

Supplementary Materials: SFARI Gene Set GO Biological Process Enrichment

All tables and data below are intended for the supporting online material file accompanying the manuscript, not the main manuscript body. They are cited in the manuscript text and Figure 2 legend as Supplementary Table S1, Supplementary Table S2, Supplementary Data S3, and Supplementary Data S4, respectively.

Supplementary Table S1. Summary of enriched Gene Ontology Biological Process (GO BP) themes across SFARI gene groups.

SFARI group	Functional theme	n sig.terms	Top GO Biological Process term	Top adj. p	Median adj. p	Mean-log10(p)	$\Sigma - \log_{10}(p)$
All SFARI genes(n=1211)	Neuro development & differentiation	312	<i>neurogenesis</i>	4.96×10^{-62}	0.0006	7.25	2263
	Synapse organization & signaling	96	<i>trans-synaptic signaling</i>	1.49×10^{-70}	0.0000	13.10	1258
	Chromatin / RNA / transcription	170	<i>regulation of cellular component organization</i>	2.75×10^{-45}	0.0027	4.93	839
	Other	1108	<i>cell adhesion</i>	1.07×10^{-28}	0.0015	4.26	4726
Score 1 (high confidence)(n=233)	Neuro development & differentiation	167	<i>cognition</i>	8.25×10^{-23}	0.0025	5.05	844
	Synapse organization & signaling	66	<i>anterograde trans-synaptic signaling</i>	8.25×10^{-23}	0.0000	7.43	490
	Chromatin / RNA / transcription	116	<i>chromatin organization</i>	9.40×10^{-24}	0.0088	3.89	451
	Other	521	<i>negative regulation of nucleobase-containing compound metabolic process</i>	1.11×10^{-16}	0.0063	2.77	1442
Score 2 (strong candidate)(n=705)	Neuro development & differentiation	204	<i>neurogenesis</i>	5.56×10^{-23}	0.0013	4.35	887
	Synapse organization & signaling	70	<i>trans-synaptic signaling</i>	6.26×10^{-37}	0.0005	7.56	529
	Chromatin / RNA / transcription	69	<i>regulation of cellular component organization</i>	4.98×10^{-17}	0.0065	2.96	204
	Other	712	<i>cell adhesion</i>	1.39×10^{-22}	0.0063	3.01	2142
Score 3 (suggestive evidence)(n=179)	Neuro development & differentiation	66	<i>neurogenesis</i>	2.14×10^{-10}	0.0067	2.85	188
	Synapse organization & signaling	28	<i>regulation of membrane potential</i>	1.40×10^{-7}	0.0005	3.46	97
	Chromatin / RNA / transcription	27	<i>regulation of cellular component organization</i>	2.13×10^{-7}	0.0092	2.40	65

SFARI group	Functional theme	n sig.terms	Top GO Biological Process term	Top adj. p	Median adj. p	Mean-log10(p)	Σ -log10(p)
	Other	256	<i>cellular response to oxygen-containing compound</i>	1.28×10^{-9}	0.0141	2.22	569
Syndromic(n=301)	Neuro development & differentiation	166	<i>neurogenesis</i>	9.74×10^{-21}	0.0023	4.45	739
	Synapse organization & signaling	47	<i>synapse organization</i>	1.85×10^{-12}	0.0005	4.59	216
	Chromatin / RNA / transcription	137	<i>chromatin organization</i>	1.55×10^{-35}	0.0022	4.66	639
	Other	520	<i>negative regulation of nucleobase-containing compound metabolic process</i>	3.22×10^{-16}	0.0061	2.78	1443

Genes from the SFARI Gene database (release 2025-01-13; protein-coding genes used for enrichment, $n = 1,211$ of 1,219 total) were grouped by SFARI gene score (1, high confidence; 2, strong candidate; 3, suggestive evidence) and syndromic status, and tested for GO BP enrichment using g:Profiler (Benjamini-Hochberg FDR < 0.05; term size 10-2,500; background = *H. sapiens* genome). Significant terms were assigned to one of four themes by GO ontology tree anchor descent. n sig. terms, number of significantly enriched GO BP terms assigned to that theme; Top adj. p, BH-adjusted p-value of the most significant term in the theme; Mean -log10(p), average of -log10(adjusted p) across all terms in the theme; Σ -log10(p), sum of -log10(adjusted p) across all terms in the theme, used as an aggregate enrichment-strength measure.

