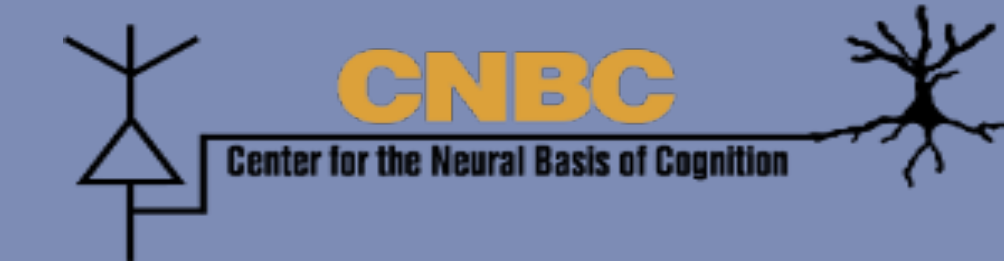
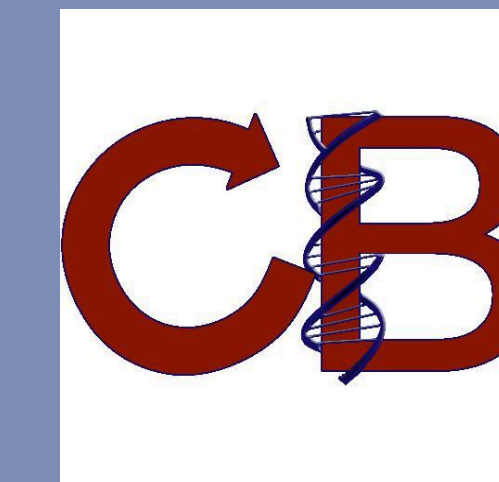




Transcriptional clustering reveals molecular convergence between human and songbird vocal learning circuits

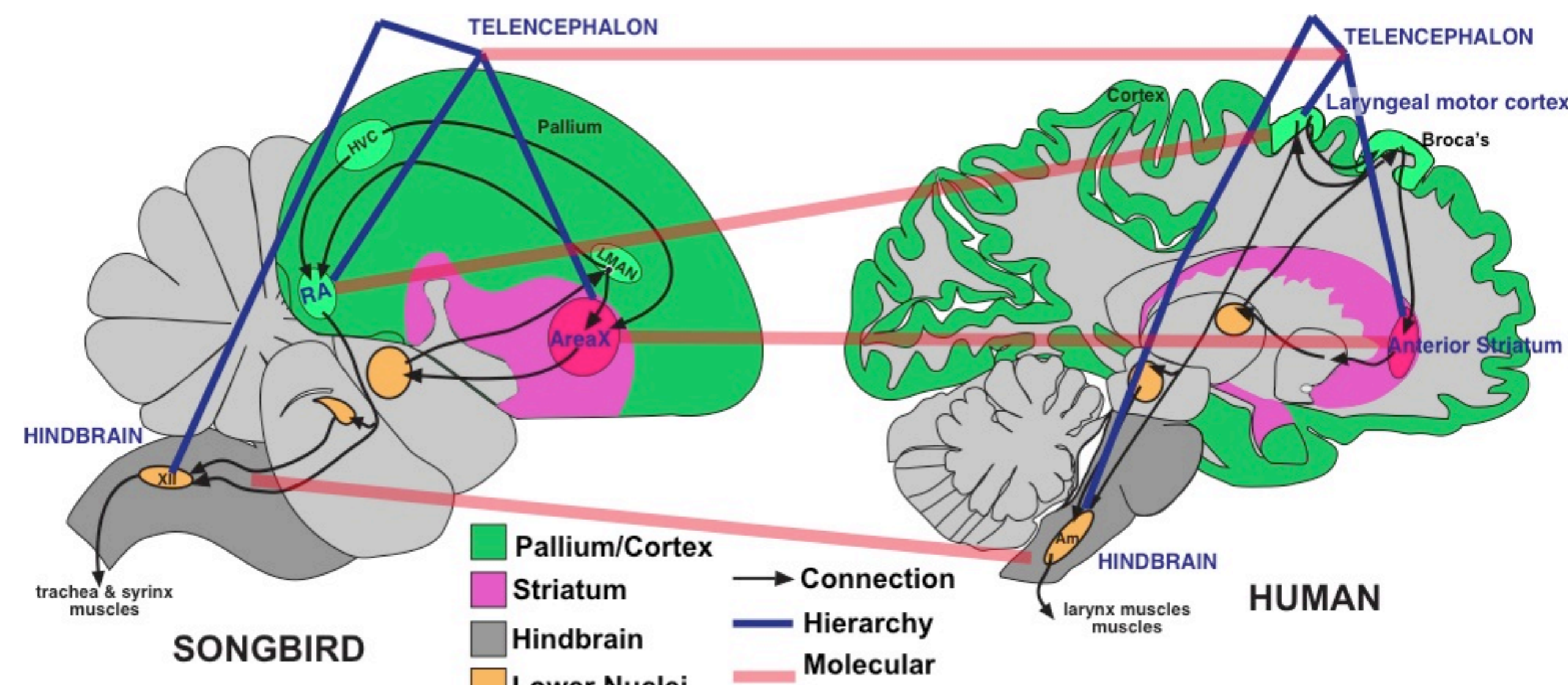
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Introduction

