

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 lighting is high-contrast, with bright highlights on the clouds and deep shadows in the desert.

**What can the transcriptome tell us about
hippocampal subregion differences?**

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OUR FOCUS

**Identify the transcriptional differences between
selected hippocampal sub-regions**

OUR RATIONALE

Aging is associated with cognitive decline

The hippocampal formation is known to be particularly vulnerable

Each sub-region within the hippocampus has unique susceptibilities and possesses unique anatomy and molecular physiology

CA1 → particularly susceptible to AD-related pathology

CA3 → more vulnerable to stress/glucocorticoids

DG → reduced neurogenesis with aging

OUR QUESTION

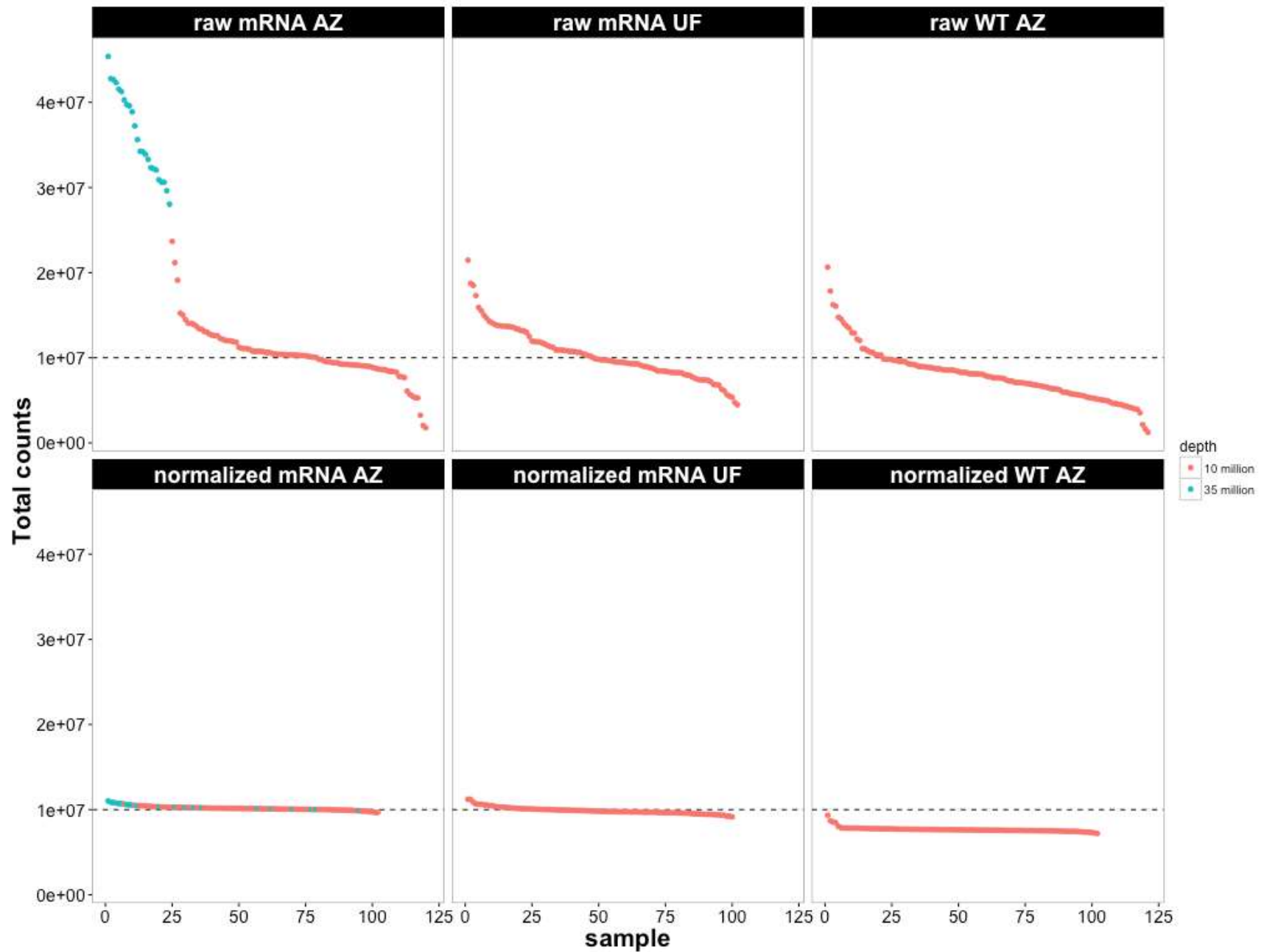
Do the transcriptional differences across the hippocampal sub-regions throughout the lifespan (i.e. ignoring age-related changes) help explain their unique age-related susceptibilities?