Supplementary Table S2. Top five most significant GO Biological Process terms within each SFARI group × theme combination.

SFARI group	Theme	Rank	GO ID	Term name	Term size	Intersection size	Adj. p
All SFARI genes	Neuro development & differentiation	1	GO:0022008	<i>neurogenesis</i>	1769	285	4.96×10^{-62}
All SFARI genes	Neuro development & differentiation	2	GO:0048699	<i>generation of neurons</i>	1523	254	1.84×10^{-57}
All SFARI genes	Neuro development & differentiation	3	GO:0030182	<i>neuron differentiation</i>	1444	240	1.20×10^{-53}
All SFARI genes	Neuro development & differentiation	4	GO:0048666	<i>neuron development</i>	1167	203	8.82×10^{-48}
All SFARI genes	Neuro development & differentiation	5	GO:0007417	<i>central nervous system development</i>	1035	186	1.41×10^{-45}
All SFARI genes	Synapse organization & signaling	1	GO:0099537	<i>trans-synaptic signaling</i>	772	192	1.49×10^{-70}
All SFARI genes	Synapse organization & signaling	2	GO:0099536	<i>synaptic signaling</i>	803	194	4.00×10^{-69}
All SFARI genes	Synapse organization & signaling	3	GO:0098916	<i>anterograde trans-synaptic signaling</i>	765	188	3.12×10^{-68}
All SFARI genes	Synapse organization & signaling	4	GO:0007268	<i>chemical synaptic transmission</i>	765	188	3.12×10^{-68}
All SFARI genes	Synapse organization & signaling	5	GO:0050808	<i>synapse organization</i>	561	151	1.04×10^{-59}
All SFARI genes	Chromatin / RNA / transcription	1	GO:0051128	<i>regulation of cellular component organization</i>	2427	310	2.75×10^{-45}
All SFARI genes	Chromatin / RNA / transcription	2	GO:0006325	<i>chromatin organization</i>	1216	187	4.08×10^{-36}
All SFARI genes	Chromatin / RNA / transcription	3	GO:0006338	<i>chromatin remodeling</i>	1057	166	6.49×10^{-33}
All SFARI genes	Chromatin / RNA / transcription	4	GO:0051254	<i>positive regulation of RNA metabolic process</i>	1804	226	2.61×10^{-30}
All SFARI genes	Chromatin / RNA / transcription	5	GO:1902680	<i>positive regulation of RNA biosynthetic process</i>	1674	214	9.12×10^{-30}
All SFARI genes	Other	1	GO:0007155	<i>cell adhesion</i>	1512	198	1.07×10^{-28}
All SFARI genes	Other	2	GO:0003008	<i>system process</i>	2290	254	3.58×10^{-26}
All SFARI genes	Other	3	GO:0030900	<i>forebrain development</i>	403	84	2.44×10^{-24}
All SFARI genes	Other	4	GO:0099173	<i>postsynapse organization</i>	233	62	9.84×10^{-24}
All SFARI genes	Other	5	GO:0051240	<i>positive regulation of multicellular organismal process</i>	1639	196	1.94×10^{-23}
Score 1 (high confidence)	Neuro development & differentiation	1	GO:0050890	<i>cognition</i>	315	35	8.25×10^{-23}
Score 1 (high confidence)	Neuro development & differentiation	2	GO:0022008	<i>neurogenesis</i>	1769	73	2.41×10^{-22}
Score 1 (high confidence)	Neuro development & differentiation	3	GO:0007611	<i>learning or memory</i>	268	32	6.54×10^{-22}
Score 1 (high confidence)	Neuro development & differentiation	4	GO:0048699	<i>generation of neurons</i>	1523	67	7.88×10^{-22}
Score 1 (high confidence)	Neuro development & differentiation	5	GO:0030182	<i>neuron differentiation</i>	1444	63	2.91×10^{-20}