Previous studies have discovered that multiple human and zebra finch circuits that serve analogous functions also display significant transcriptional correlation



Penning, 2014

Marker genes have been found in zebra finch vocal learning circuits can either be suppressed or enriched

PVALB – RA POS

SNCA – RA NEG

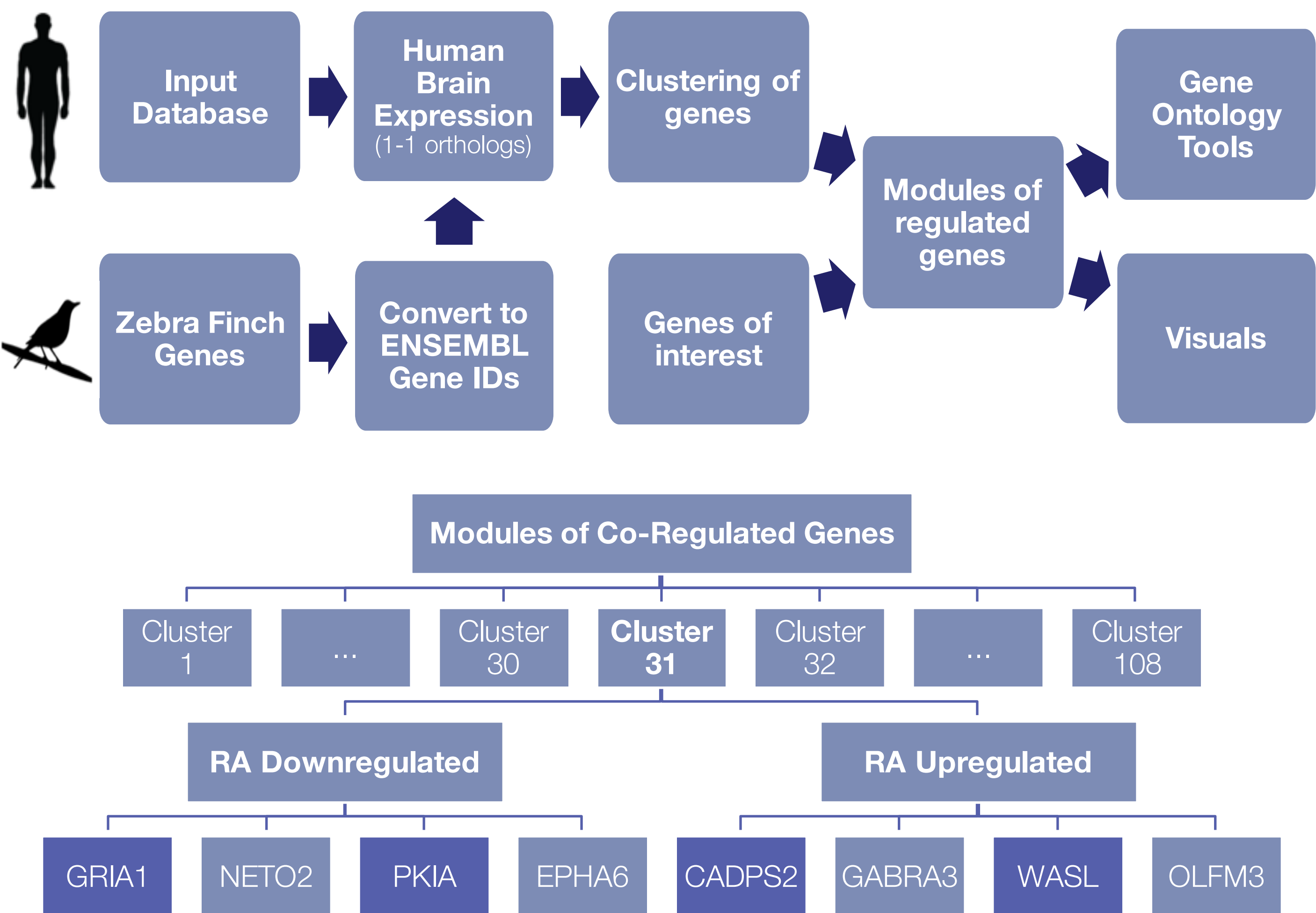


ZEBRA

