

Supplemental Figure S6. Gene ontology analyses of putative regulatory targets of genetic loci harboring human-specific SNCs using the Enrichr bioinformatics platform (see Methods for details).

GO Molecular Function: 8,045 genes

cadherin binding (GO:0045296)

transcription regulatory region DNA binding (GO:0044212)

transcription factor activity, RNA polymerase II core promoter proximal region sequence-specific binding (GO:00

RNA polymerase II transcription factor binding (GO:0001085)

transcription regulatory region sequence-specific DNA binding (GO:0000976)

transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding (GO

protein kinase binding (GO:0019901)

RNA polymerase II regulatory region sequence-specific DNA binding (GO:0000977)

protein kinase activity (GO:0004672)

transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding (GO

GO Biological Process: 8,045 genes

positive regulation of transcription from RNA polymerase II promoter (GO:0045944)

regulation of transcription from RNA polymerase II promoter (GO:0006357)

positive regulation of transcription, DNA-templated (GO:0045893)

nervous system development (GO:0007399)

regulation of apoptotic process (GO:0042981)

neuron differentiation (GO:0030182)

axonogenesis (GO:0007409)

negative regulation of apoptotic process (GO:0043066)

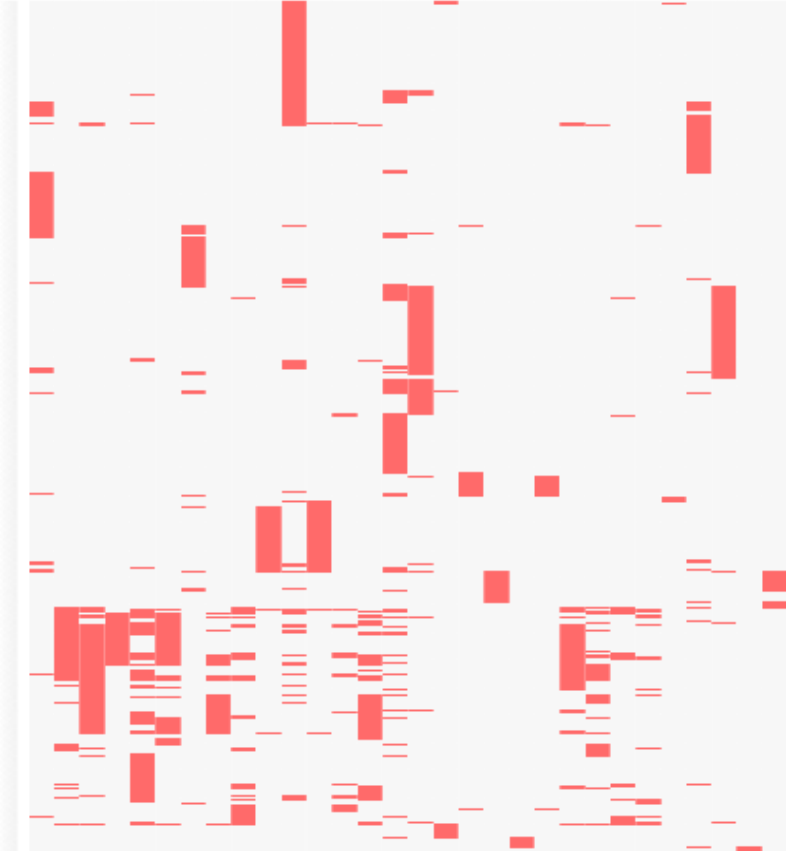
negative regulation of transcription, DNA-templated (GO:0045892)

generation of neurons (GO:0048699)