KEY DESIGN POINTS

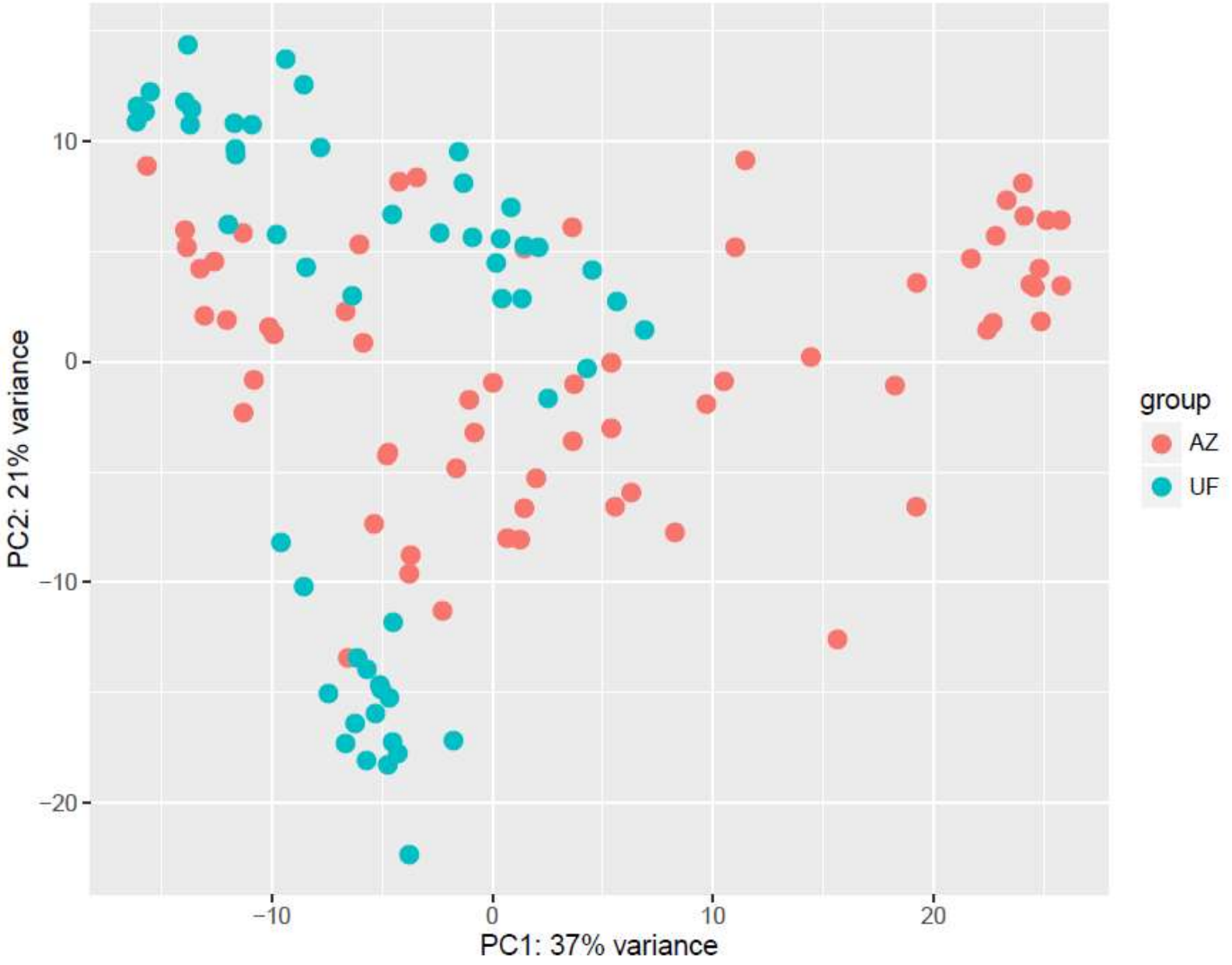
Only considered genes that met correction for all of our parallel hypotheses [B&H FDR $p < 0.05$]

