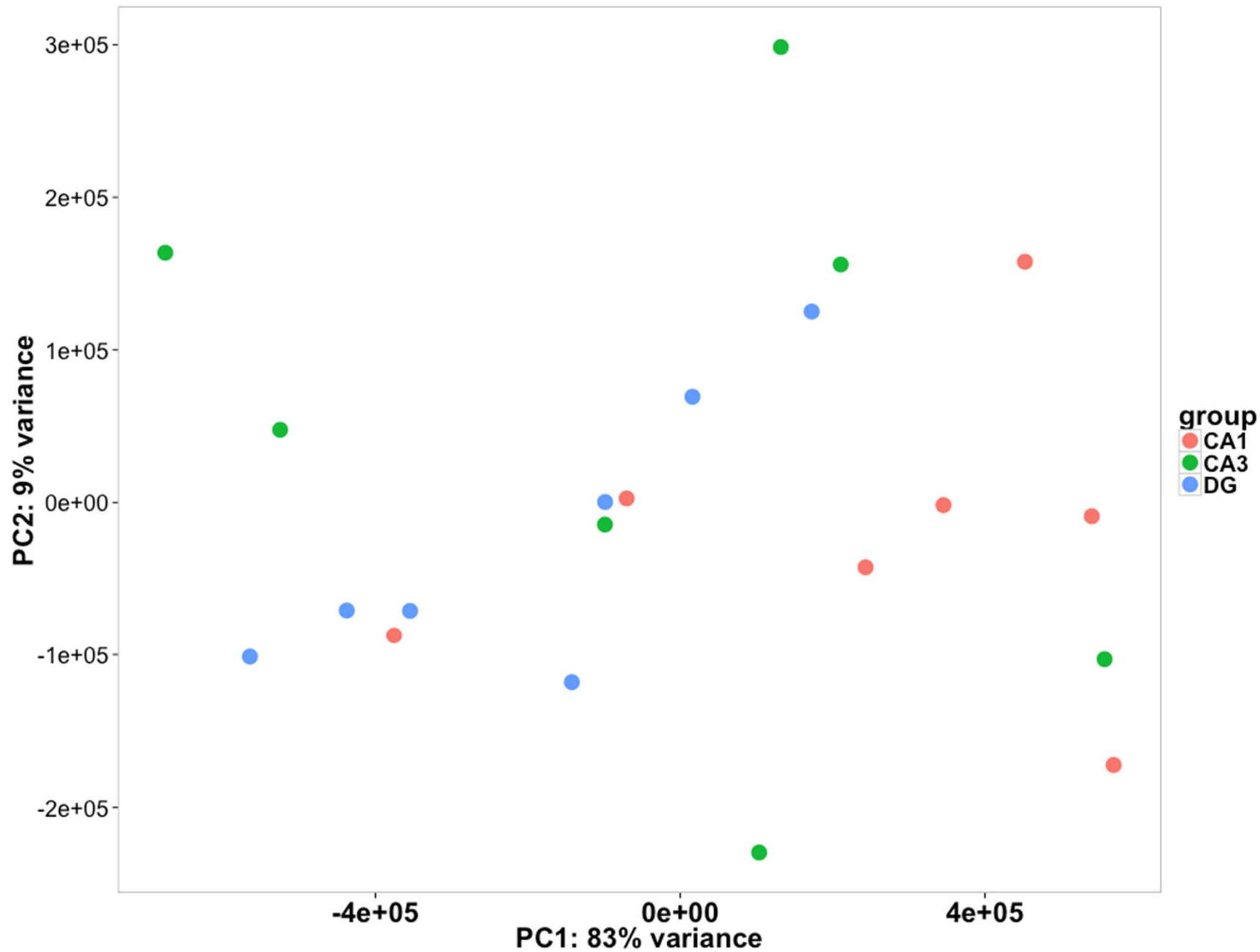


RNA-Seq Quality Control Stats – AZ and UF

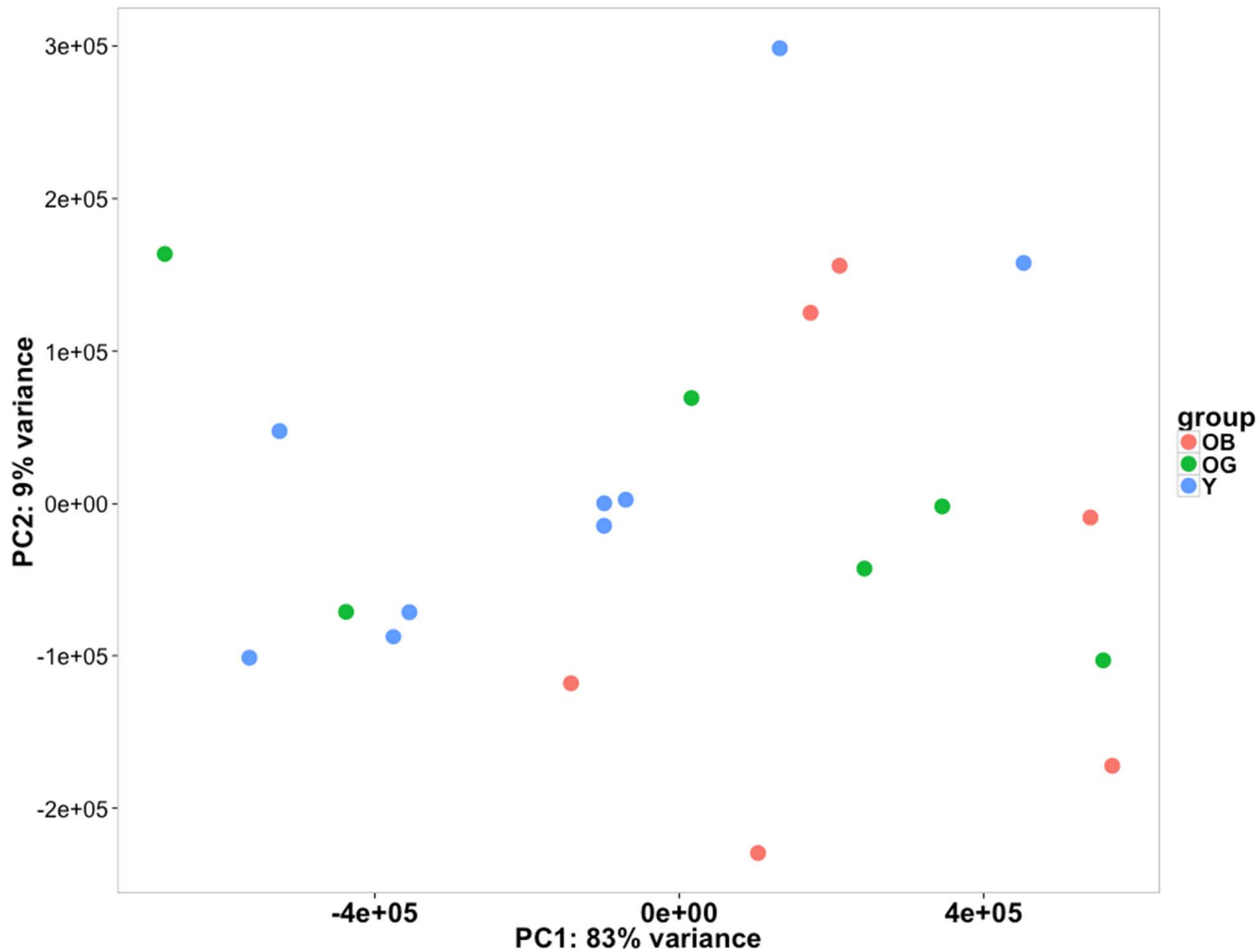
Institute	Mapping Rate per Sample	Total Counts per Sample	Mean Counts per Gene	Genes Detected per Sample
