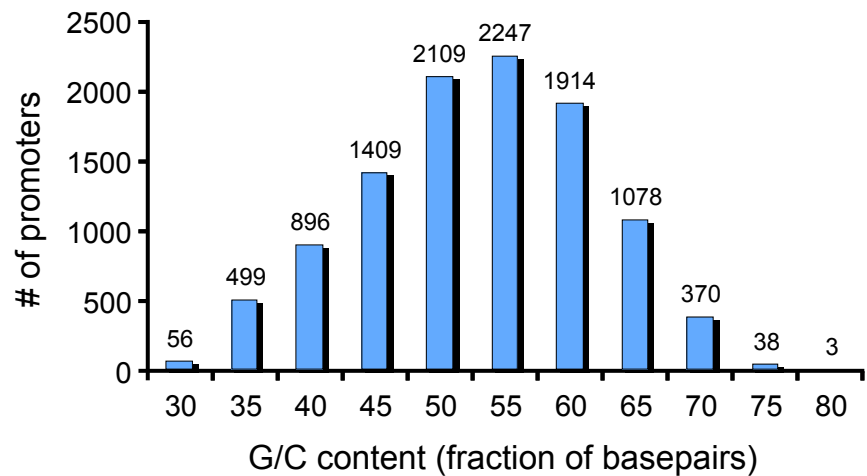


Supplementary Table 1. Shown are Gene Ontology gene sets whose average G/C content in their promoter region is significantly different than that in an average human promoter region (0.505), as determined by a *t*-test ($P < 0.05$, FDR=0.05).

<u>Gene Ontology set</u>	<u>G/C content</u>	<u># of genes</u>	<u>P-value</u>
olfactory_receptor_activity	0.37	39	4.33E-16
perception_of_smell	0.39	43	6.21E-12
transcription_factor_activity	0.53	553	1.61E-10
DNA_binding	0.52	1104	2.85E-10
perception_of_taste	0.36	19	3.29E-10
transcription_regulator_activity	0.53	748	3.44E-10
regulation_of_metabolism	0.52	1141	3.62E-10
organismal_physiological_process	0.48	841	4.71E-10
sensory_perception	0.46	239	1.89E-09
regulation_of_biological_process	0.52	1668	7.15E-09
interferonalpha2_receptor_binding	0.34	10	9.49E-09
development	0.52	881	1.93E-08
rhodopsinlike_receptor_activity	0.47	292	5.13E-08
nucleic_acid_binding	0.52	1626	1.46E-07
taste_receptor_activity	0.35	11	2.82E-07
Gprotein_coupled_receptor_protein_signaling_pathway	0.48	433	4.32E-07
regulation_of_transcription_from_Pol_II_promoter	0.54	169	7.13E-07
calciumdependent_cellcell_adhesion	0.39	12	2.84E-06
frizzled2_signaling_pathway	0.59	17	5.80E-05
cytokine_activity	0.47	154	5.81E-05
small_GTPase_mediated_signal_transduction	0.53	172	8.37E-05
transmembrane_receptor_activity	0.49	626	0.0001183
hematopoietininterferonclass_D200domain_cytokine_receptor_binding	0.42	38	0.0001226
RNA_polymerase_II_transcription_factor_activity	0.53	141	0.0001388
homophilic_cell_adhesion	0.45	53	0.0001669
cell_surface_receptor_linked_signal_transduction	0.49	678	0.0002226
neurogenesis	0.53	175	0.0002304
taxis	0.47	79	0.0002704
intracellular_signaling_cascade	0.52	538	0.0004065
immune_response	0.49	442	0.0004868
GTPase_activity	0.54	108	0.0005463
ossification	0.41	18	0.0005633
response_to_external_biotic_stimulus	0.48	284	0.0006621
alcohol_metabolism	0.53	148	0.0006845
endocytosis	0.53	72	0.0007814
nucleolus	0.55	33	0.000863
glucuronosyltransferase_activity	0.38	11	0.0008657
GTP_binding	0.53	226	0.0009273
cellcell_adhesion	0.47	86	0.001037
neurotransmitter_transport	0.56	24	0.001044
hexose_metabolism	0.54	80	0.00107
chemokine_activity	0.46	39	0.001075
response_to_bacteria	0.46	39	0.001212
response_to_stimulus	0.49	830	0.001347
RNA_binding	0.52	271	0.001486
nucleotide_binding	0.52	956	0.001745
cytosolic_large_ribosomal_subunit_sensu_Eukaryota	0.56	19	0.001813
vesiclemediated_transport	0.53	159	0.0021
transcription_corepressor_activity	0.54	65	0.002256
microsome	0.47	80	0.002378
carbohydrate_catabolism	0.55	54	0.002426
nitric_oxide_metabolism	0.58	11	0.002663
Wnt_receptor_signaling_pathway	0.55	57	0.002877