Must be statistically significant across both sites

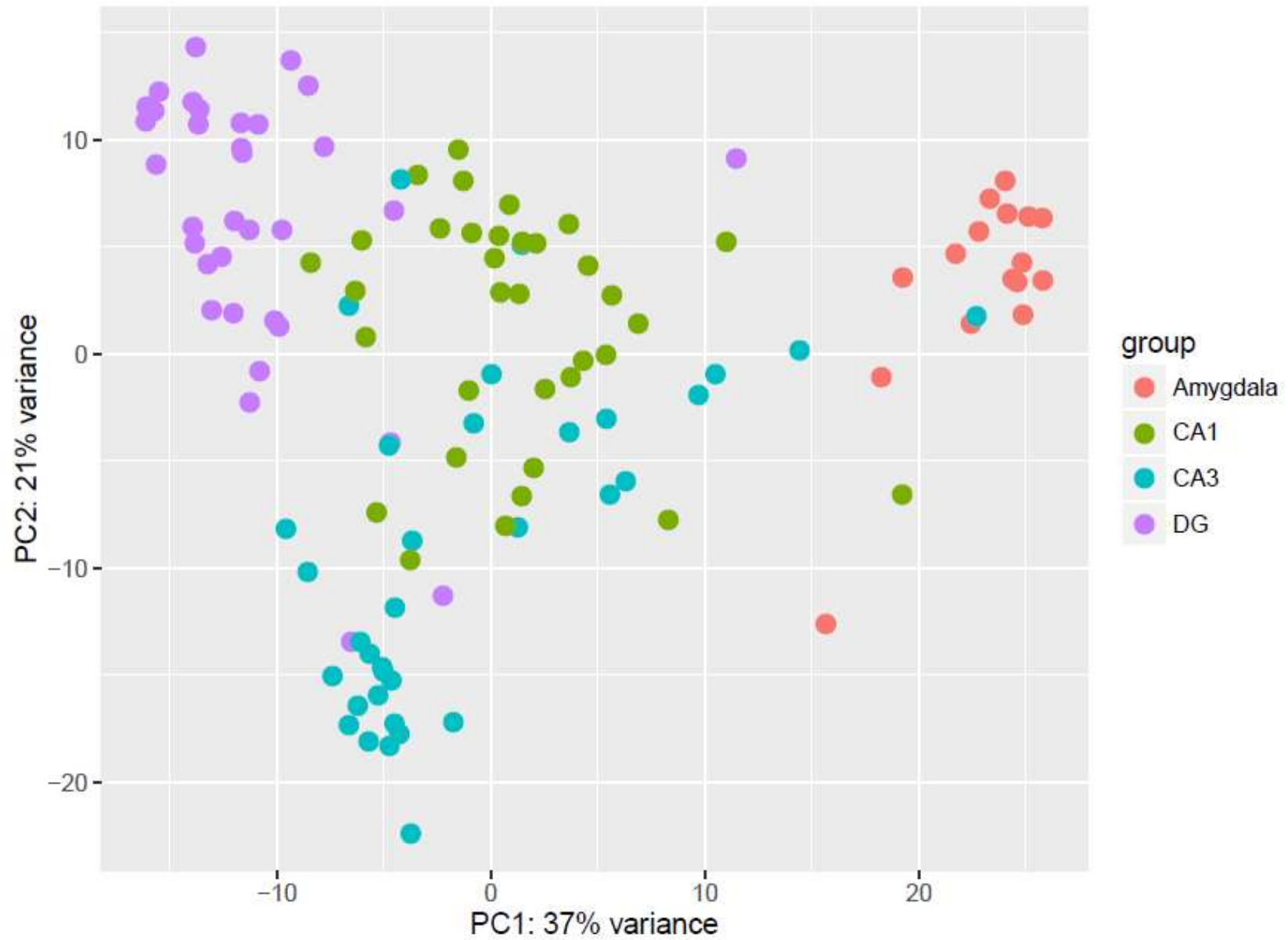
APPLES TO APPLES



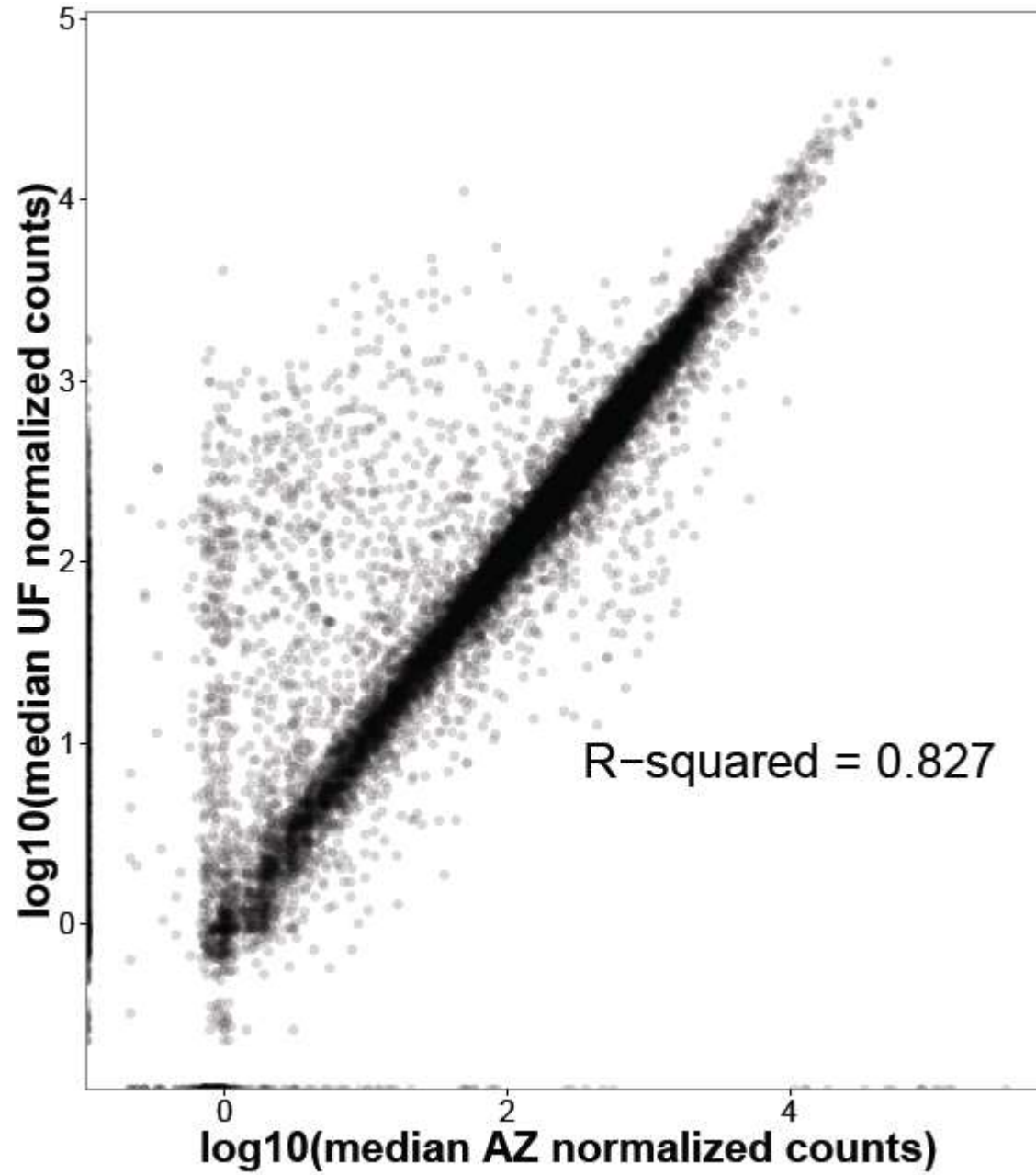
