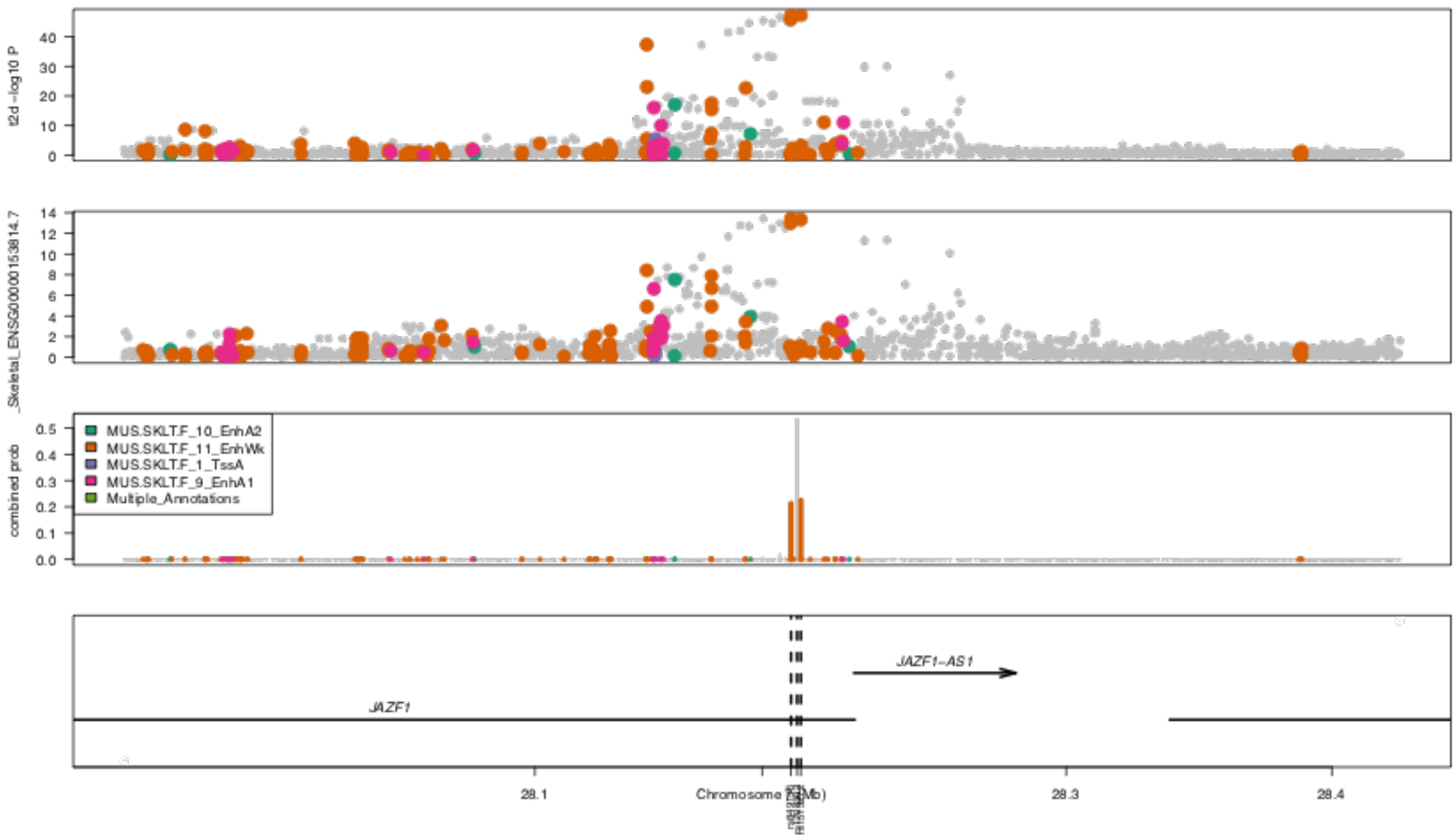
jazf1-regulation.md

Implications of SPP regulation reports for JAZF1 regulation

We are interested in studying JAZF1 regulation in adipose cells and skeletal muscle cells. The following data illustrate our motivation:

Association of SNPs with T2D risk and JAZF1 expression at the JAZF1 locus



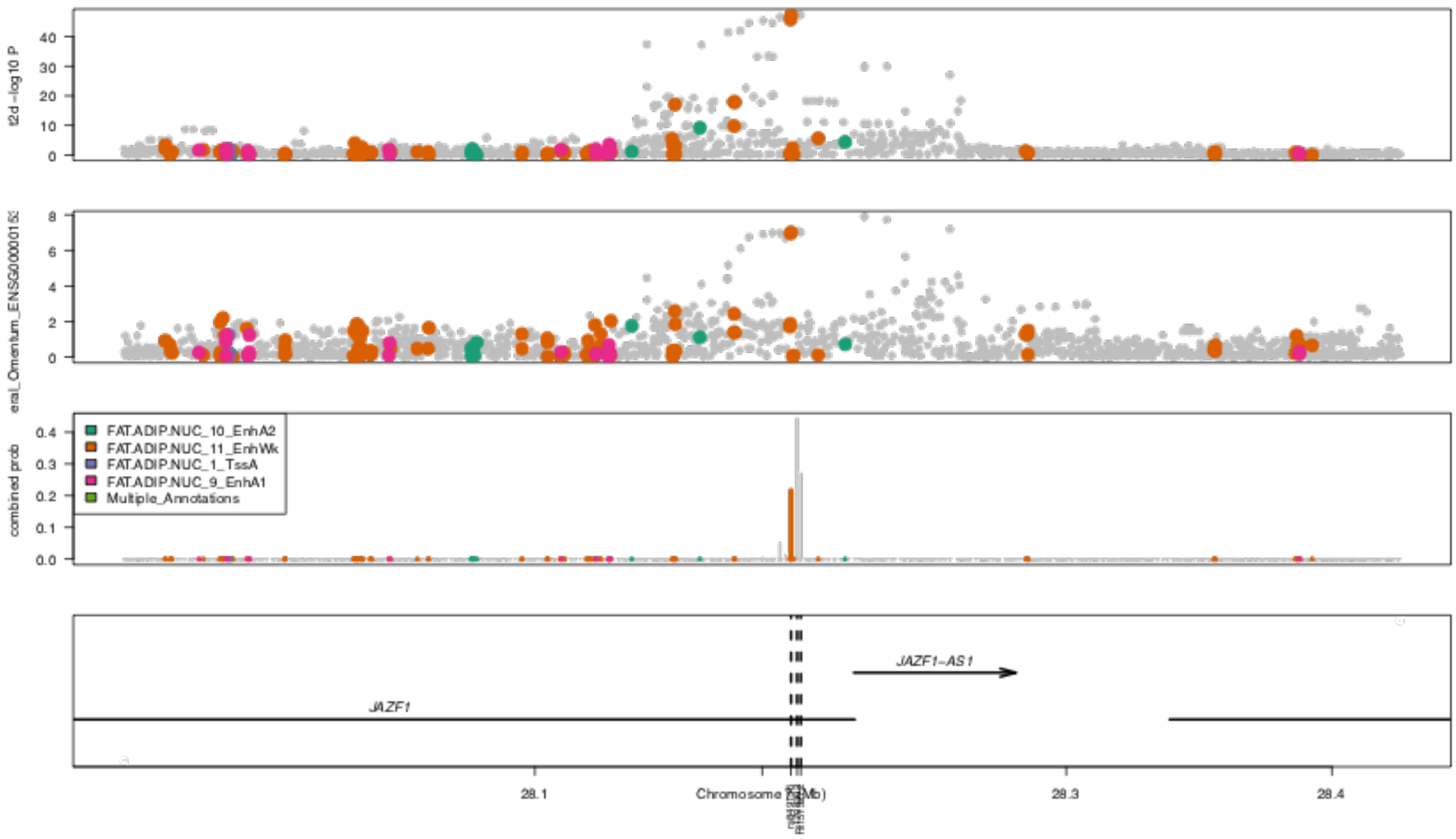
The x-axis of this figure represents a genomic region of roughly 500 kilobases. All points and bars in the first three plots represent SNPs. SNPs that occupy skeletal muscle regulatory sites are colored according to the legend.

