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Defining a set of genes responding to disrupted iron homeostasis

Extract 3' and 5' UTRs from zebrafish reference genome assembly (GRCz11)

Use SIREs to search for genes with Iron Responsive Elements

393
genes with
5' IREs

1,207
genes with 3' IREs

Using Fisher's exact test, we tested whether the IRE gene sets were over-represented in any gene sets from MSigDB.

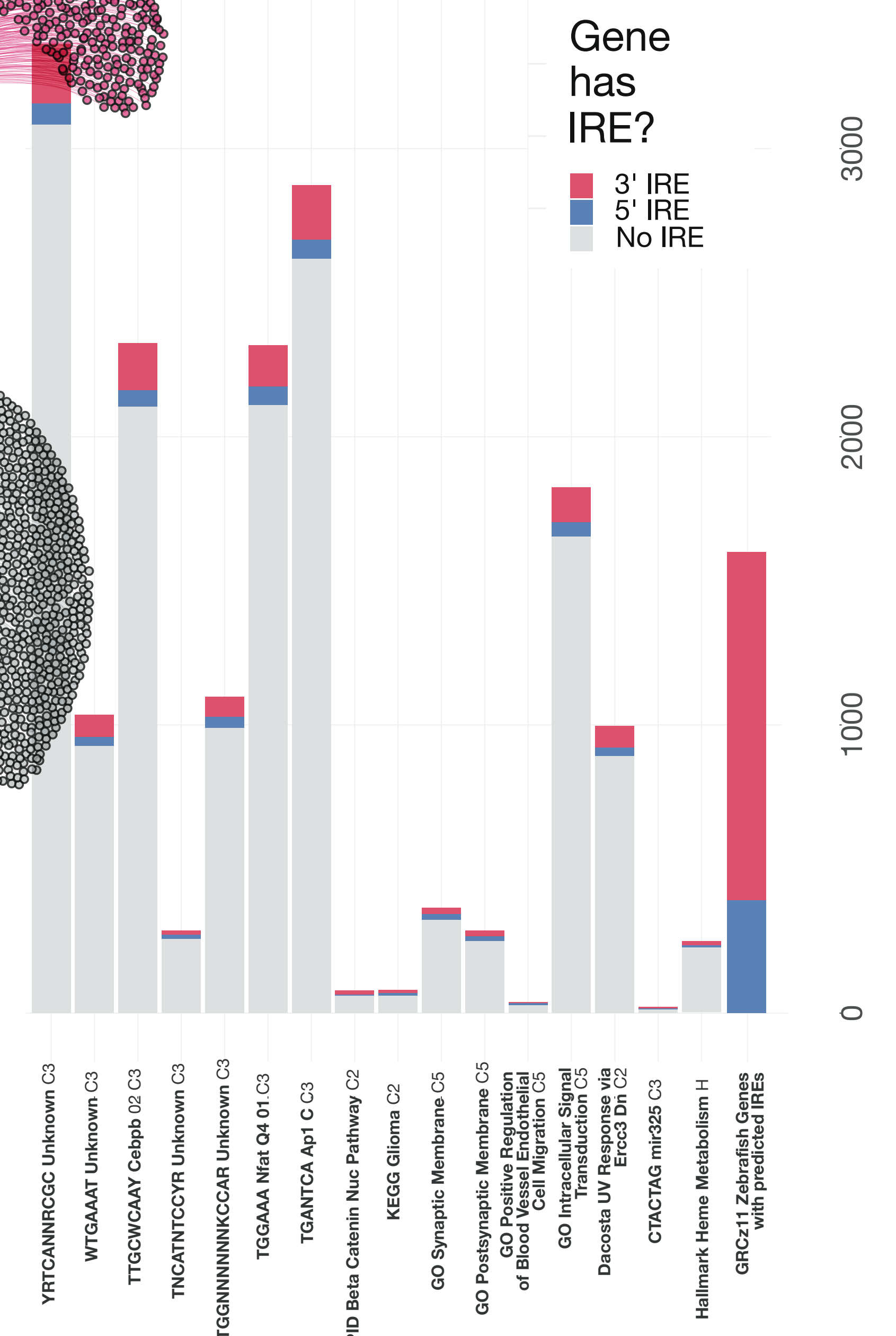
Surprisingly, many genes with IREs were not well-represented in existing gene sets, even the *Hallmark Heme Metabolism* gene set.

Iron enriched

We defined and characterised a set of genes responding to disrupted iron homeostasis.