GO Molecular Function: 8,045 genes

Enriched Terms

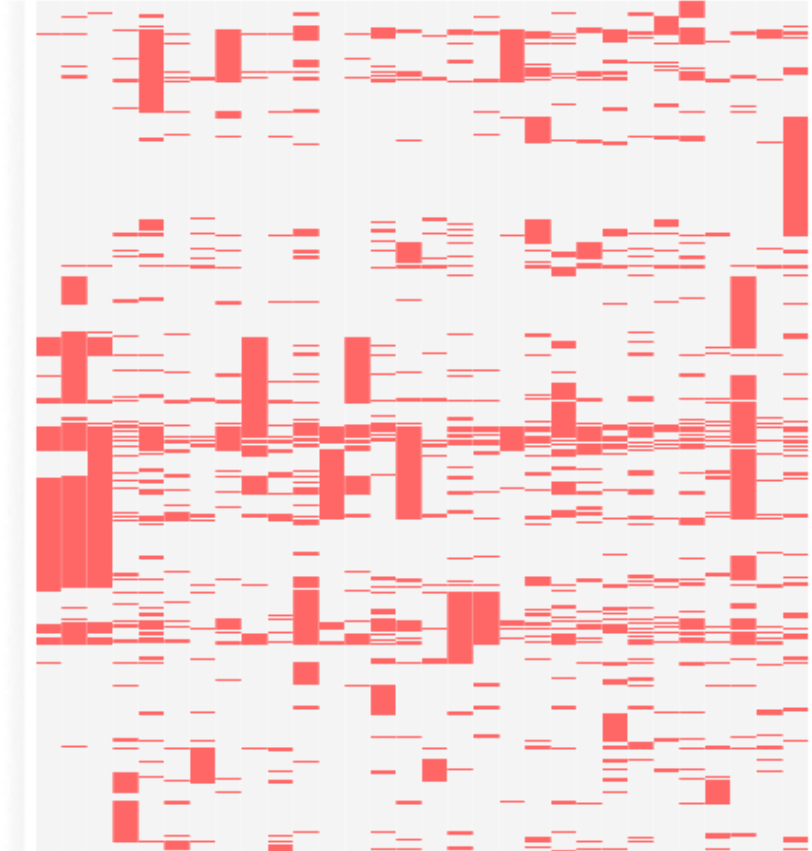
cadherin binding (GO:0043022)
transcription factor ac...
RNA polymerase II re...
transcriptional activat...
actin binding (GO:0005511)
RNA polymerase II tra...
GTPase activator acti...
protein homodimeriza...
GTPase activator acti...
repressing transcrip...
transcriptional transcri...
protein kinase regulator...
motor kinase binding...
amyloid-beta binding...
voltage-gated calcium c...
polyubiquitin binding...
microtubule N-acetylgl...
core promoter cation c...
transcriptional motor act...
activating transcrip...
transcriptional repres...
BMP receptor activat...
calcium ion binding (GO:0005511)
protein serine/threonine...
sodium/amino acid sy...
voltage-gated potassi...



GO Biological Process: 8,045 genes

Enriched Terms

positive regulation of...
regulation of transcri...
nervous system deve...
regulation of transcri...
neuron system of deve...
axon differentiation...
negative regulation of...
negative regulation of...
generation of neuron...
regulation of neuron...
positive regulation of...
regulation of cell proli...
axon guidance (GO:0007344)
negative regulation of...
negative regulation of...
protein regulation of...
negative regulation of...
positive regulation of...
transmembrane protei...
positive regulation of...
activation of protein k...
positive regulation of...
central nervous syste...
regulation of protein k...
positive regulation of...
cellular protein modifi...