UF	96.51%	11,000,000	410	15,212
AZ	97.05%	36,000,000	1377	15,657
P-value	0.14	2.67e-23	2.00e-23	2.44e-04



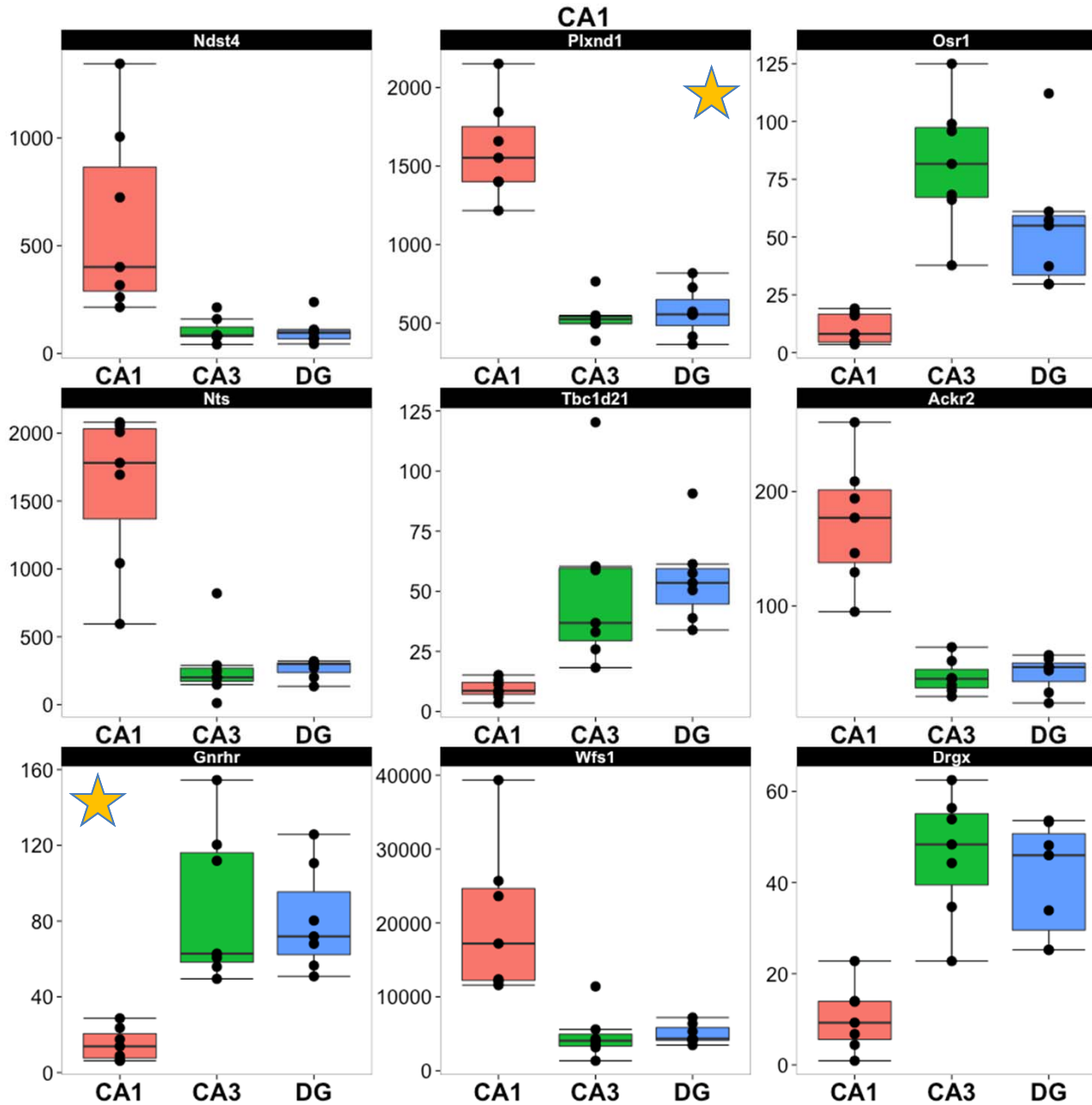
Principal Components Analysis – by HCF sub-region