Transcripts with a binding site and correlated to FOXP2 expression have been experimentally promising to be activating in Area X

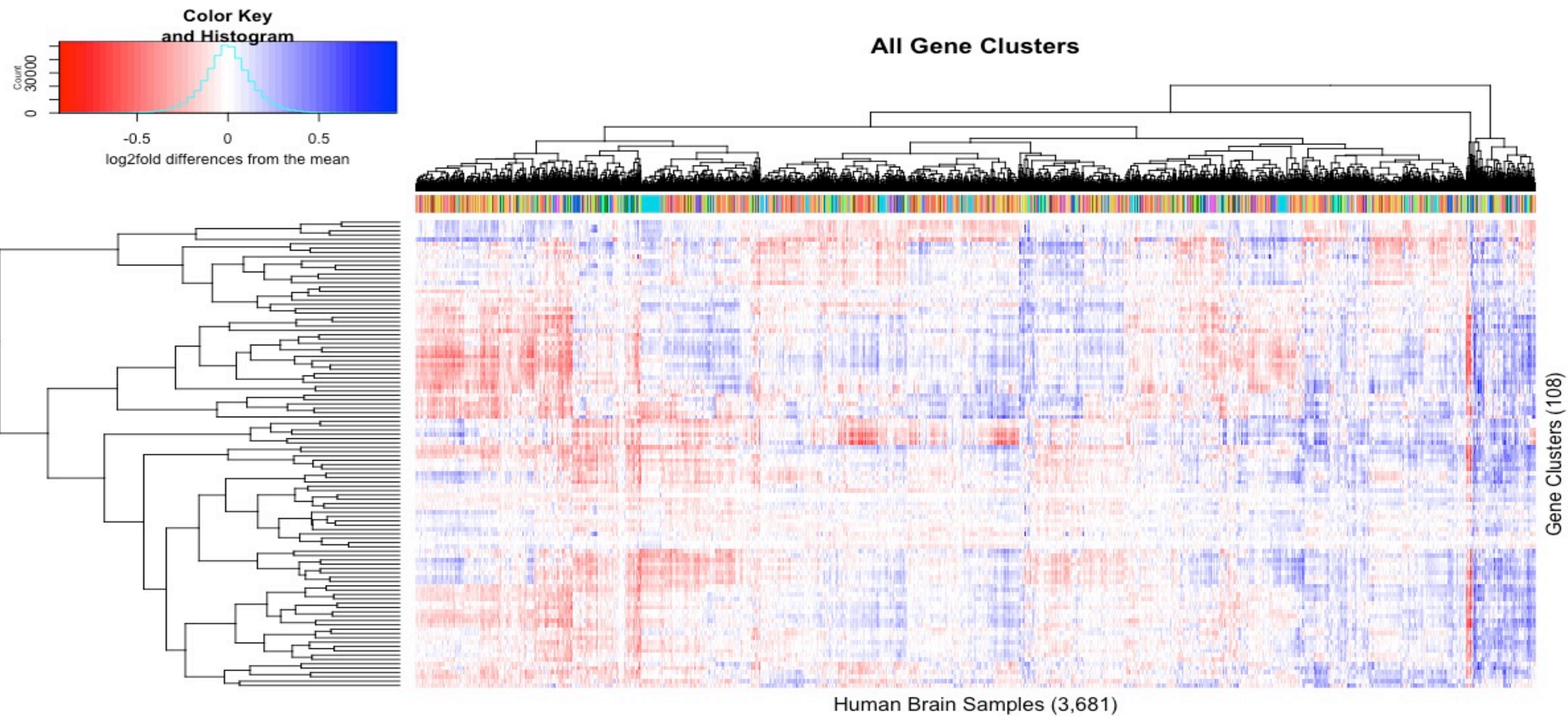
Goal - Develop computational algorithms to cluster human genes and statistically relate the similarity of cluster transcriptional specialization across human and songbird anatomical regions