Input Genes

Input Genes

GO Biological Process (8,045 genes): Top 35 of 308 significant records

Term	Overlap	P-value	Adjusted P-value
positive regulation of transcription from RNA polymerase II promoter (GO:0045944)	485/849	1.12E-19	5.67E-16
regulation of transcription from RNA polymerase II promoter (GO:0006357)	786/1479	2.51E-19	6.37E-16
positive regulation of transcription, DNA-templated (GO:0045893)	611/1121	3.46E-18	5.85E-15
nervous system development (GO:0007399)	276/456	7.07E-16	8.98E-13
regulation of apoptotic process (GO:0042981)	453/816	1.74E-15	1.77E-12
neuron differentiation (GO:0030182)	100/140	1.57E-12	1.33E-09
axonogenesis (GO:0007409)	146/224	1.88E-12	1.37E-09
negative regulation of apoptotic process (GO:0043066)	279/486	3.63E-12	2.31E-09
negative regulation of transcription, DNA-templated (GO:0045892)	437/814	5.44E-12	3.07E-09
generation of neurons (GO:0048699)	93/131	1.66E-11	7.69E-09
regulation of cell proliferation (GO:0042127)	400/741	1.67E-11	7.69E-09
positive regulation of nucleic acid-templated transcription (GO:1903508)	284/503	2.98E-11	1.26E-08
negative regulation of transcription from RNA polymerase II promoter (GO:0000122)	314/566	4.51E-11	1.76E-08
regulation of cell migration (GO:0030334)	190/317	7.61E-11	2.76E-08
positive regulation of gene expression (GO:0010628)	410/772	1.69E-10	5.73E-08
axon guidance (GO:0007411)	106/159	2.78E-10	8.82E-08
negative regulation of cellular process (GO:0048523)	295/535	4.21E-10	1.26E-07
negative regulation of cell proliferation (GO:0008285)	210/364	9.35E-10	2.64E-07
negative regulation of programmed cell death (GO:0043069)	232/409	1.08E-09	2.88E-07
protein phosphorylation (GO:0006468)	261/471	2.26E-09	5.62E-07
negative regulation of gene expression (GO:0010629)	332/619	2.32E-09	5.62E-07
positive regulation of macromolecule metabolic process (GO:0010604)	165/277	2.5E-09	5.78E-07
transmembrane receptor protein tyrosine kinase signaling pathway (GO:0007169)	224/397	3.91E-09	8.63E-07
positive regulation of cell differentiation (GO:0045597)	122/195	5.25E-09	1.11E-06
activation of protein kinase activity (GO:0032147)	142/234	5.85E-09	1.19E-06
positive regulation of protein phosphorylation (GO:0001934)	231/413	6.36E-09	1.24E-06
central nervous system development (GO:0007417)	133/218	1.1E-08	2.06E-06
negative regulation of cellular macromolecule biosynthetic process (GO:2000113)	278/513	1.29E-08	2.34E-06
regulation of transcription, DNA-templated (GO:0006355)	776/1599	2.65E-08	4.64E-06
positive regulation of epithelial cell migration (GO:0010634)	55/75	3.67E-08	6.13E-06
cellular protein modification process (GO:0006464)	504/1002	3.74E-08	6.13E-06
positive regulation of cell migration (GO:0030335)	133/222	5.27E-08	8.35E-06
positive regulation of cell proliferation (GO:0008284)	233/425	5.42E-08	8.35E-06
neuron projection morphogenesis (GO:0048812)	103/164	5.98E-08	8.94E-06
positive regulation of multicellular organismal process (GO:0051240)	123/203	6.72E-08	9.66E-06