Principal Components Analysis – by animal performance



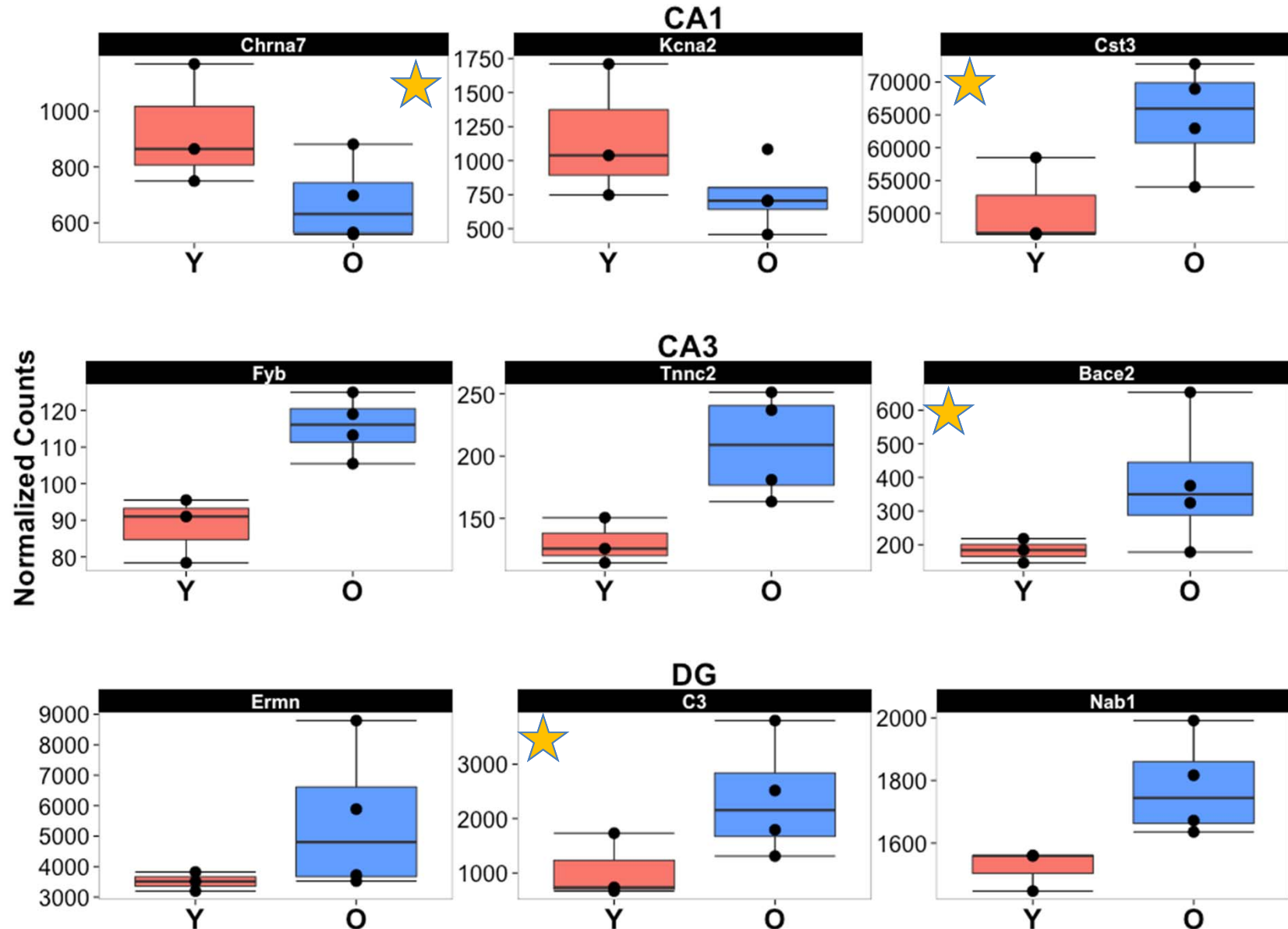
Region Differential Expression – CA1



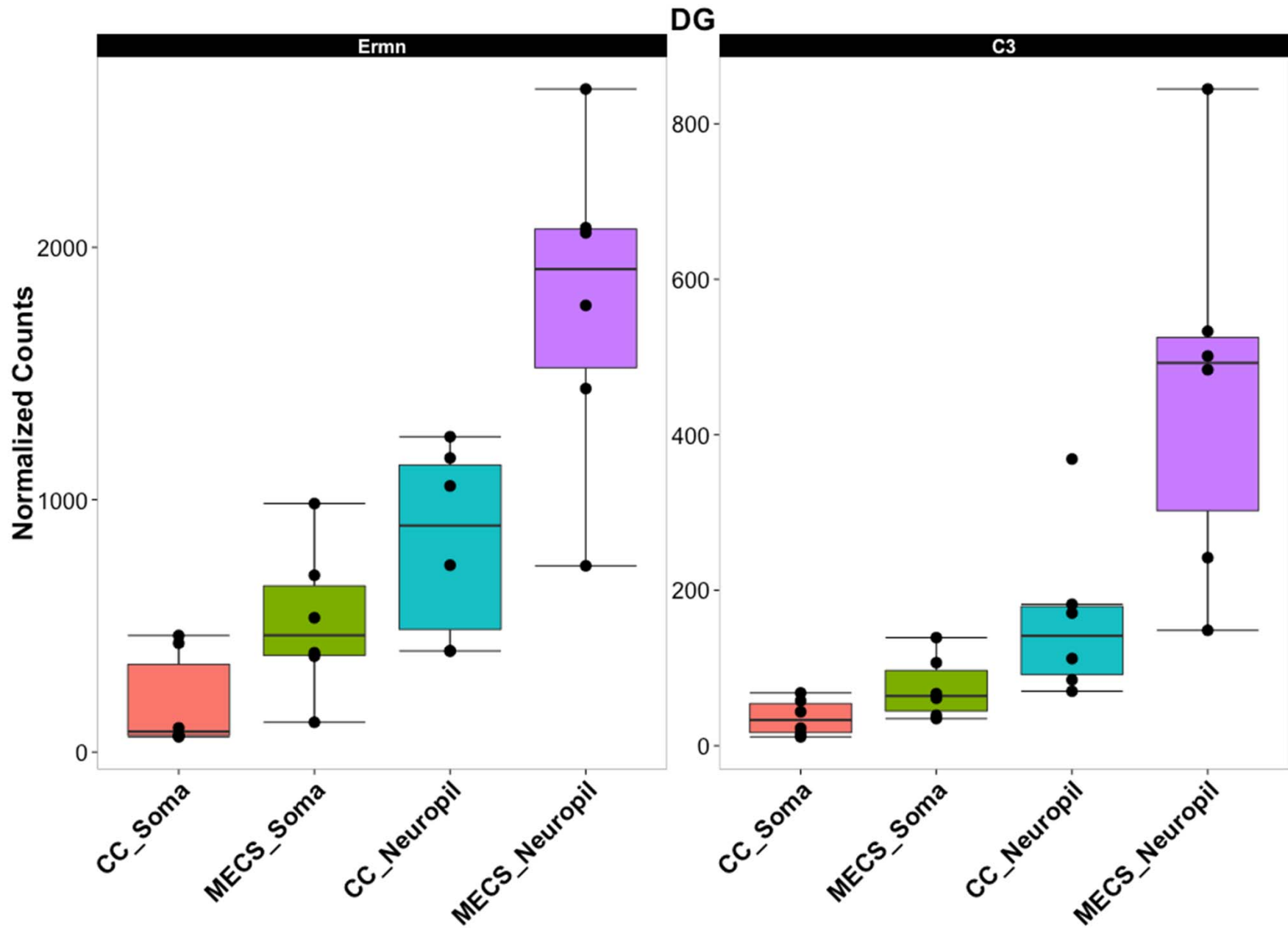
CA1 vs. CA3 = sig
CA1 vs. DG = sig