PCA – BY SITE



PCA – BY REGION

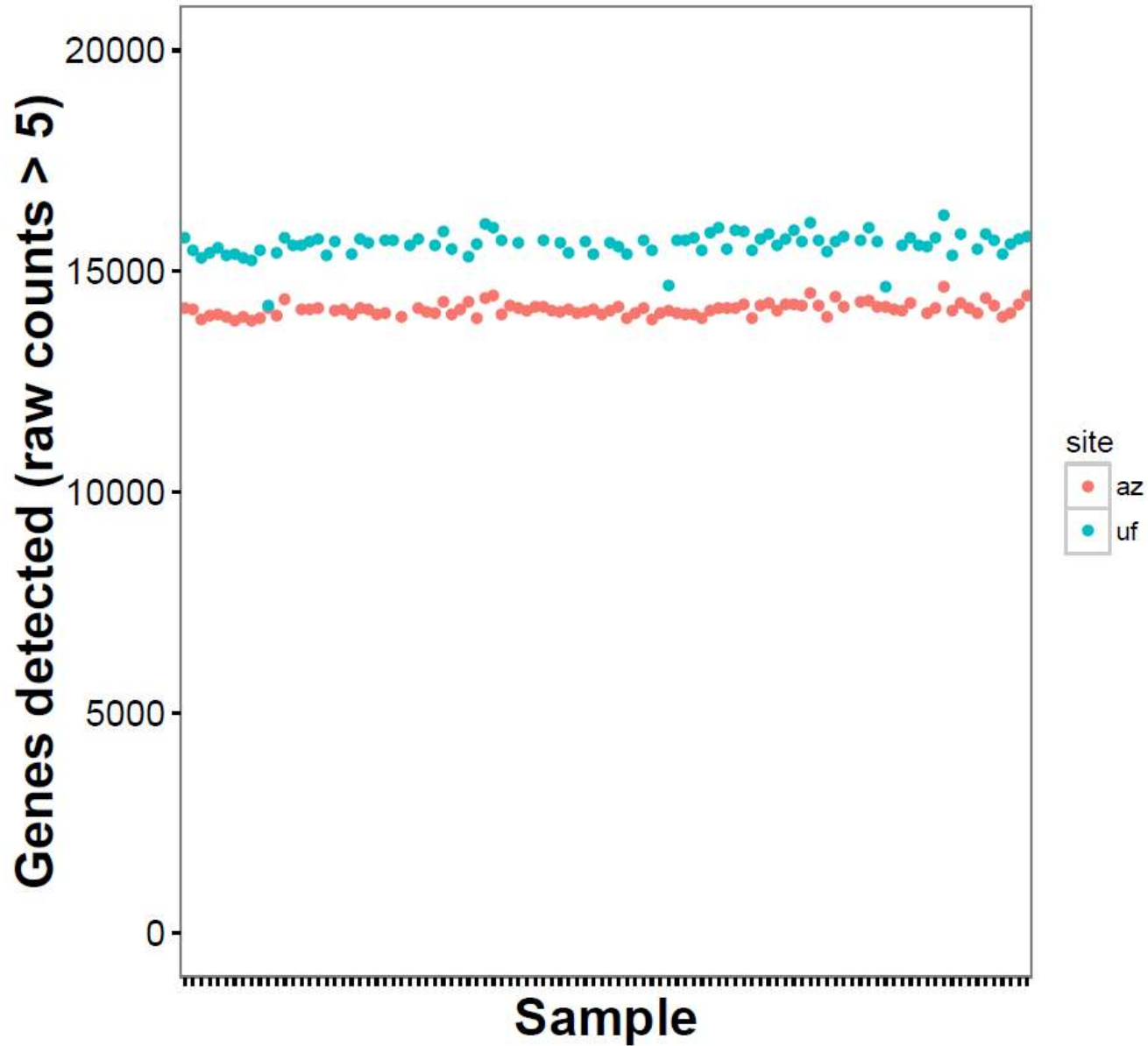


CROSS SITE CORRELATION

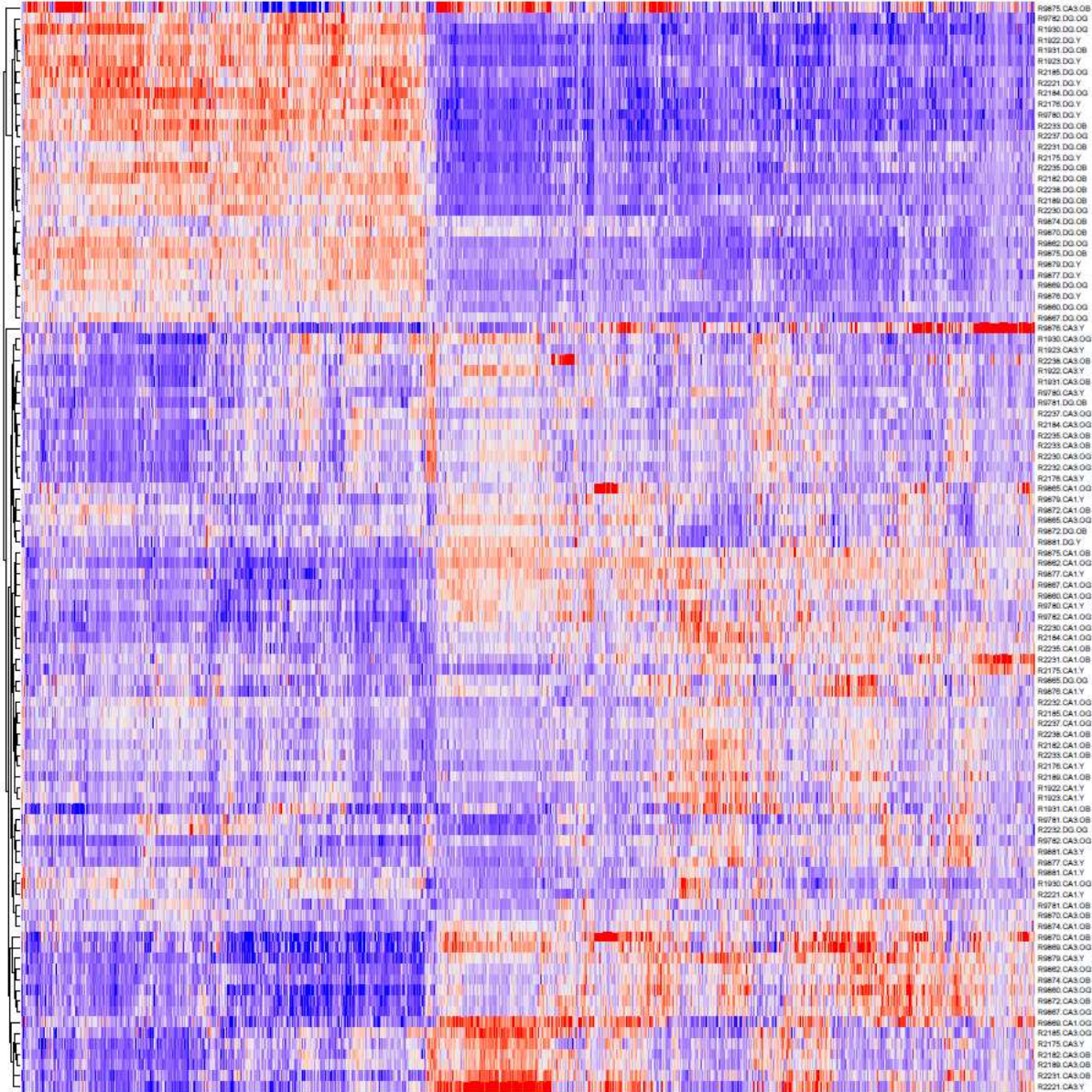