Methodology



RA Markers of Songbird Vocal Motor Nucleus are Enriched in Coexpressed Clusters in Human Brain Samples

Statistical and GO Analysis reveals significant RA enriched and suppressed clusters in DNA Microarray Data sampled across all human brain samples



RA Negative			
Cluster Number	Expected Value	Actual Value	P-Value
87	6.217	35	< 0.0001
20	2.241	12	0.0001
45	3.299	12	0.0145

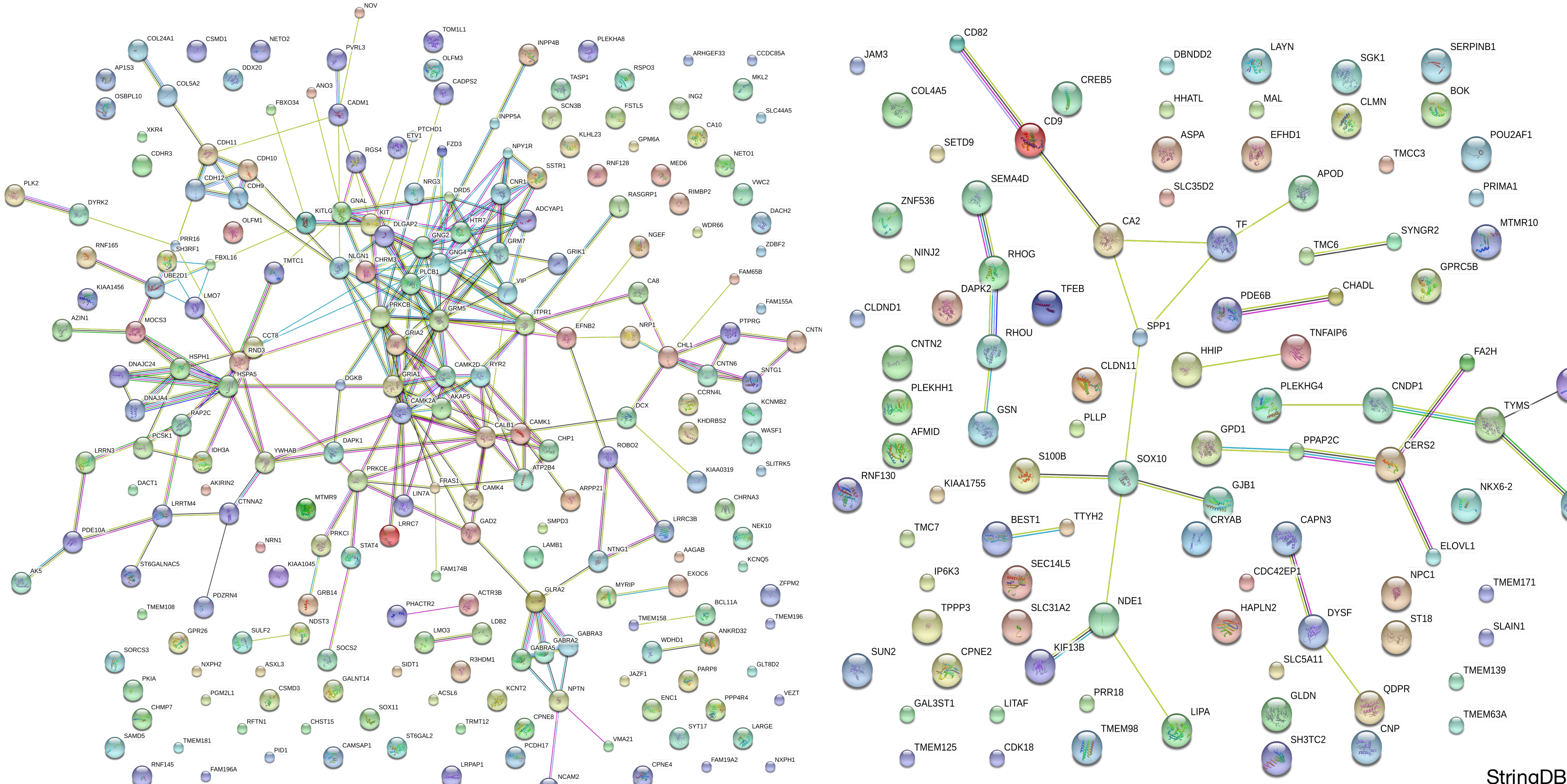
Annotation Cluster 87 Enrichment Score : 8.46		
GO Term in Cluster	Count	P-Value
Synapse	26	4.8E-13
postsynaptic membrane	17	3.1E-09
Cell junction	29	3.7E-09
Postsynaptic cell membrane	15	1.8E-08
cell junction	22	1.2E-07
synapse	14	1.5E-07