DG vs. CA3 = non-sig
AZ = UF
 Disregard Age
 Disregard Perf.

HCF Sub-Region Expression & Aging – Old vs. Young

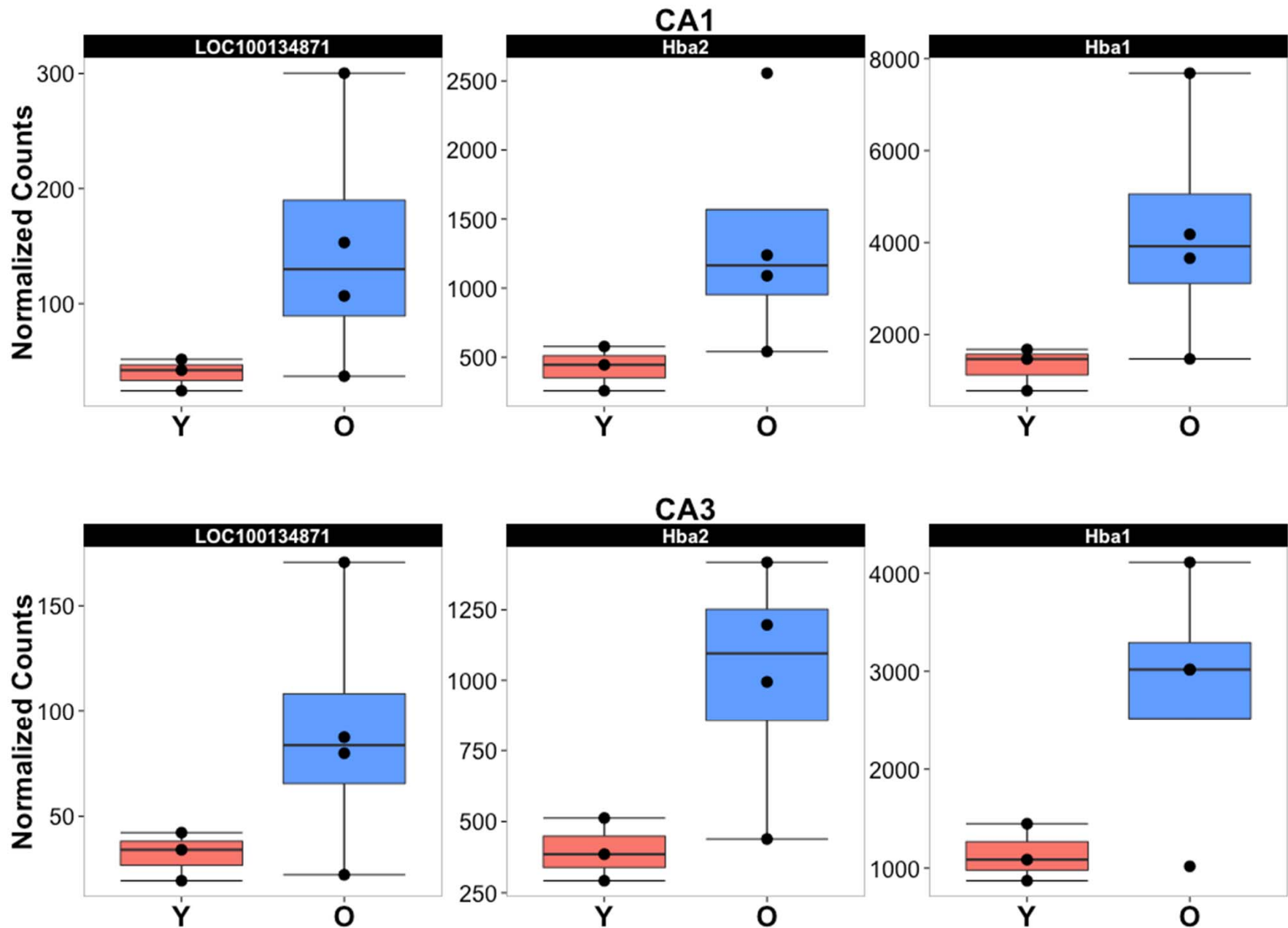
Disregard performance, Old vs. Young = sig, AZ = UF