SFARI group	Theme	Rank	GO ID	Term name	Term size	Intersection size	Adj. p
Score 1 (high confidence)	Synapse organization & signaling	1	GO:0098916	<i>anterograde trans-synaptic signaling</i>	765	50	8.25×10^{-23}
Score 1 (high confidence)	Synapse organization & signaling	2	GO:0099177	<i>regulation of trans-synaptic signaling</i>	504	42	8.25×10^{-23}
Score 1 (high confidence)	Synapse organization & signaling	3	GO:0007268	<i>chemical synaptic transmission</i>	765	50	8.25×10^{-23}
Score 1 (high confidence)	Synapse organization & signaling	4	GO:0050804	<i>modulation of chemical synaptic transmission</i>	503	42	8.25×10^{-23}
Score 1 (high confidence)	Synapse organization & signaling	5	GO:0099537	<i>trans-synaptic signaling</i>	772	50	1.18×10^{-22}
Score 1 (high confidence)	Chromatin / RNA / transcription	1	GO:0006325	<i>chromatin organization</i>	1216	63	9.40×10^{-24}
Score 1 (high confidence)	Chromatin / RNA / transcription	2	GO:0051254	<i>positive regulation of RNA metabolic process</i>	1804	75	4.43×10^{-23}
Score 1 (high confidence)	Chromatin / RNA / transcription	3	GO:0006338	<i>chromatin remodeling</i>	1057	57	2.91×10^{-22}
Score 1 (high confidence)	Chromatin / RNA / transcription	4	GO:0045893	<i>positive regulation of DNA-templated transcription</i>	1672	69	4.46×10^{-21}
Score 1 (high confidence)	Chromatin / RNA / transcription	5	GO:1902680	<i>positive regulation of RNA biosynthetic process</i>	1674	69	4.63×10^{-21}
Score 1 (high confidence)	Other	1	GO:0045934	<i>negative regulation of nucleobase-containing compound metabolic process</i>	1510	59	1.11×10^{-16}
Score 1 (high confidence)	Other	2	GO:0051703	<i>biological process involved in intraspecies interaction between organisms</i>	60	16	1.32×10^{-16}
Score 1 (high confidence)	Other	3	GO:0031644	<i>regulation of nervous system process</i>	114	16	4.47×10^{-12}
Score 1 (high confidence)	Other	4	GO:0099173	<i>postsynapse organization</i>	233	21	4.65×10^{-12}
Score 1 (high confidence)	Other	5	GO:0044087	<i>regulation of cellular component biogenesis</i>	1006	39	1.37×10^{-10}
Score 2 (strong candidate)	Neuro development & differentiation	1	GO:0022008	<i>neurogenesis</i>	1769	144	5.56×10^{-23}
Score 2 (strong candidate)	Neuro development & differentiation	2	GO:0048699	<i>generation of neurons</i>	1523	128	2.36×10^{-21}
Score 2 (strong candidate)	Neuro development & differentiation	3	GO:0030182	<i>neuron differentiation</i>	1444	120	1.81×10^{-19}
Score 2 (strong candidate)	Neuro development & differentiation	4	GO:0048666	<i>neuron development</i>	1167	103	2.83×10^{-18}
Score 2 (strong candidate)	Neuro development & differentiation	5	GO:0031175	<i>neuron projection development</i>	1010	93	1.50×10^{-17}
Score 2 (strong candidate)	Synapse organization & signaling	1	GO:0099537	<i>trans-synaptic signaling</i>	772	110	6.26×10^{-37}
Score 2 (strong candidate)	Synapse organization & signaling	2	GO:0099536	<i>synaptic signaling</i>	803	111	3.32×10^{-36}
Score 2 (strong candidate)	Synapse organization & signaling	3	GO:0007268	<i>chemical synaptic transmission</i>	765	106	8.83×10^{-35}
Score 2 (strong candidate)	Synapse organization & signaling	4	GO:0098916	<i>anterograde trans-synaptic signaling</i>	765	106	8.83×10^{-35}
Score 2 (strong candidate)	Synapse organization & signaling	5	GO:0007267	<i>cell-cell signaling</i>	1316	132	2.59×10^{-29}
Score 2 (strong candidate)	Chromatin / RNA / transcription	1	GO:0051128	<i>regulation of cellular component organization</i>	2427	161	4.98×10^{-17}