RA Positive			
Cluster Number	Expected Value	Actual Value	P-Value
97	1.300	7	0.0041
78	1.011	7	0.0062
61	1.239	6	0.0084
87	1.486	10	0.0175

Annotation Cluster 97 Enrichment Score : 2.07		
GO Term in Cluster	Count	P-Value
Membrane	48	9.8E-04
Integral component of membrane	35	3.4E-03
Transmembrane helix	37	4.2E-03
transmembrane	37	4.4E-03
transmembrane region	34	7.4E-03
topological domain: extracellular	19	5.6E-02
topological domain: cytoplasmic	21	1.2E-01

Gene Clusters (108)

RA Clusters are enriched for protein-protein interactions

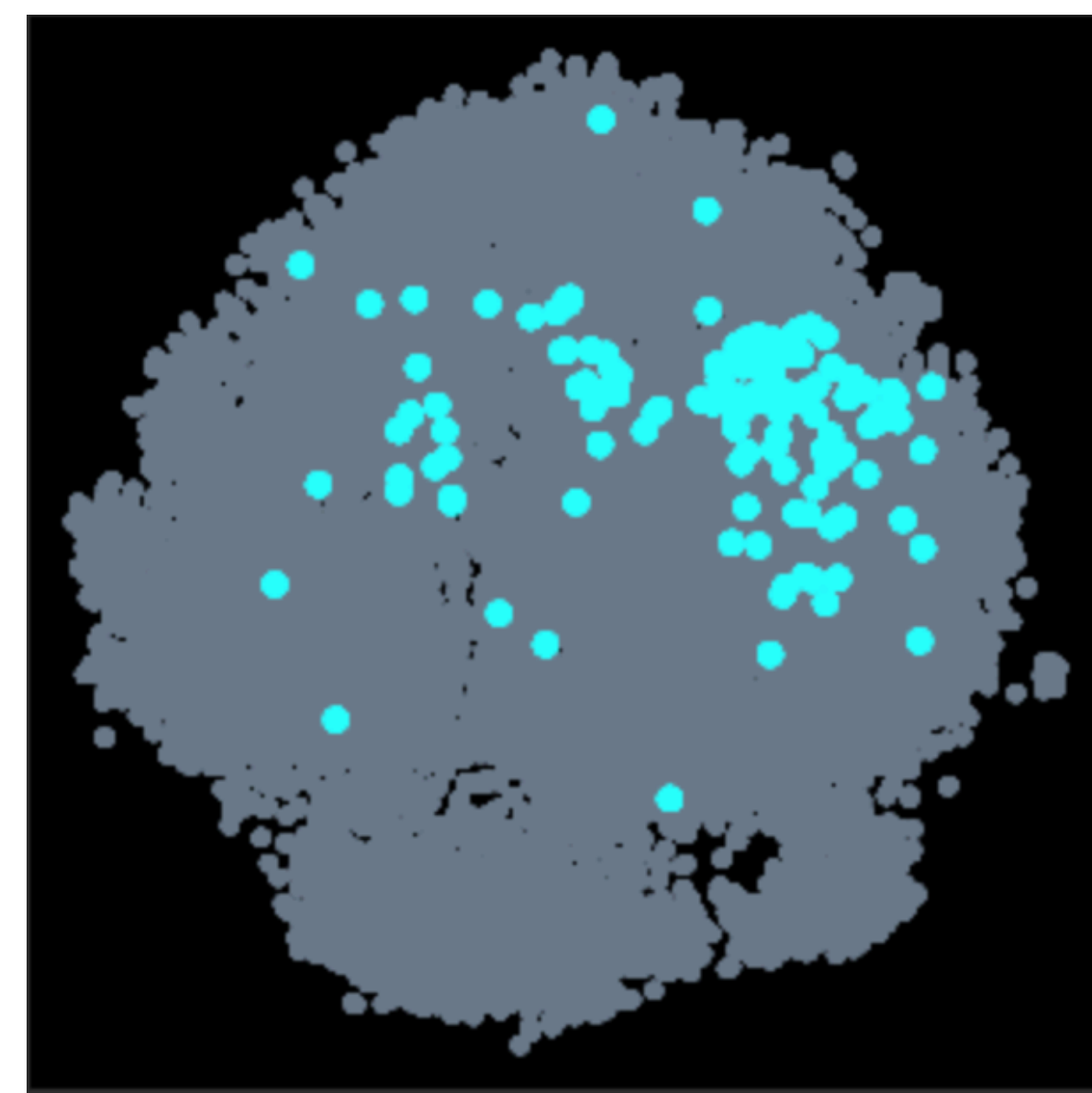
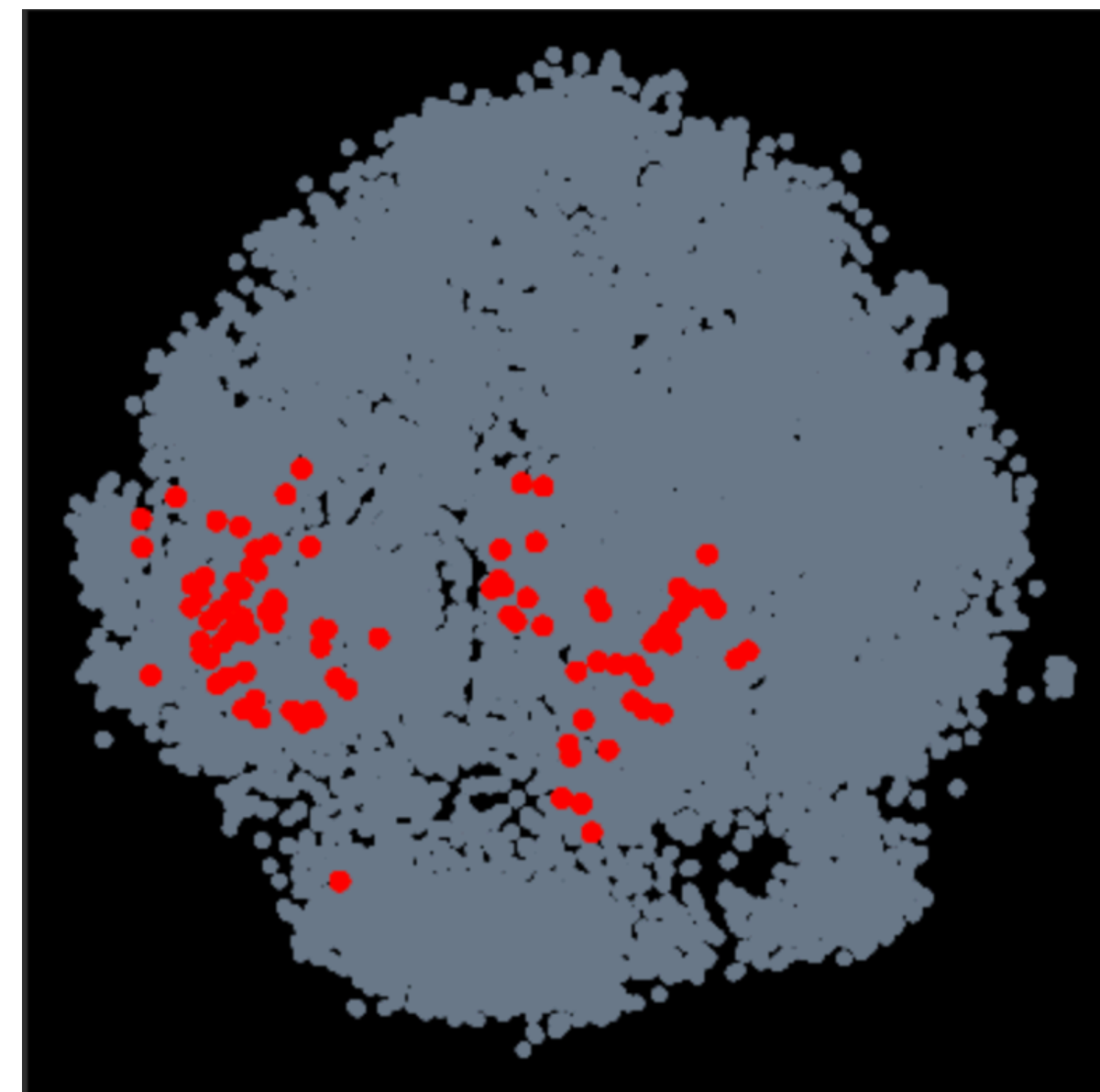