Mechanism of Action w/ Aging? – DG IEGs

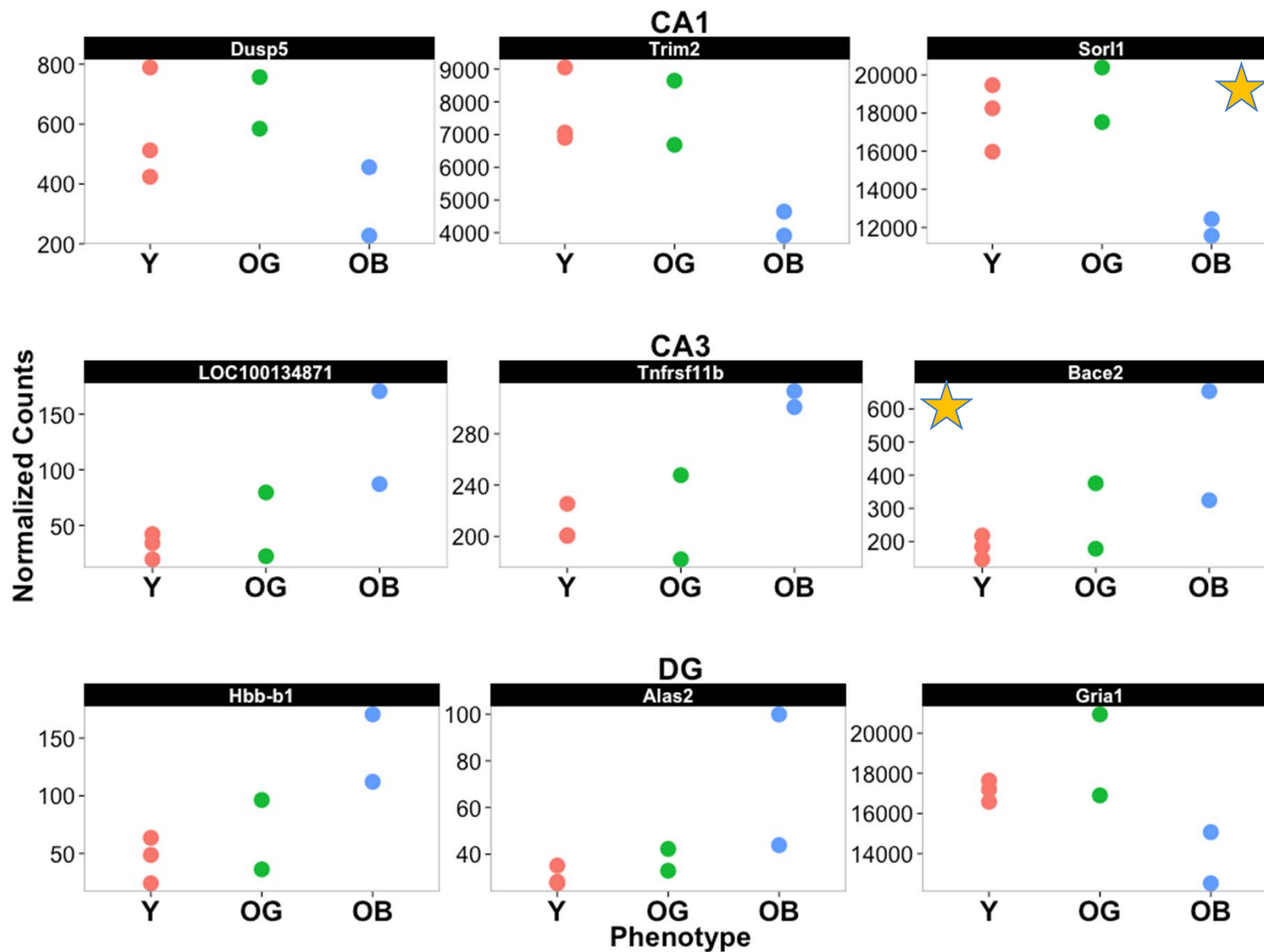


Therapeutic Opportunity? Aging / Cognition – HBB

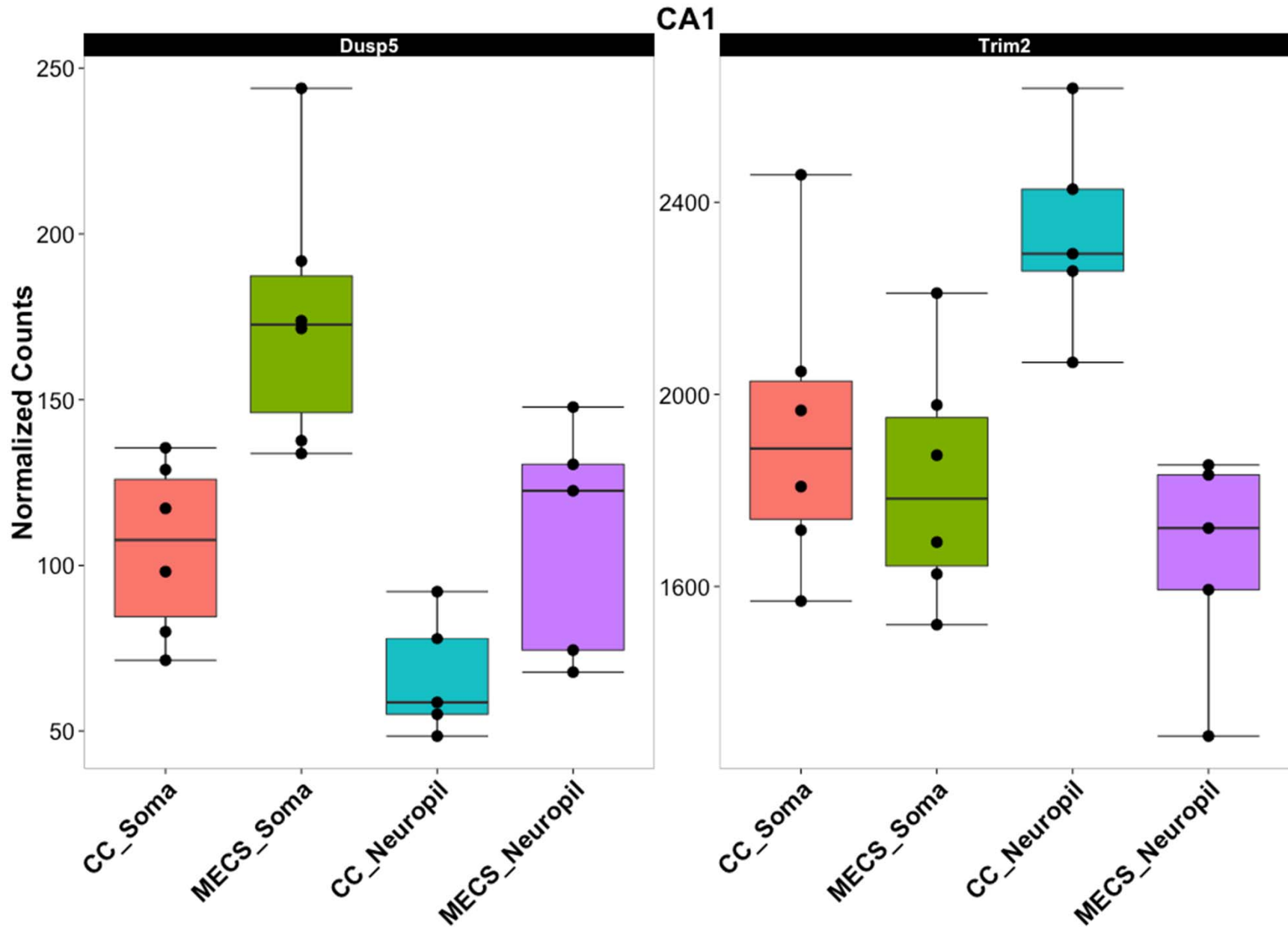


Differential Expression - Cognition

Y vs. Old Good = non-sig, Old Good vs. Old Bad = sig, Y vs. Old Bad = sig
AZ = UF, Region Specific Results