From top to bottom, the subfigures are:

- Association with T2D risk (-log10 p-value)
- Association with JAZF1 expression in skeletal muscle tissue (-log10 p-value)
- Posterior probability of being the causal variant after bayesian fine-mapping (PPA)
- RefSeq transcript annotations

It is visually apparent (and statistically demonstrable) that the T2D GWAS association and JAZF1 gene expression association signals are highly similar, and it is likely that they share a causal variant. Indeed, multiple variants with high probability of being causal occupy weak enhancers in skeletal muscle.

The below figure contains the same information, but considers adipose (visceral omentum) tissue in place of skeletal muscle



This motivates our interest in JAZF1 regulation. As a next step we can query SPP for more information about molecular regulators of JAZF1 expression.

Transcriptomic report

Using the following parameters to query SPP for a transcriptomic report on JAZF1:

Target gene(s) of interest

Single Gene

'Omics Category

Transcriptomics

Start typing and select from the suggested gene symbols

JAZF1 (JAZF1)

Signaling Pathway Module Category

All Signaling Pathway Module Categories

Biosample Category

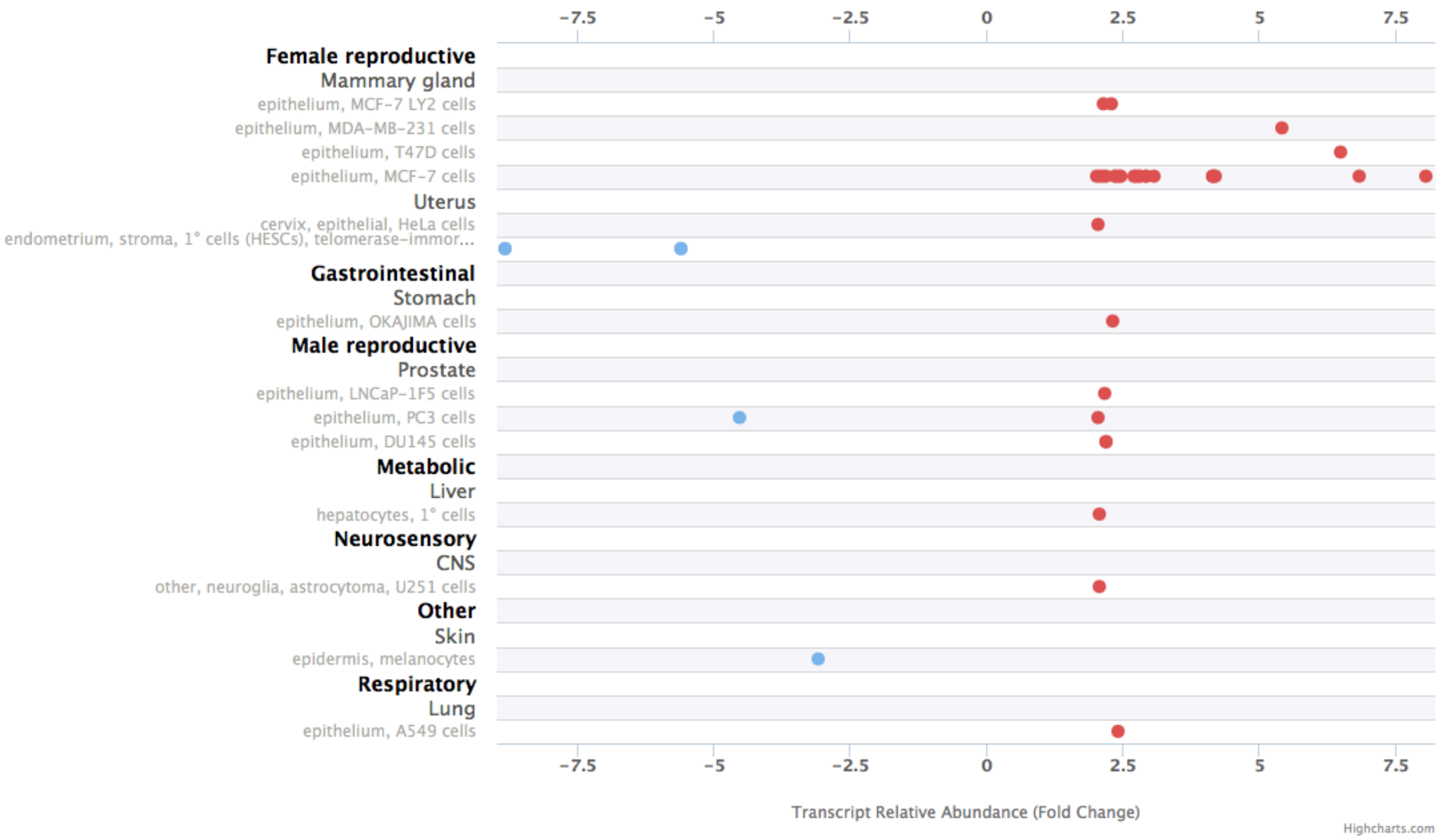
Human

All Physiological Systems

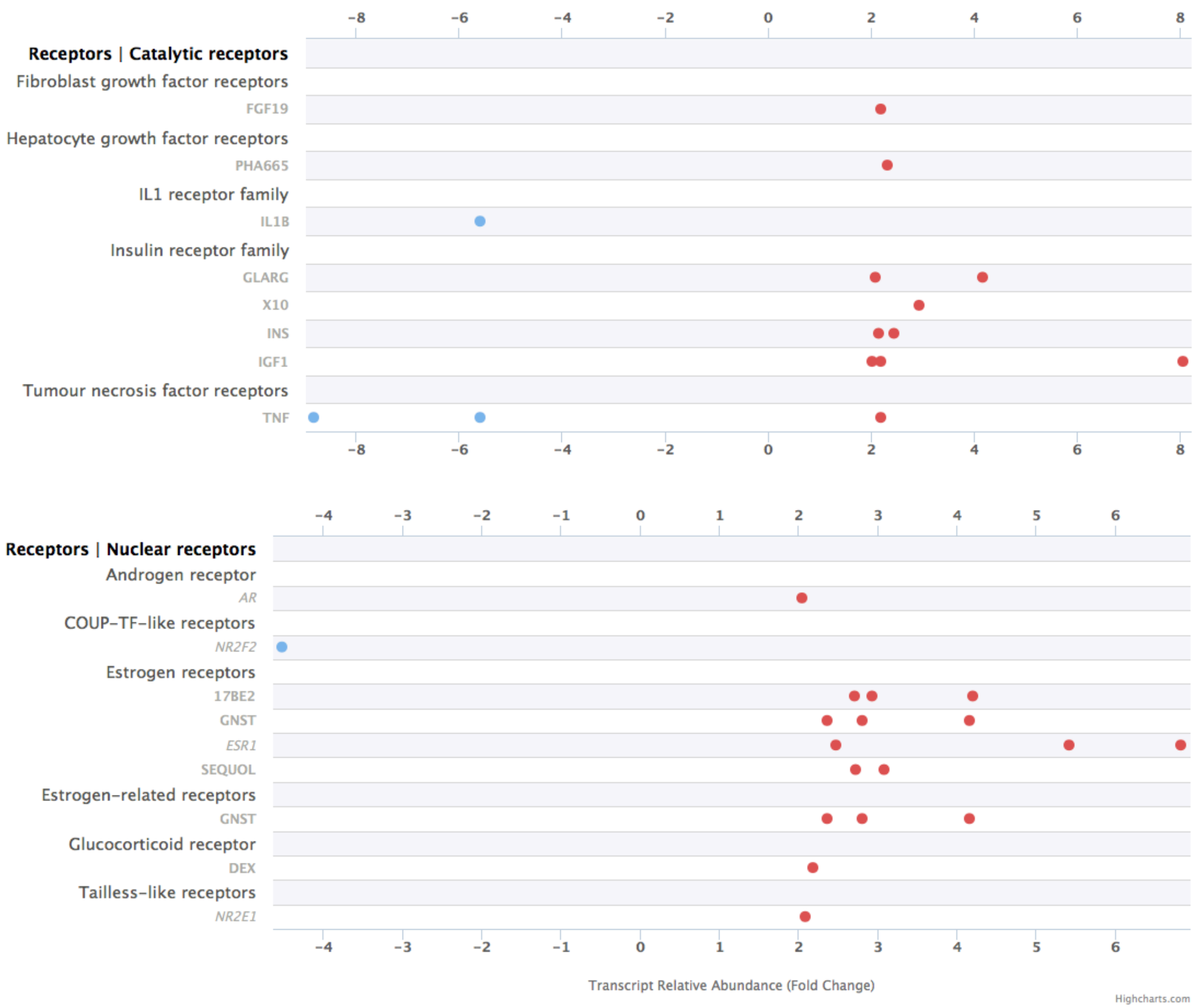
FDR Significance cut-off

5E-02

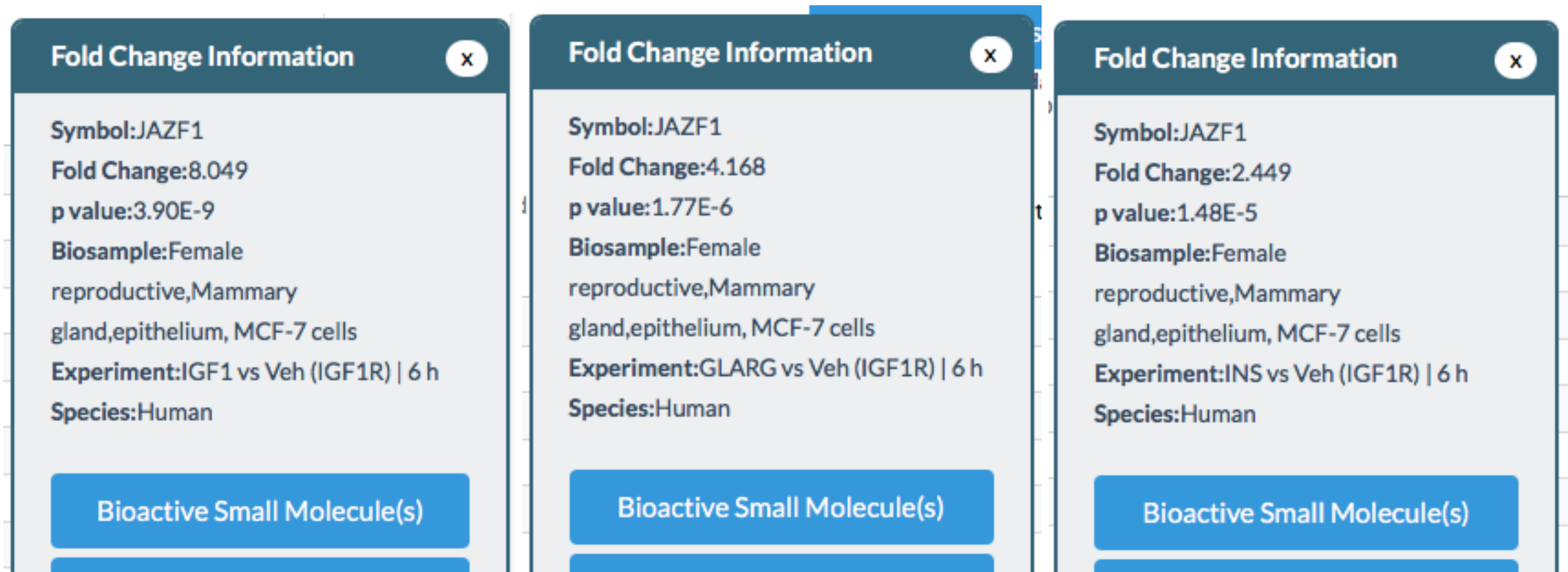
SPP returns a substantial number of nodes, primarily from experiments in mammary gland cells. See also the online transcriptomic report with results organized by module category.