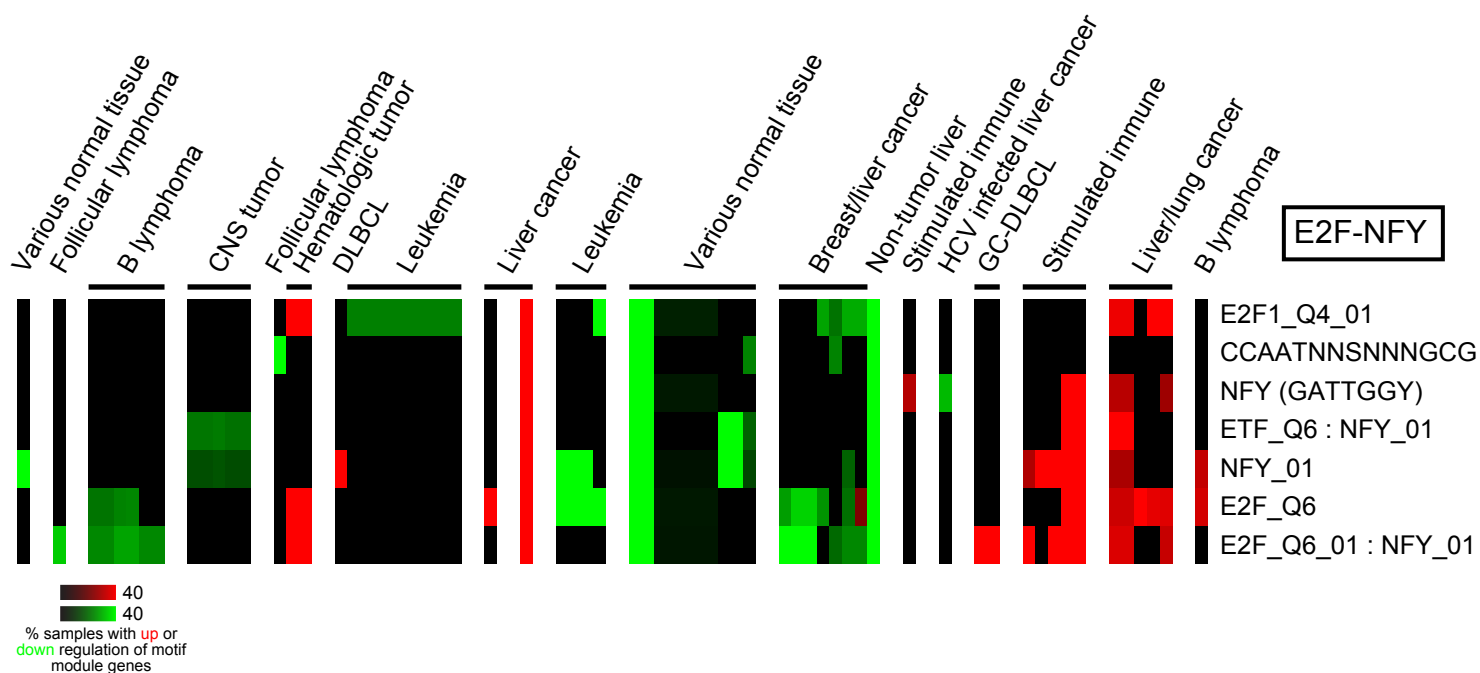
hexose catabolism	0.55	41	0.002974
delayed_rectifier_potassium_channel_activity	0.56	11	0.003041
glucose_metabolism	0.54	57	0.003043
inflammatory_response	0.48	118	0.003716
nucleoplasm	0.55	27	0.003742
response_to_pathogen	0.43	15	0.004205
extracellular_matrix_organization_and_biogenesis	0.43	16	0.00445
structural_constituent_of_ribosome	0.53	101	0.004588
enzyme_inhibitor_activity	0.48	145	0.004652
insulin_receptor_binding	0.57	11	0.005115
kinase_activity	0.52	508	0.005116
positive_regulation_of_protein_biosynthesis	0.44	14	0.005499
response_to_pathogenic_bacteria	0.42	11	0.005804
MHC_class_II_receptor_activity	0.45	11	0.006603
nucleotide_receptor_activity	0.43	25	0.006885
positive_regulation_of_biosynthesis	0.45	18	0.007196