GO Molecular Function (8,045 genes): Top 30 of 81 significant records

Term	Overlap	P-value	Adjusted P-value
cadherin binding (GO:0045296)	191/314	1.1E-11	1.26E-08
transcription regulatory region DNA binding (GO:0044212)	216/375	6.56E-10	3.76E-07
transcription factor activity, RNA polymerase II core promoter proximal region sequence-specific binding (GO:0000982)	168/281	1.22E-09	4.66E-07
RNA polymerase II transcription factor binding (GO:0001085)	84/122	1.79E-09	5.11E-07
transcription regulatory region sequence-specific DNA binding (GO:0000976)	171/293	1.06E-08	2.43E-06
transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding (GO:0001228)	166/285	2.1E-08	4.01E-06
protein kinase binding (GO:0019901)	268/496	3.35E-08	5.4E-06
RNA polymerase II regulatory region sequence-specific DNA binding (GO:0000977)	251/461	3.78E-08	5.4E-06
protein kinase activity (GO:0004672)	276/514	4.5E-08	5.72E-06
transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding (GO:0001077)	109/176	7.35E-08	8.4E-06
GTPase regulator activity (GO:0030695)	154/276	2.44E-06	0.000254
amyloid-beta binding (GO:0001540)	37/50	4.47E-06	0.000426
protein serine/threonine kinase activity (GO:0004674)	197/369	5.99E-06	0.000518
repressing transcription factor binding (GO:0070491)	39/54	6.67E-06	0.000518
RNA polymerase II regulatory region DNA binding (GO:0001012)	116/202	6.8E-06	0.000518
GTPase activator activity (GO:0005096)	139/250	9.43E-06	0.000675
voltage-gated cation channel activity (GO:0022843)	64/101	1.2E-05	0.000807
motor activity (GO:0003774)	56/86	1.28E-05	0.000811
regulatory region DNA binding (GO:0000975)	126/225	1.52E-05	0.000916
core promoter proximal region sequence-specific DNA binding (GO:0000987)	152/279	1.65E-05	0.000943
protein homodimerization activity (GO:0042803)	332/665	1.79E-05	0.000973
actin binding (GO:0003779)	140/255	2.09E-05	0.001086
PDZ domain binding (GO:0030165)	43/63	2.29E-05	0.001141
RNA polymerase II core promoter proximal region sequence-specific DNA binding (GO:0000978)	143/263	3.29E-05	0.001569
transcriptional repressor activity, RNA polymerase II transcription regulatory region sequence-specific binding (GO:0001227)	92/160	5.43E-05	0.002452
protein tyrosine kinase activity (GO:0004713)	86/148	5.57E-05	0.002452
microtubule motor activity (GO:0003777)	41/61	6.16E-05	0.002608
tubulin binding (GO:0015631)	138/256	7.7E-05	0.003145
microtubule binding (GO:0008017)	109/196	8.13E-05	0.003208
acetylgalactosaminyltransferase activity (GO:0008376)	34/49	9.81E-05	0.003742

GO Cellular Component (8,045 genes): 29 significant records

Term	Overlap	P-value	Adjusted P-value
cytoskeleton (GO:0005856)	284/521	4.18E-09	1.85E-06
dendrite (GO:0030425)	131/216	2.35E-08	5.12E-06
axon (GO:0030424)	92/142	3.47E-08	5.12E-06
actin cytoskeleton (GO:0015629)	169/295	7.67E-08	8.23E-06
integral component of plasma membrane (GO:0005887)	711/1464	9.29E-08	8.23E-06
focal adhesion (GO:0005925)	194/357	1.52E-06	0.000112
Golgi subcompartment (GO:0098791)	250/480	4.46E-06	0.000282
perinuclear region of cytoplasm (GO:0048471)	198/379	3.32E-05	0.001839
cytoplasmic vesicle membrane (GO:0030659)	38/55	4.48E-05	0.002203
Golgi membrane (GO:0000139)	225/443	0.000104	0.004546
cortical cytoskeleton (GO:0030863)	36/53	0.000123	0.004546
cortical actin cytoskeleton (GO:0030864)	36/53	0.000123	0.004546
caveola (GO:0005901)	38/57	0.000148	0.00505
filopodium (GO:0030175)	40/61	0.000173	0.005461
membrane raft (GO:0045121)	70/120	0.000224	0.006622
endoplasmic reticulum lumen (GO:0005788)	142/271	0.000339	0.009382
microtubule organizing center (GO:0005815)	251/508	0.000401	0.010456
cytoplasmic vesicle (GO:0031410)	115/216	0.000546	0.013065
chromatin (GO:0000785)	153/297	0.00056	0.013065
nuclear chromatin (GO:0000790)	132/254	0.000826	0.018285
catenin complex (GO:0016342)	21/29	0.0009	0.018978
ionotropic glutamate receptor complex (GO:0008328)	27/40	0.001001	0.020165
dendrite membrane (GO:0032590)	16/21	0.001571	0.030261
cation channel complex (GO:0034703)	40/66	0.00177	0.032667
centrosome (GO:0005813)	225/462	0.00199	0.035259
main axon (GO:0044304)	23/34	0.002257	0.038461
junctional sarcoplasmic reticulum membrane (GO:0014701)	10-Sep	0.002537	0.040494
microtubule cytoskeleton (GO:0015630)	191/389	0.002642	0.040494
actin-based cell projection (GO:0098858)	42/71	0.002651	0.040494
ruffle membrane (GO:0032587)	33/54	0.003598	0.053124