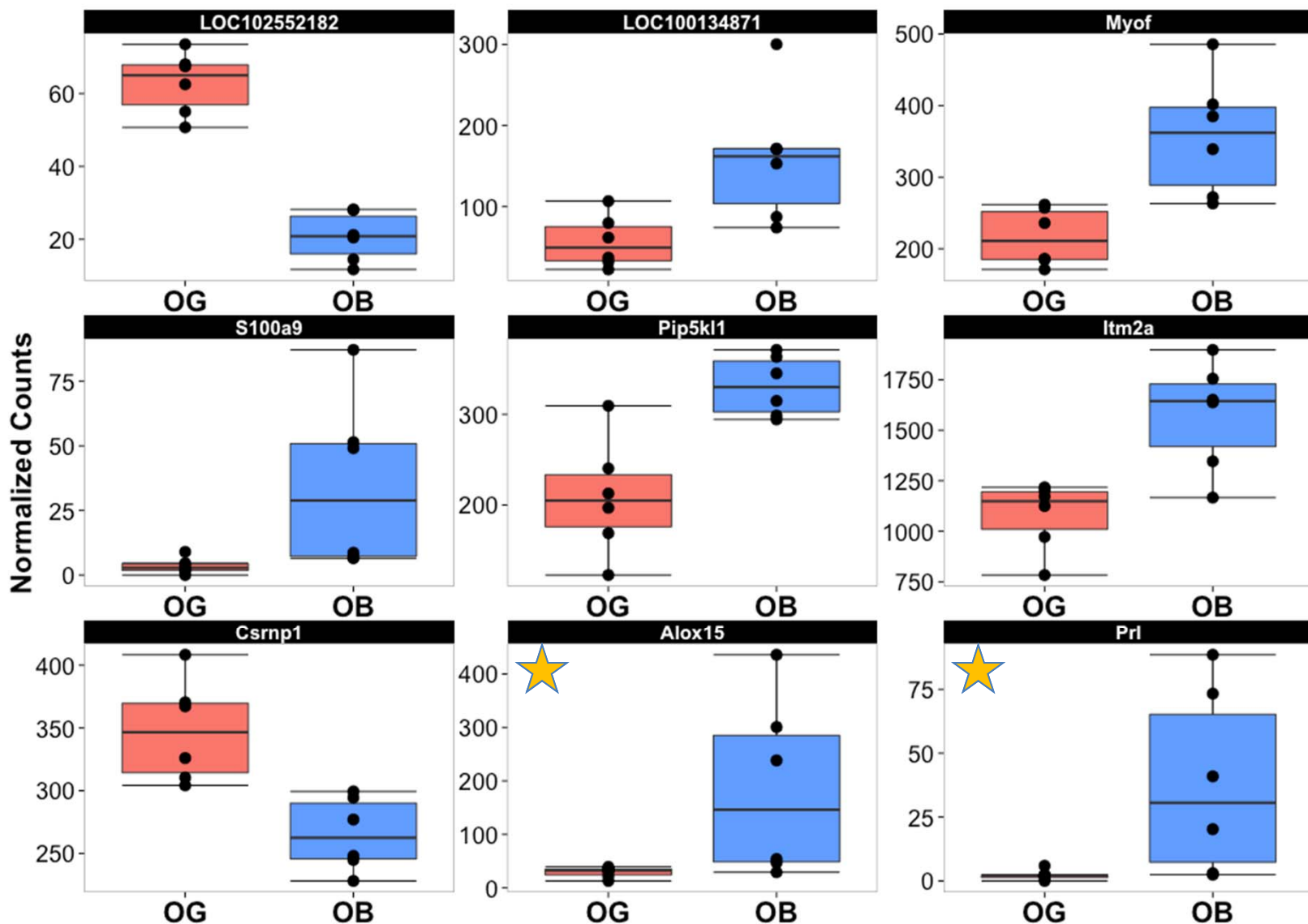


Differential Expression – Cognition, Mechanism? CA1 IEGs



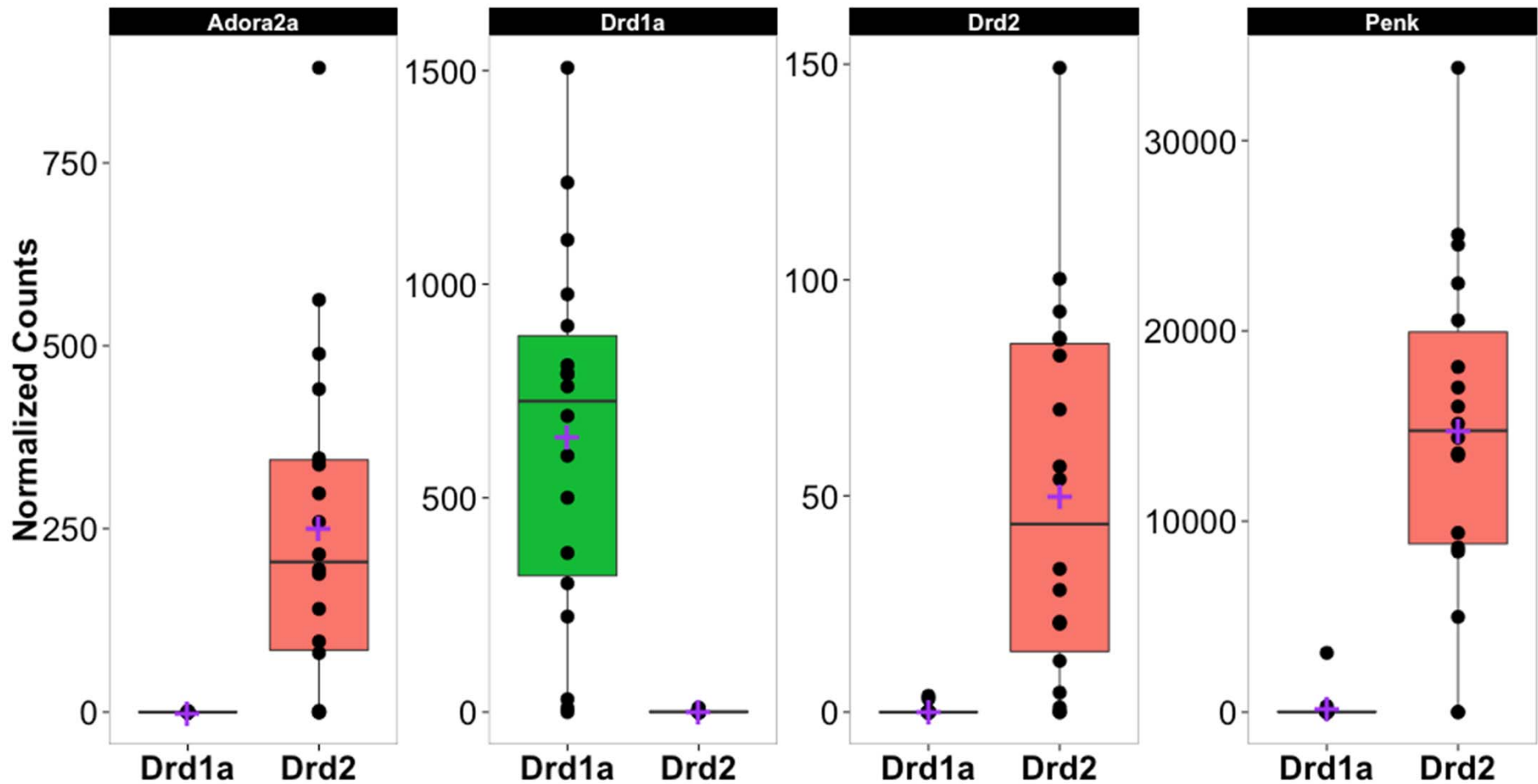
Differential Expression – Cognition, HCF-Generic