Figure S1



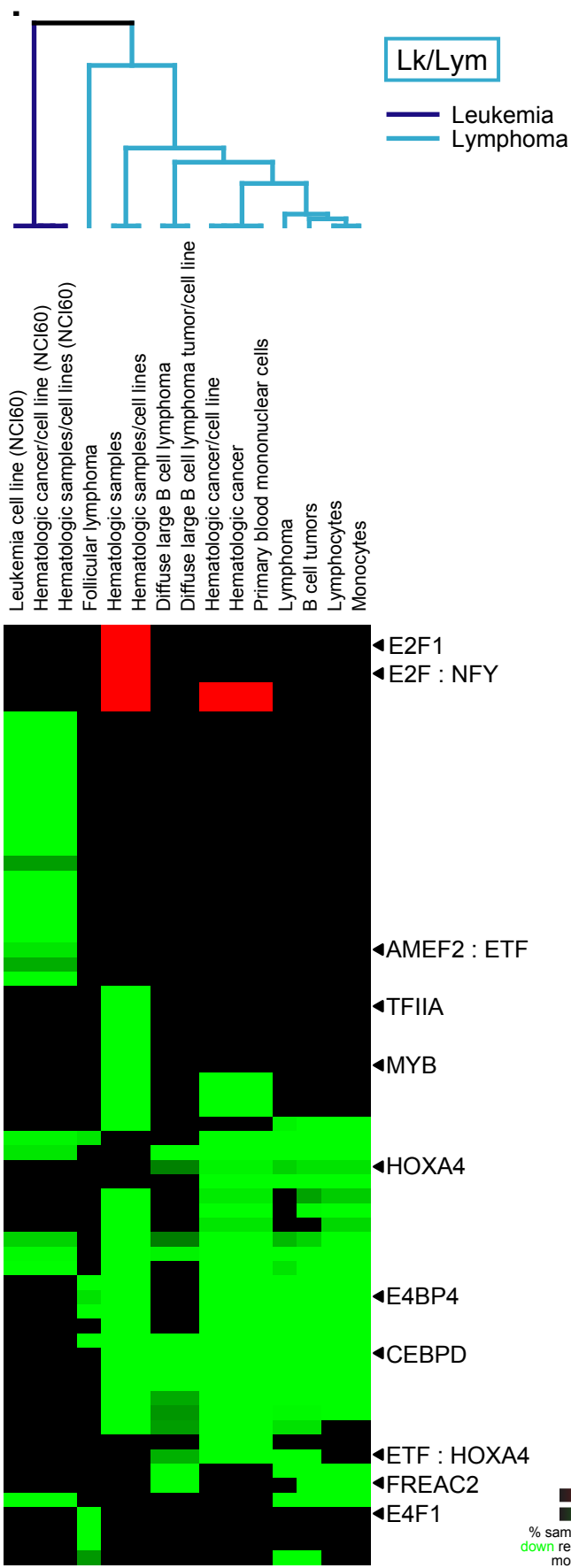
Supplementary Figure 1. Human promoters greatly vary in their G/C content. Shown is a histogram of the number of human promoters at each percentage of G/C nucleotides.