FOXP2-Regulated Genes in Songbird Area X are Enriched in Analogous Human Striatal Regions

Visual and statistical analysis shows that there are significant FOXP2 clusters in DNA Microarray data from analogous basal ganglia and striatum than RNASeq data from non-analogous cortical regions (Dorsolateral prefrontal cortex and primary motor cortex)

Striatum				DLPFC			
Cluster Number	Expected Value	Actual Value	P-Value	Cluster Number	Expected Value	Actual Value	P-Value
45	1.146	5	0.0061	31	0.853	5	0.0545
73	1.301	5	0.0102	8	0.736	3	0.1679
17	0.551	3	0.0179	18	0.224	1	0.2017

Similar gene expression-based clustering confirms spatial enrichment of FOXP2 regulated gene set



BrainSpan

Discussion and Conclusion

Results suggests that there are conserved gene regulatory modules in vocal learning circuits between songbirds and humans

- GO analysis (synapse, membrane, cell junctions, transmembrane domains) of RA enriched and suppressed clusters suggests genes that relate to signaling of neuromodulators across neurons
- FOXP2 related gene transcripts are correlated to Area X analogous regions in human brain sample, especially in basal ganglia (BG and Str),

However, further refinement of the algorithm needs to be implemented for more accurate results

- Implementing ENSEMBL Gene IDs for RA background and markers
- Smaller clustering size for FoxP2 data analysis
- RNASeq analysis on RA background and markers
- Incorporating epigenetic data to verify results from gene correlation

Acknowledgements

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