The majority of these hits fall into the catalytic or nuclear receptor categories, with the insulin and estrogen receptor families most prominent:

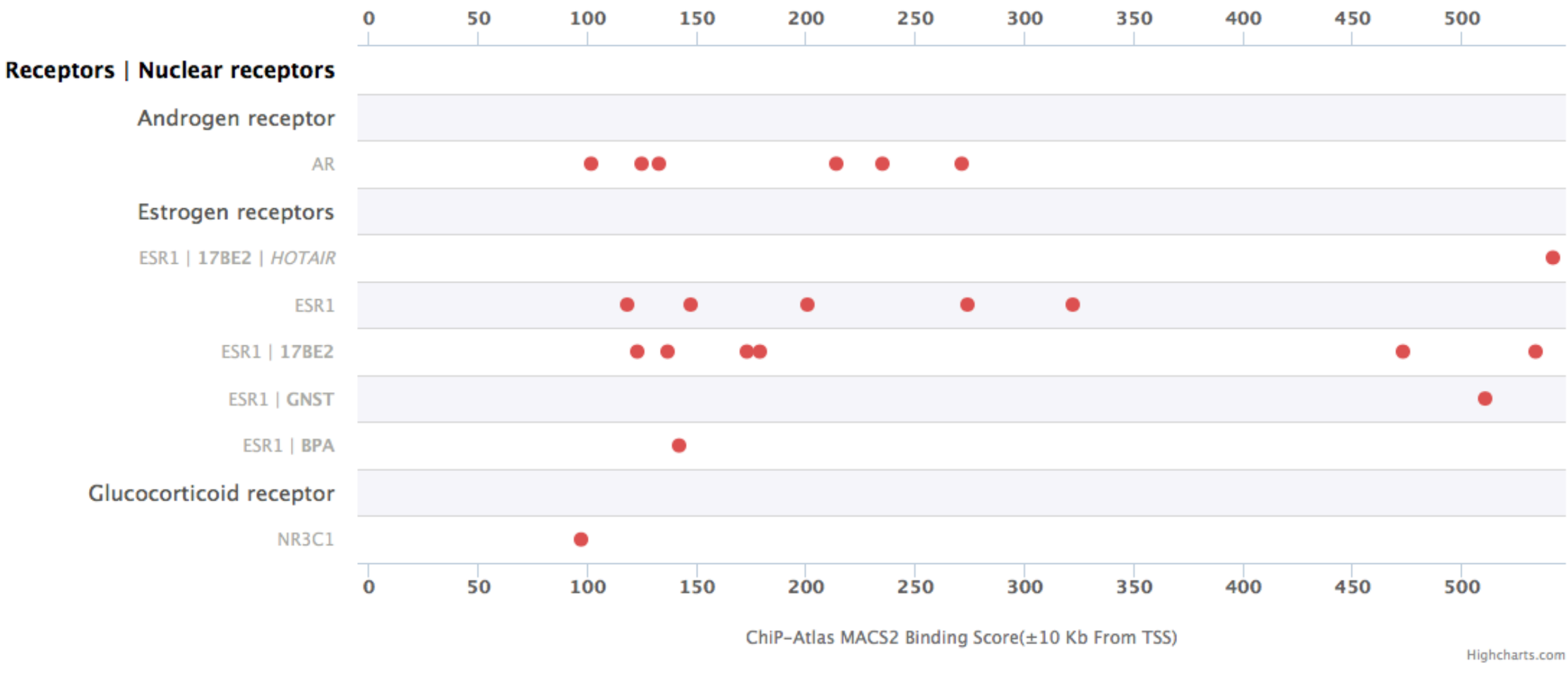


The nodes in the insulin receptor family indicate experiments where mammary gland cells were treated with insulin-related small molecules, including insulin-like growth factor 1 (IGF1), insulin glargine (GLARG), and insulin (INS). Generally it appears that JAZF1 was up-regulated in response to insulin stimulation.



Cistromic report

Estrogen receptors also feature prominently in the cistromic report, along with a variety of other nodes (see the full online cstromic report.)



Conclusions

Since JAZF1 regulation in adipose is likely involved with T2D risk, it seems intriguing that JAZF1 expression apparently responded strongly to stimulation by insulin & related molecules in mammary gland cells. Estrogen also appears to be a hormone that influences JAZF1 regulation.