These gene sets were enriched in two RNA-seq datasets: a zebrafish model of familial Alzheimer's disease, and human patients with sporadic Alzheimer's disease.

Hallmark Heme Metabolism (200 genes)

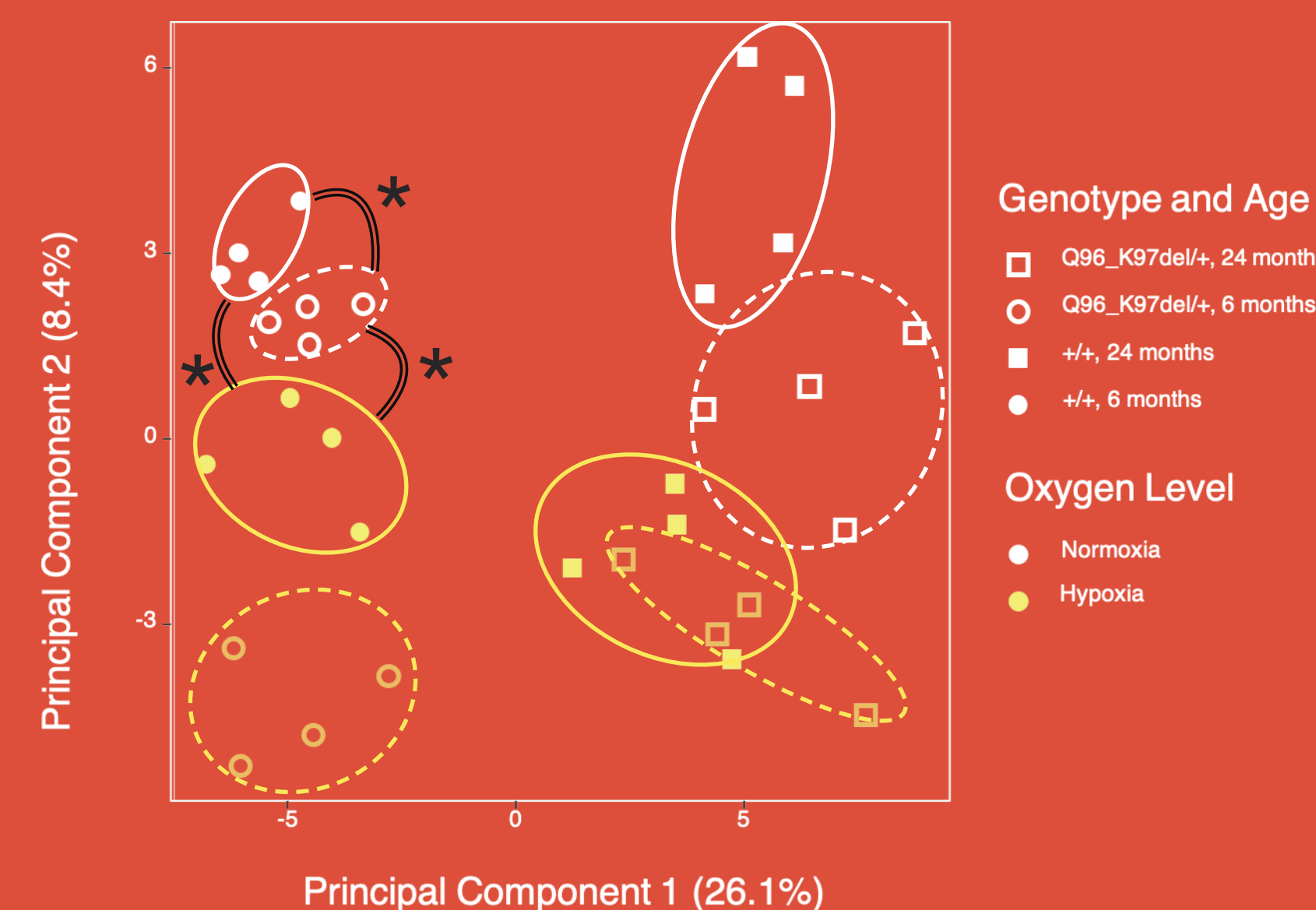


2

Gene set testing in RNA-seq datasets

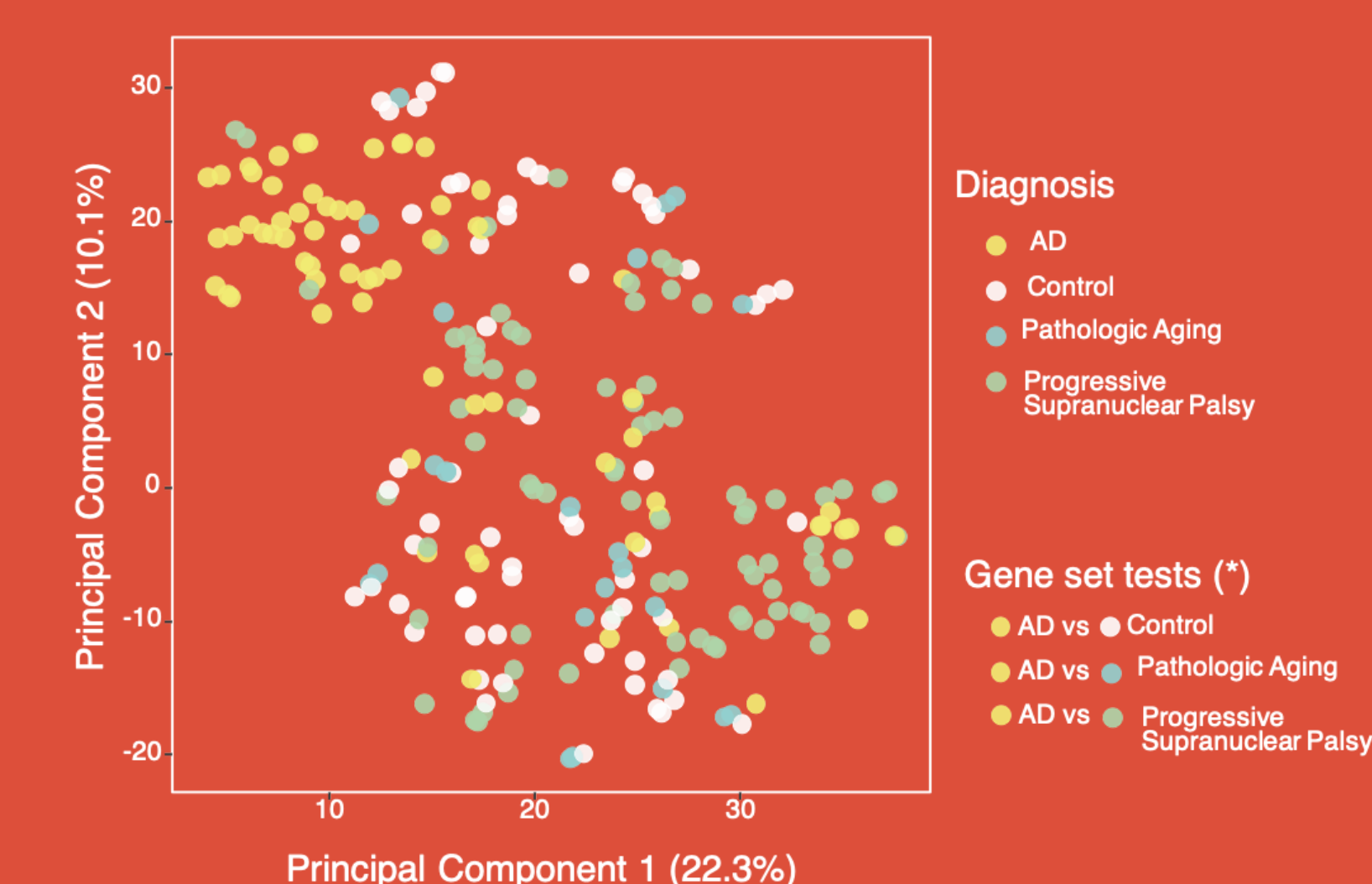
We performed gene set tests using the IRE genes for different comparisons representing Alzheimer's disease vs. control in zebrafish and human datasets. The 3' IRE gene set was consistently significantly enriched in all AD conditions.

Zebrafish



In the zebrafish dataset, this PCA of 3' IRE genes indicates each condition (age, hypoxia, Q96K97 familial AD mutation) seems to have its own distinct expression pattern of 3' IRE genes. Potentially, expression changes in the familial AD mutation may be mimicking some of the changes happening during hypoxia. Importantly, a PCA showing all genes is not sensitive enough to distinguish between hypoxia and the familial AD mutants.

Human



The human dataset shows more variation between samples on the 3' IRE PCA, but the 3' IRE gene sets are still significantly enriched in AD compared to healthy controls.

* Indicates that combined gene set testing using *fgsea*, *fry*, and *camera* gave FDR-adj. $p < 0.05$.



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QR code goes to lab page: facebook.com/forgetfulfish | We are also on Twitter: @UofABioinfoHub and @nhihin

References

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