GENES DETECTED

Genes detected in 750,000 counts

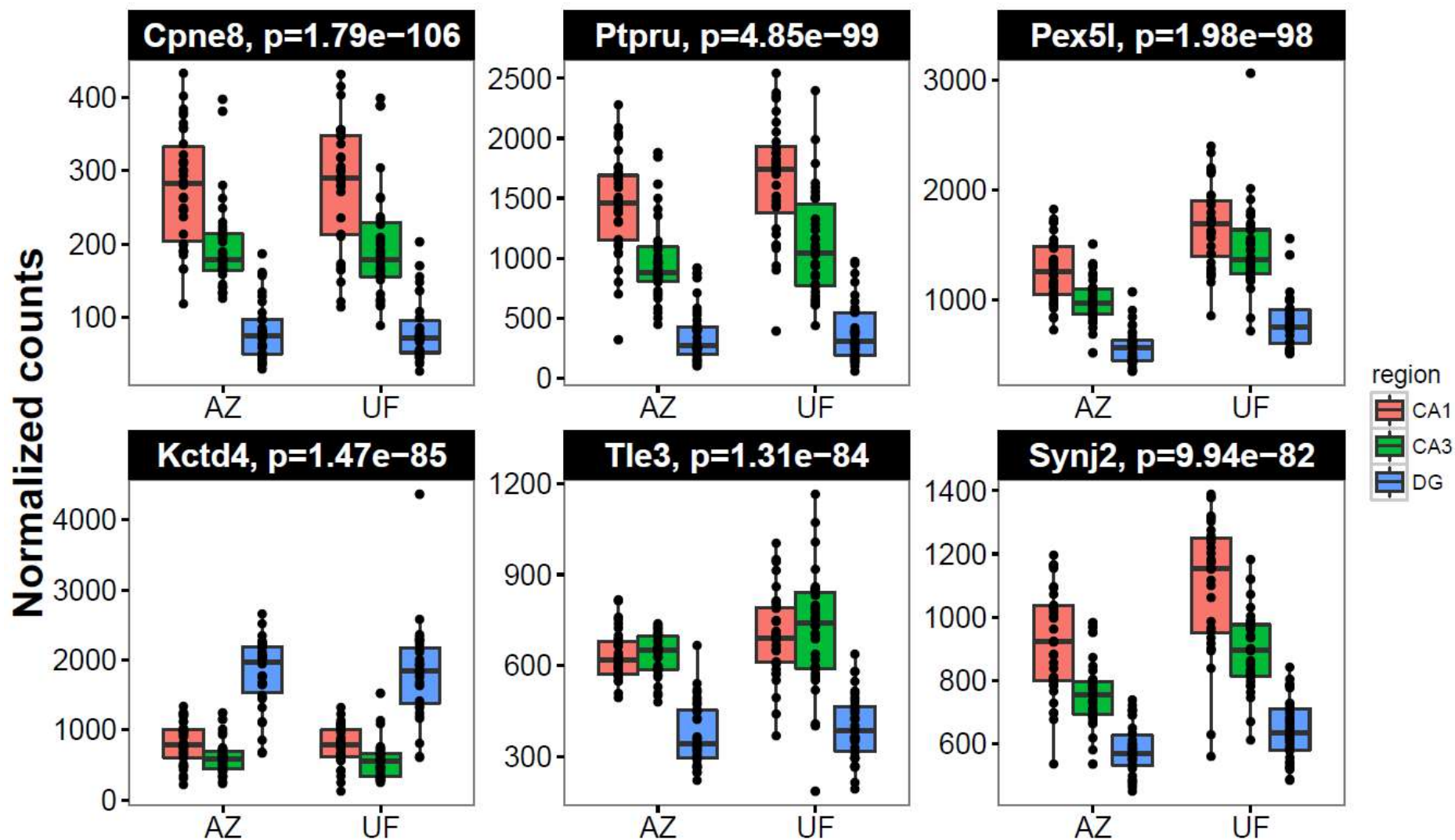


DG HEATMAP



Significantly (B&H) different vs. CA1 and CA3 at both sites