SFARI group	Theme	Rank	GO ID	Term name	Term size	Intersection size	Adj. p
Score 2 (strong candidate)	Chromatin / RNA / transcription	2	GO:0051130	<i>positive regulation of cellular component organization</i>	1091	78	2.96×10^{-9}
Score 2 (strong candidate)	Chromatin / RNA / transcription	3	GO:0010975	<i>regulation of neuron projection development</i>	426	41	3.41×10^{-8}
Score 2 (strong candidate)	Chromatin / RNA / transcription	4	GO:0031344	<i>regulation of cell projection organization</i>	639	52	6.90×10^{-8}
Score 2 (strong candidate)	Chromatin / RNA / transcription	5	GO:1901888	<i>regulation of cell junction assembly</i>	258	30	8.30×10^{-8}
Score 2 (strong candidate)	Other	1	GO:0007155	<i>cell adhesion</i>	1512	130	1.39×10^{-22}
Score 2 (strong candidate)	Other	2	GO:0098609	<i>cell-cell adhesion</i>	965	91	8.36×10^{-18}
Score 2 (strong candidate)	Other	3	GO:0003008	<i>system process</i>	2290	152	5.24×10^{-16}
Score 2 (strong candidate)	Other	4	GO:0003013	<i>circulatory system process</i>	595	64	5.28×10^{-15}
Score 2 (strong candidate)	Other	5	GO:0008015	<i>blood circulation</i>	511	57	5.32×10^{-14}
Score 3 (suggestive evidence)	Neuro development & differentiation	1	GO:0022008	<i>neurogenesis</i>	1769	47	2.14×10^{-10}
Score 3 (suggestive evidence)	Neuro development & differentiation	2	GO:0048699	<i>generation of neurons</i>	1523	40	1.31×10^{-8}
Score 3 (suggestive evidence)	Neuro development & differentiation	3	GO:0030182	<i>neuron differentiation</i>	1444	38	2.77×10^{-8}
Score 3 (suggestive evidence)	Neuro development & differentiation	4	GO:0045664	<i>regulation of neuron differentiation</i>	190	13	8.11×10^{-7}
Score 3 (suggestive evidence)	Neuro development & differentiation	5	GO:0032879	<i>regulation of localization</i>	1914	39	6.70×10^{-6}
Score 3 (suggestive evidence)	Synapse organization & signaling	1	GO:0042391	<i>regulation of membrane potential</i>	443	20	1.40×10^{-7}
Score 3 (suggestive evidence)	Synapse organization & signaling	2	GO:0007268	<i>chemical synaptic transmission</i>	765	24	1.95×10^{-6}
Score 3 (suggestive evidence)	Synapse organization & signaling	3	GO:0098916	<i>anterograde trans-synaptic signaling</i>	765	24	1.95×10^{-6}
Score 3 (suggestive evidence)	Synapse organization & signaling	4	GO:0099537	<i>trans-synaptic signaling</i>	772	24	2.24×10^{-6}
Score 3 (suggestive evidence)	Synapse organization & signaling	5	GO:0099536	<i>synaptic signaling</i>	803	24	4.23×10^{-6}
Score 3 (suggestive evidence)	Chromatin / RNA / transcription	1	GO:0051128	<i>regulation of cellular component organization</i>	2427	49	2.13×10^{-7}
Score 3 (suggestive evidence)	Chromatin / RNA / transcription	2	GO:0030307	<i>positive regulation of cell growth</i>	155	10	4.09×10^{-5}
Score 3 (suggestive evidence)	Chromatin / RNA / transcription	3	GO:0001558	<i>regulation of cell growth</i>	399	15	6.41×10^{-5}