Figure S2



Supplementary Figure 2. *Cis*-regulation of E2F and NFY motif modules in cancer. Shown is the clinical annotation enrichment of the array signature of E2F and NFY-containing motif modules (E2F-NFY). The samples and motifs are shown in the same order as found in the global map in Figure 4a.

Figure S3



Supplementary Figure 3. *Cis*-regulation of motif modules in leukemia and lymphoma. Motif modules enriched in the leukemia/lymphoma (Lk/Lym) cluster. Location of several motif modules is indicated.

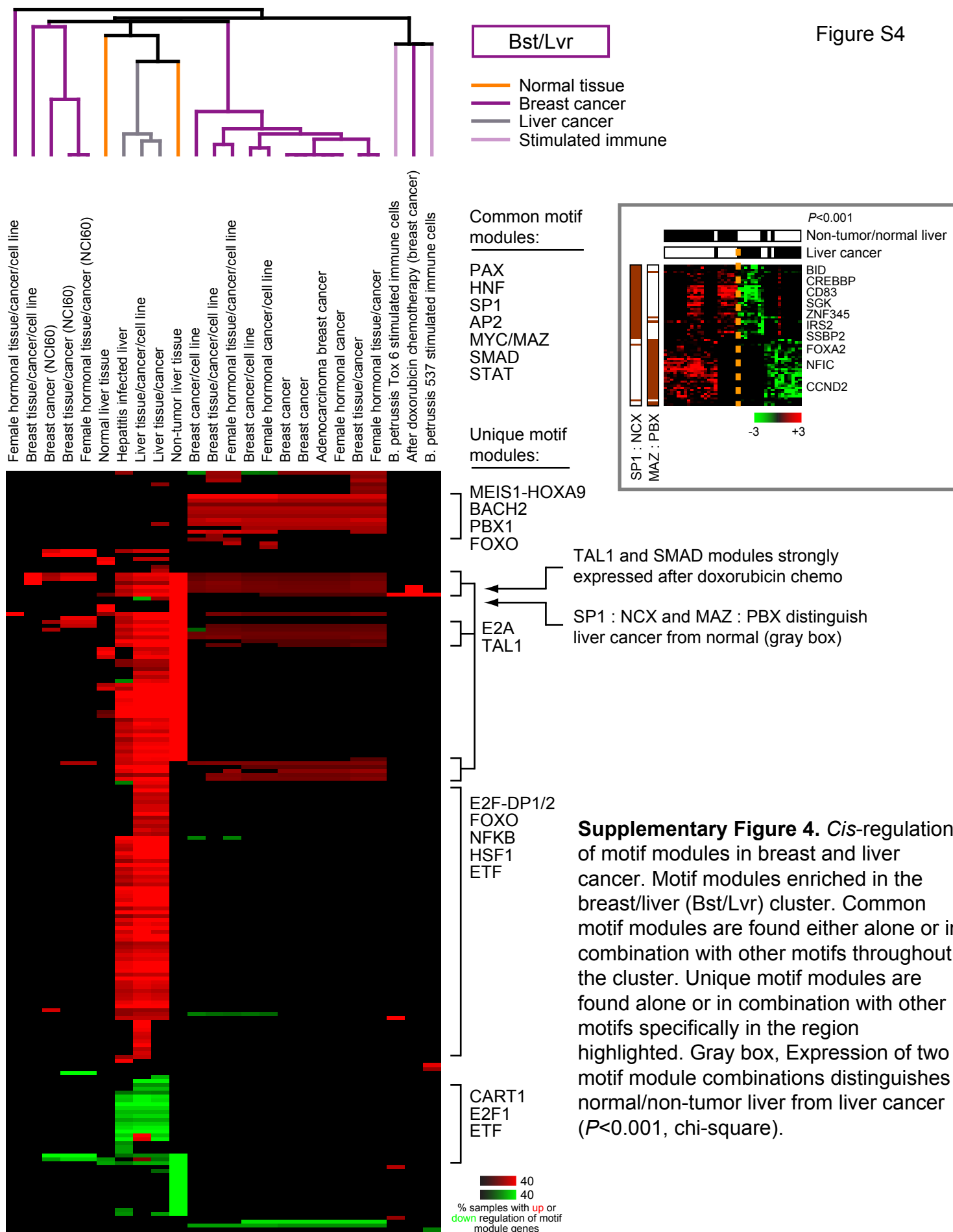
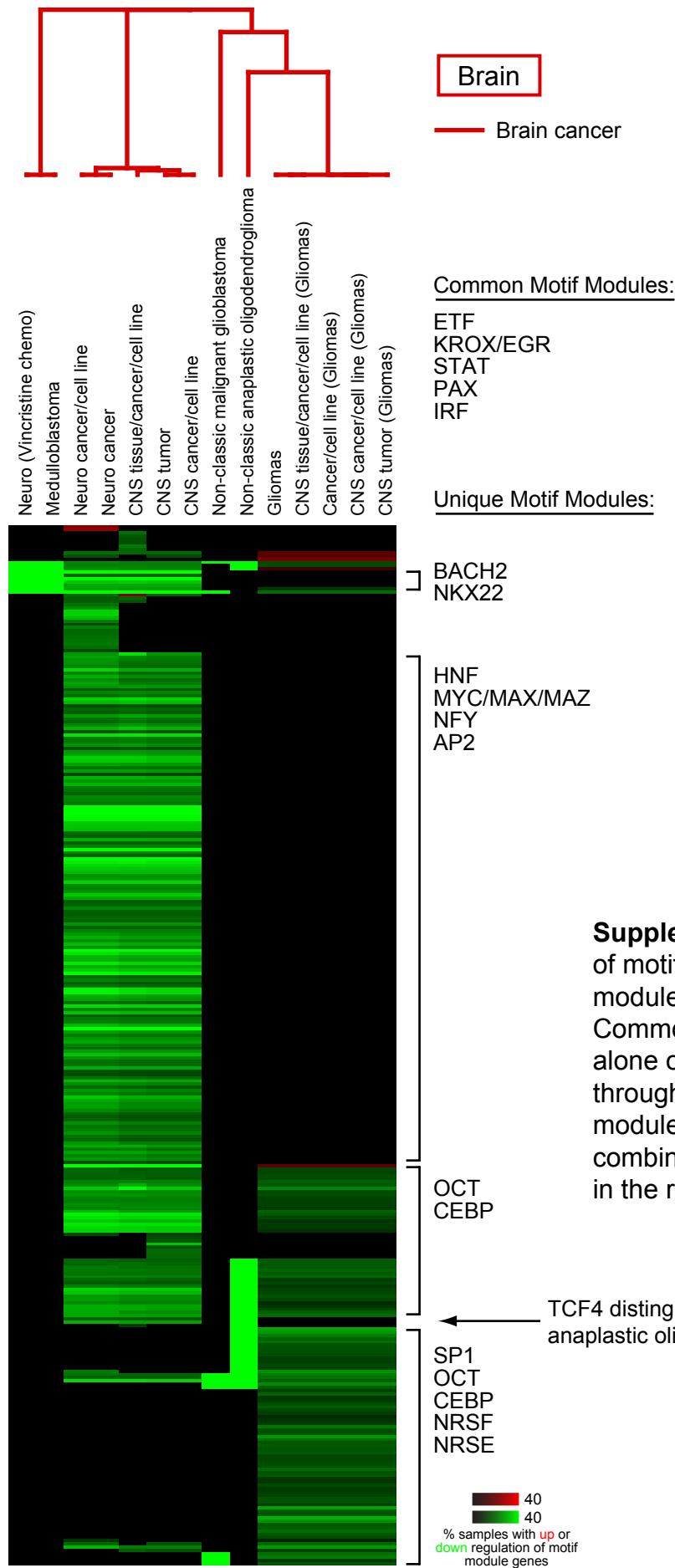
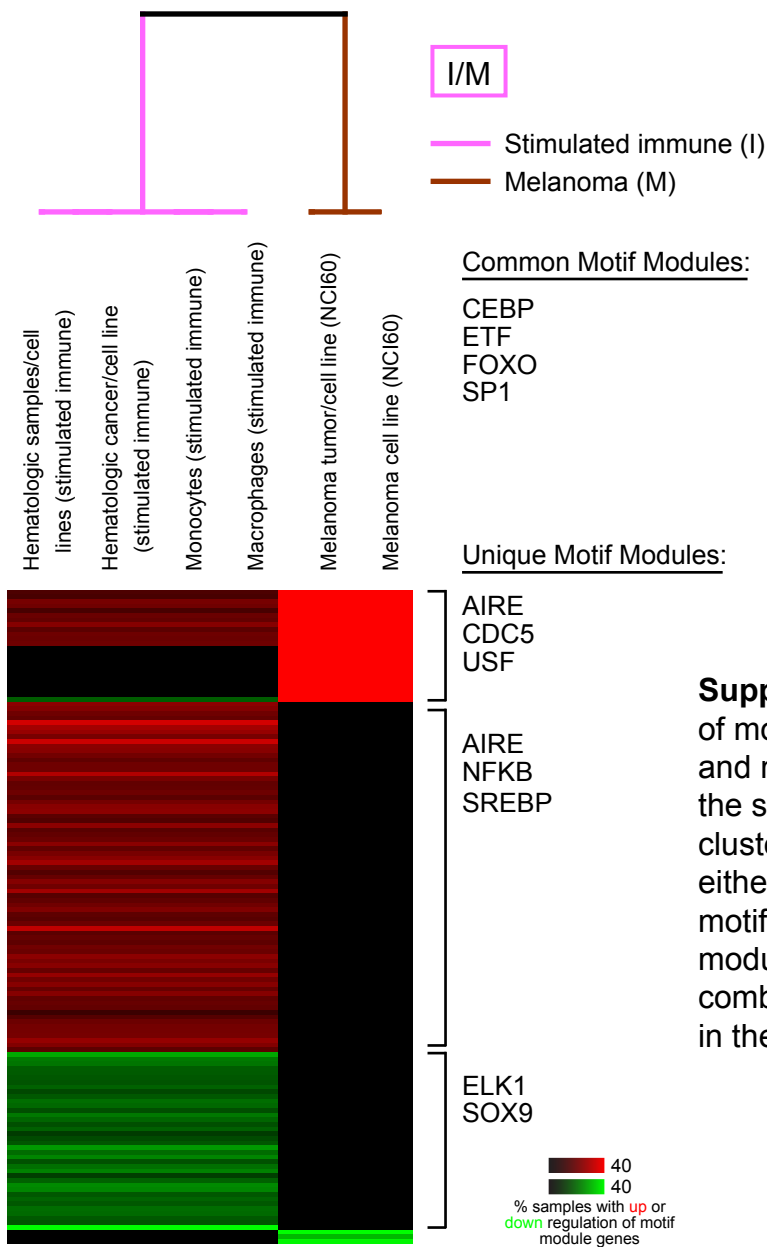


Figure S5



Supplementary Figure 5. *Cis*-regulation of motif modules in brain cancer. Motif modules enriched in the brain cluster. Common motif modules are found either alone or in combination with other motifs throughout the cluster. Unique motif modules are found alone or in combination with other motifs specifically in the region highlighted.

Figure S6



Supplementary Figure 6. *Cis*-regulation of motif modules in stimulated immune and melanoma. Motif modules enriched in the stimulated immune/melanoma (I/M) cluster. Common motif modules are found either alone or in combination with other motifs throughout the cluster. Unique motif modules are found alone or in combination with other motifs specifically in the region highlighted.