TOP HITS – DG SPECIFIC (meta p-value, Fisher's combined)

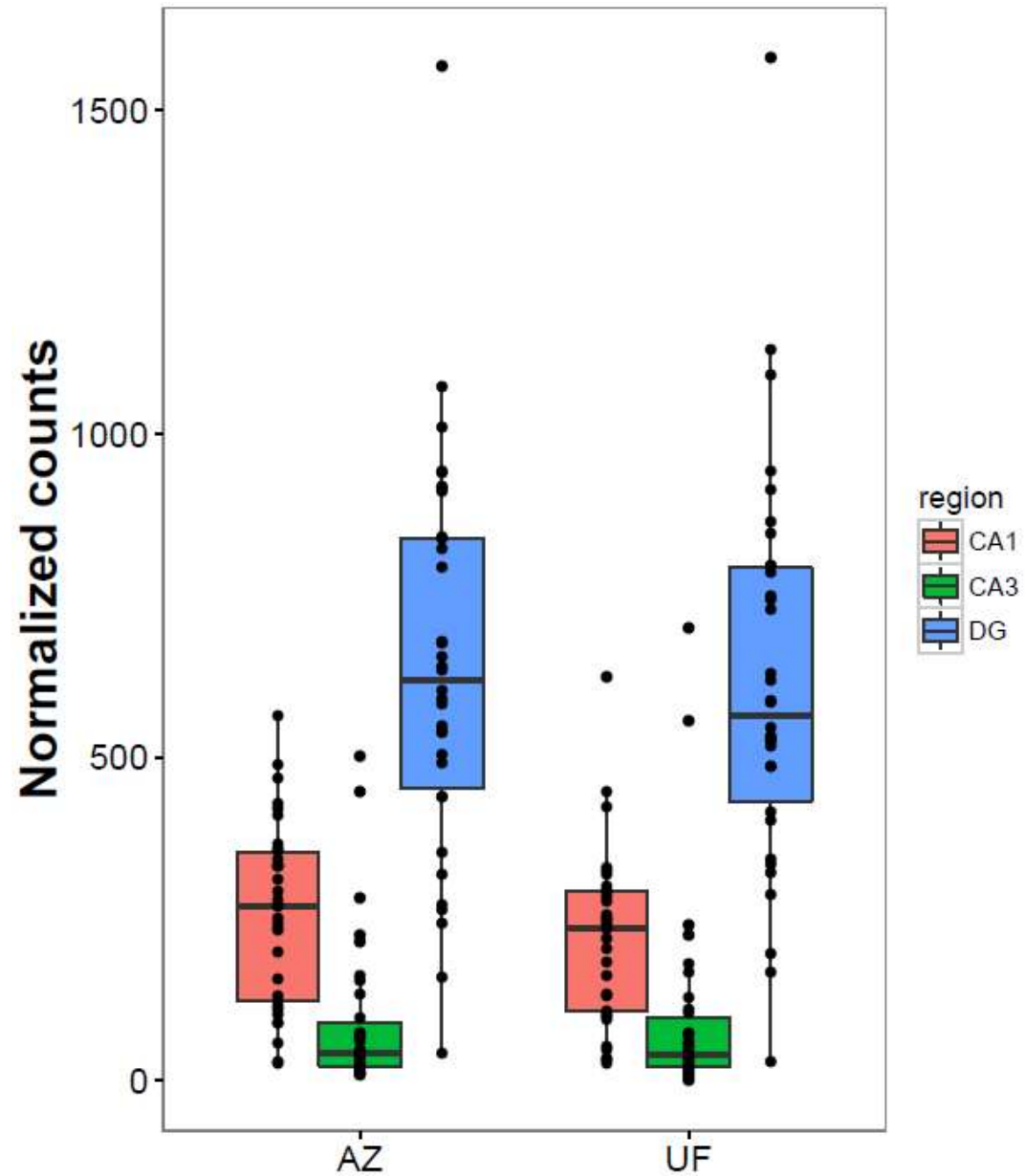
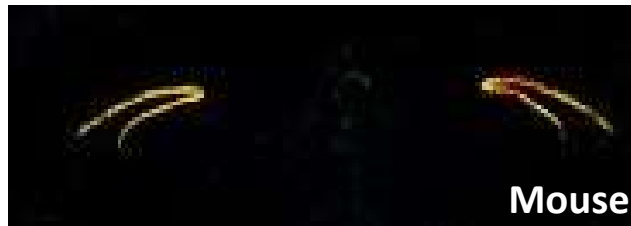