Old Good vs. Old Bad = sig, Disregard Young Group, Disregard Region
AZ = UF



Future Goals – Circuit Identification + Single Cell Seq

Striatal MSNs, genetically labeled and sorted by Drd1a vs. Drd2
Over 95% library prep success rate from FACS'd single cells

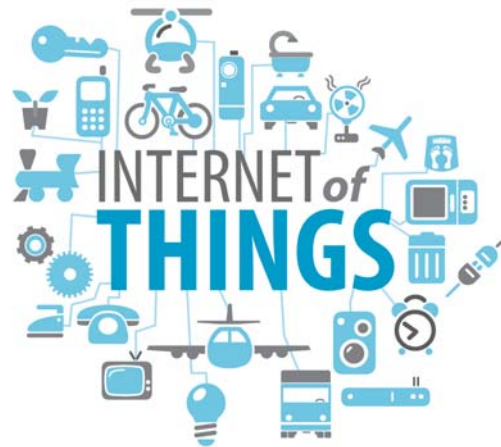


Human Translational Efforts

Large Sample Sizes + Wearables + Genomics



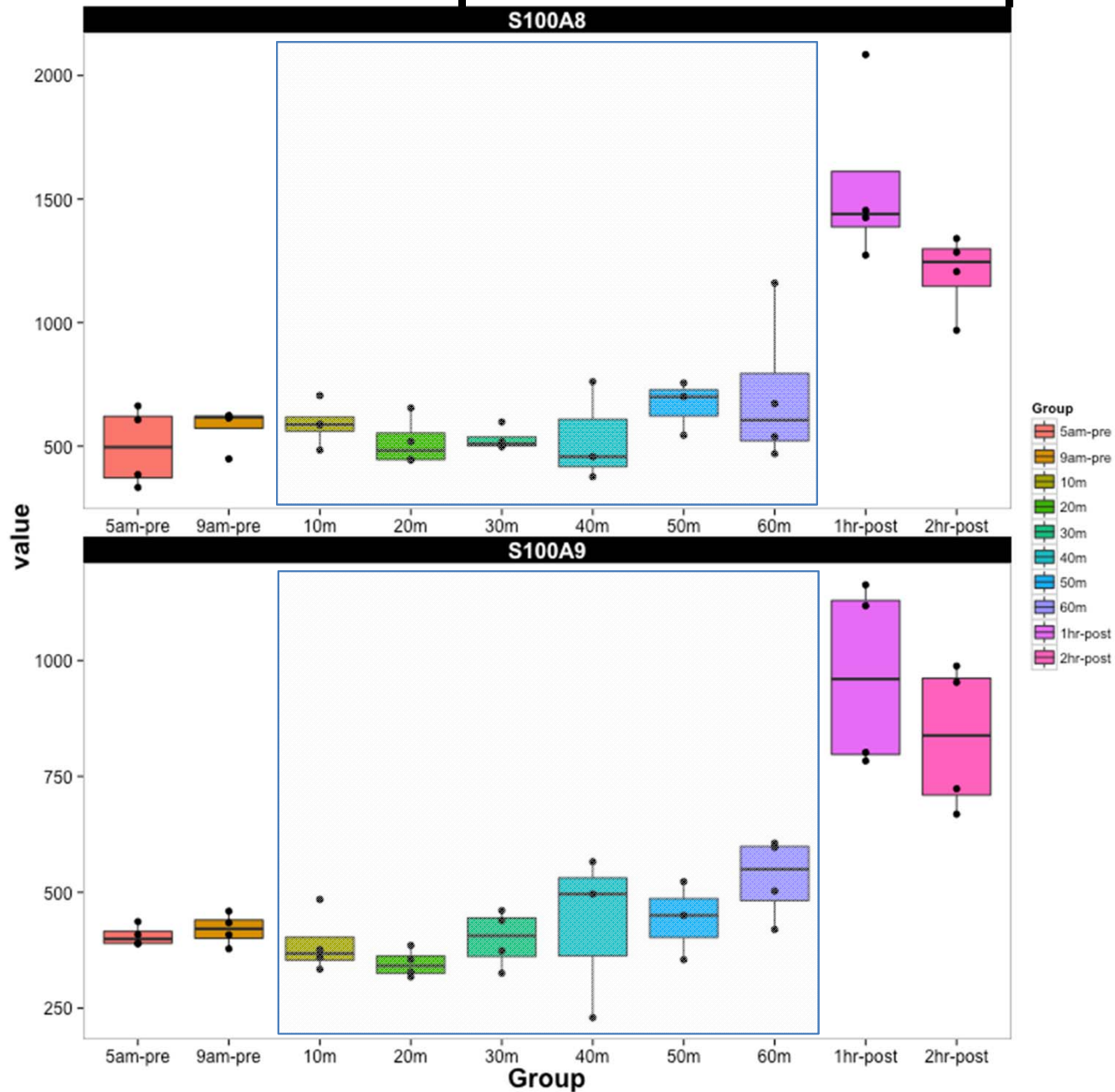
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+



Dried Blood Spot – Proof of Concept



S100A8 + S100A9 = "Calprotectin", secreted by skeletal muscle in response to exercise