SFARI group	Theme	Rank	GO ID	Term name	Term size	Intersection size	Adj. p
Score 3 (suggestive evidence)	Chromatin / RNA / transcription	4	GO:0006325	<i>chromatin organization</i>	1216	26	2.87×10^{-4}
Score 3 (suggestive evidence)	Chromatin / RNA / transcription	5	GO:0051254	<i>positive regulation of RNA metabolic process</i>	1804	33	3.54×10^{-4}
Score 3 (suggestive evidence)	Other	1	GO:1901701	<i>cellular response to oxygen-containing compound</i>	1194	37	1.28×10^{-9}
Score 3 (suggestive evidence)	Other	2	GO:0036211	<i>protein modification process</i>	2360	52	7.42×10^{-9}
Score 3 (suggestive evidence)	Other	3	GO:0070887	<i>cellular response to chemical stimulus</i>	2199	49	1.46×10^{-8}
Score 3 (suggestive evidence)	Other	4	GO:1901700	<i>response to oxygen-containing compound</i>	1632	41	2.07×10^{-8}
Score 3 (suggestive evidence)	Other	5	GO:0040007	<i>growth</i>	920	26	3.63×10^{-6}
Syndromic	Neuro development & differentiation	1	GO:0022008	<i>neurogenesis</i>	1769	82	9.74×10^{-21}
Syndromic	Neuro development & differentiation	2	GO:0050793	<i>regulation of developmental process</i>	2431	97	1.73×10^{-20}
Syndromic	Neuro development & differentiation	3	GO:0048699	<i>generation of neurons</i>	1523	74	1.19×10^{-19}
Syndromic	Neuro development & differentiation	4	GO:0030182	<i>neuron differentiation</i>	1444	70	1.99×10^{-18}
Syndromic	Neuro development & differentiation	5	GO:0048666	<i>neuron development</i>	1167	61	2.37×10^{-17}
Syndromic	Synapse organization & signaling	1	GO:0050808	<i>synapse organization</i>	561	36	1.85×10^{-12}
Syndromic	Synapse organization & signaling	2	GO:0050804	<i>modulation of chemical synaptic transmission</i>	503	34	2.22×10^{-12}
Syndromic	Synapse organization & signaling	3	GO:0099177	<i>regulation of trans-synaptic signaling</i>	504	34	2.32×10^{-12}
Syndromic	Synapse organization & signaling	4	GO:0098916	<i>anterograde trans-synaptic signaling</i>	765	39	1.67×10^{-10}
Syndromic	Synapse organization & signaling	5	GO:0007268	<i>chemical synaptic transmission</i>	765	39	1.67×10^{-10}
Syndromic	Chromatin / RNA / transcription	1	GO:0006325	<i>chromatin organization</i>	1216	88	1.55×10^{-35}
Syndromic	Chromatin / RNA / transcription	2	GO:0006338	<i>chromatin remodeling</i>	1057	80	2.07×10^{-33}
Syndromic	Chromatin / RNA / transcription	3	GO:0051254	<i>positive regulation of RNA metabolic process</i>	1804	98	1.20×10^{-30}
Syndromic	Chromatin / RNA / transcription	4	GO:1902680	<i>positive regulation of RNA biosynthetic process</i>	1674	93	8.79×10^{-30}
Syndromic	Chromatin / RNA / transcription	5	GO:0045893	<i>positive regulation of DNA-templated transcription</i>	1672	93	8.79×10^{-30}
Syndromic	Other	1	GO:0045934	<i>negative regulation of nucleobase-containing compound metabolic process</i>	1510	68	3.22×10^{-16}
Syndromic	Other	2	GO:0007049	<i>cell cycle</i>	1668	65	1.71×10^{-12}

SFARI group	Theme	Rank	GO ID	Term name	Term size	Intersection size	Adj. p
Syndromic	Other	3	GO:0033554	<i>cellular response to stress</i>	1856	69	2.17×10^{-12}
Syndromic	Other	4	GO:0006974	<i>DNA damage response</i>	929	46	4.97×10^{-12}
Syndromic	Other	5	GO:0061061	<i>muscle structure development</i>	673	36	2.94×10^{-10}

Provided for drill-down reference to Supplementary Table S1. Term size, number of genes annotated to the GO term genome-wide; Intersection size, number of query genes annotated to the term; Adj. p, Benjamini-Hochberg adjusted p-value.

Supplementary Data S3. Full GO Biological Process enrichment results.

The complete enrichment result set (n = 4,858 significant GO BP terms across all five SFARI groups) is too large to present as an in-document table and is provided as a separate Supplementary Data file, citable in the manuscript as “see Supplementary Data S3.” Columns include: source, native GO ID, term name and description, p-value, term size, query size, intersection size, effective domain size, precision, recall, the SFARI group queried, and parent GO term(s).

Supplementary Data S4. Full SFARI gene curation list.

The complete curated gene list prior to protein-coding filtering (n = 1,219 SFARI Gene entries, including the 8 non-protein-coding or unresolved entries excluded from enrichment) is provided as a separate Supplementary Data file, citable in the manuscript as “see Supplementary Data S4.” Columns include: gene symbol, Ensembl gene ID, SFARI gene score, syndromic flag, Ensembl biotype, and biotype lookup source.