DG = 2,532 transcripts
CA1 = 1,068 transcripts
CA3 = 1,200 transcripts

“UNIQUE” EXPRESSION – DG

PLK5

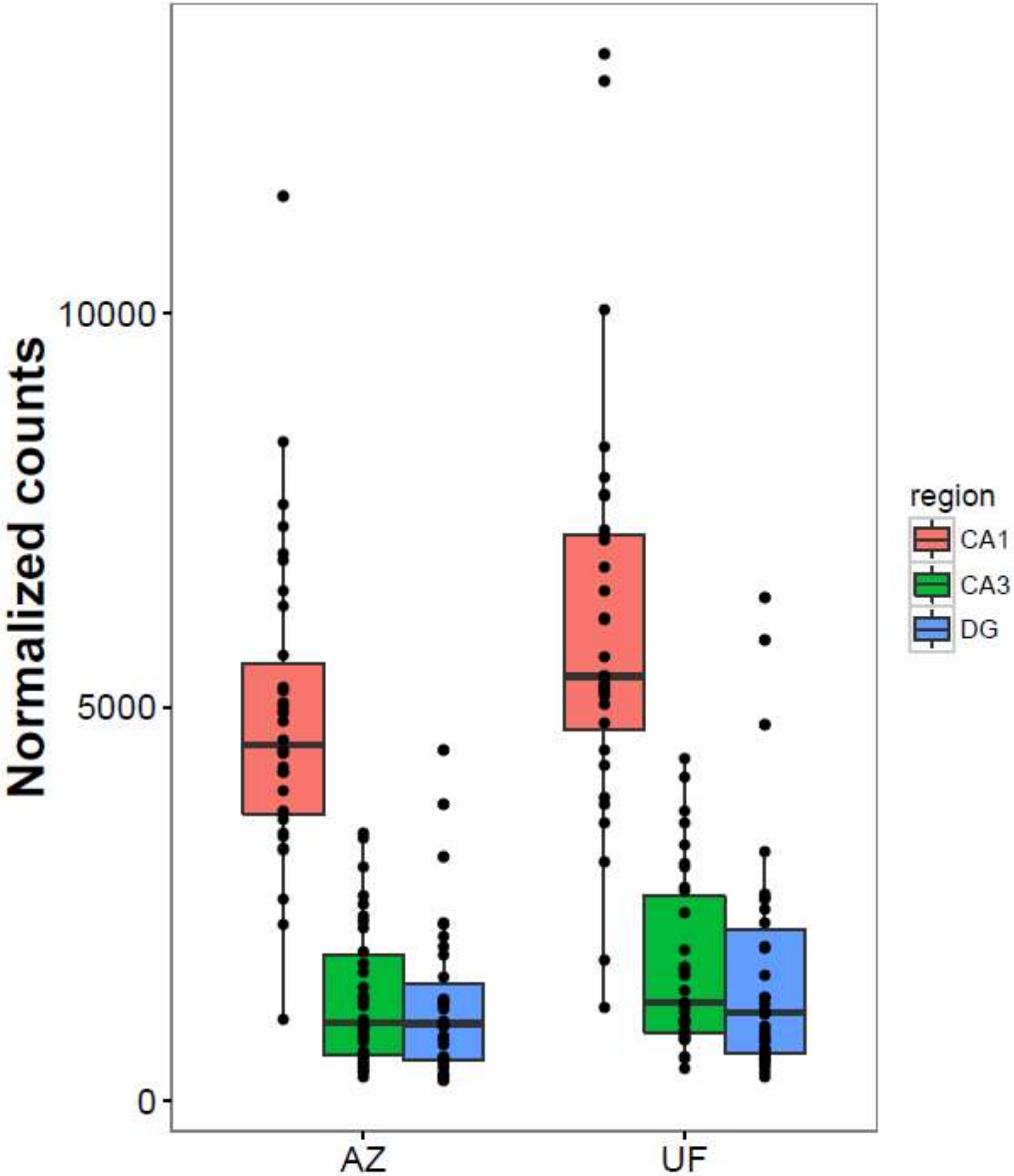
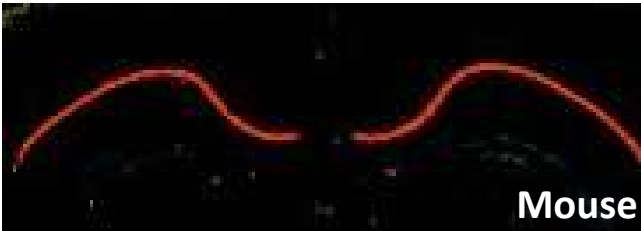
Kinase-deficient in humans, role in differentiation?



“UNIQUE” EXPRESSION – CA1

WFS1

ER-localized
glycosidase



CA3 = no strong uniquely expressed genes

So... WHAT ABOUT AGING ?

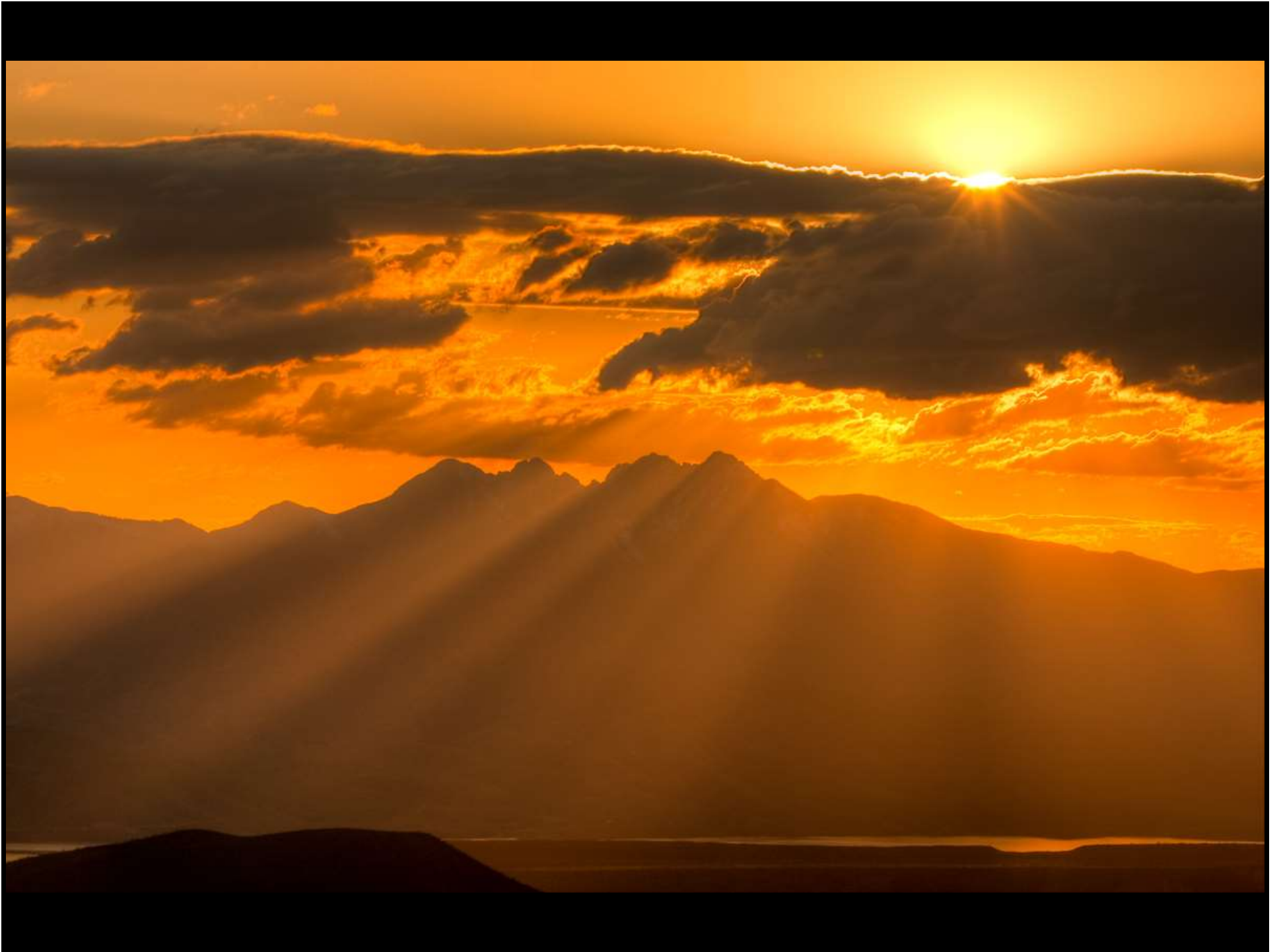
CA1 – particularly susceptible to AD-related pathology

Pathway analysis of the CA1 differentially expressed transcripts
“synaptic vesicle” transcripts are associated in CA1 but not the
other sub-regions

Thanks

Funding: McKnight Brain Research Foundation

Collaborators: UA / UF / UAB



DISCORDANT GENES

N=~450 genes that were consistently detected at UF [Ion Proton]

75 genes were explained by the use of a stranded library prep kit

Remaining have no explanation as of yet [chr / biotypes / etc...]