

Table S1. 57 HNSCC FAIME Features identified between tumor tissue and non-tumor control tissue in all three HNSCC datasets. References are provided for mechanisms that were also found by other approaches (e.g. enrichment, CORG, and/or GSEA) comparing tumor to normal tissues (**Figure 3**), and for co-expressed clusters found in **Figure 5**.

HNSCC FAIME Features	up- or down-regulated in HNSCC tumor samples (FAIME score, Methods, Fig. 3,5)	Confirmed by enrichment, GSEA or CORG (Fig. 3; # of methods; found in any of datasets A-C)	Scale	ID	# of genes (GO from NCBI on Dec. 11, 09; Bioconductor <i>kegg.db</i> v2.3.5 on Sep 16, 09)	Cluster (Fig. 5)
Bladder cancer	↑	3	KEGG	hsa05219	42	α
ECM-receptor interaction	↑	3	KEGG	hsa04512	84	α
extracellular matrix binding	↑	3	GO-MF	GO:0050840	13	α
Focal adhesion	↑	3	KEGG	hsa04510	202	α
glucuronosyl-N-acetylgalactosaminyl-proteoglycan 4-beta-N-acetylgalactosaminyltransferase activity	↑	1	GO-MF	GO:0047238	4	α
Glycosaminoglycan biosynthesis - chondroitin sulfate	↑	0	KEGG	hsa00532	22	α
L-ascorbic acid binding	↑	3	GO-MF	GO:0031418	21	α
metalloendopeptidase activity	↑	3	GO-MF	GO:0004222	104	α
N-acetylgalactosaminyl-proteoglycan 3-beta-glucuronosyltransferase activity	↑	1	GO-MF	GO:0050510	4	α
oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen	↑	2	GO-MF	GO:0016705	16	α
p53 signaling pathway	↑	3	KEGG	hsa04115	69	α
Pathways in cancer	↑	3	KEGG	hsa05200	331	α
platelet-derived growth factor binding	↑	2	GO-MF	GO:0048407	11	α
procollagen-proline 4-dioxygenase activity	↑	1	GO-MF	GO:0004656	4	α
Small cell lung cancer	↑	3	KEGG	hsa05222	86	α
Base excision repair	↑	1	KEGG	hsa03410	35	β
Cell cycle	↑	3	KEGG	hsa04110	129	β
cyclin-dependent protein kinase regulator activity	↑	1	GO-MF	GO:0016538	6	β
DNA replication	↑	2	KEGG	hsa03030	36	β
Mismatch repair	↑	0	KEGG	hsa03430	23	β
Pyrimidine metabolism	↑	2	KEGG	hsa00240	97	β
ribonuclease H activity	↑	1	GO-MF	GO:0004523	7	β
metabolism	↓	2	KEGG	hsa00650	34	γ
1- and 2-Methylnaphthalene degradation	↓	2	KEGG	hsa00624	13	γ
3-Chloroacrylic acid degradation	↓	2	KEGG	hsa00641	12	γ
3-chloroallyl aldehyde dehydrogenase activity	↓	1	GO-MF	GO:0004028	4	γ

acyl-CoA dehydrogenase activity	↓	1	GO-MF	GO:0003995	9	Y
acyl-CoA oxidase activity	↓	0	GO-MF	GO:0003997	4	Y
acylglycerol lipase activity	↓	0	GO-MF	GO:0047372	6	Y
alcohol dehydrogenase activity, zinc-dependent	↓	2	GO-MF	GO:0004024	4	Y
aldehyde dehydrogenase (NAD) activity	↓	2	GO-MF	GO:0004029	8	Y
aldehyde dehydrogenase [NAD(P)+] activity	↓	2	GO-MF	GO:0004030	6	Y
Arachidonic acid metabolism	↓	3	KEGG	hsa00590	58	Y
aromatase activity	↓	2	GO-MF	GO:0070330	24	Y
Ascorbate and aldarate metabolism	↓	1	KEGG	hsa00053	25	Y
beta-Alanine metabolism	↓	2	KEGG	hsa00410	22	Y
Drug metabolism - cytochrome P450	↓	3	KEGG	hsa00982	72	Y
epoxide hydrolase activity	↓	1	GO-MF	GO:0004301	4	Y
Fatty acid metabolism	↓	2	KEGG	hsa00071	42	Y
Glycerolipid metabolism	↓	2	KEGG	hsa00561	45	Y
Glycolysis / Gluconeogenesis	↓	2	KEGG	hsa00010	62	Y
Histidine metabolism	↓	2	KEGG	hsa00340	29	Y
Linoleic acid metabolism	↓	2	KEGG	hsa00591	30	Y
Metabolism of xenobiotics by cytochrome P450	↓	3	KEGG	hsa00980	70	Y
Phenylalanine metabolism	↓	1	KEGG	hsa00360	21	Y
polysaccharide binding	↓	1	GO-MF	GO:0030247	11	Y
Primary bile acid biosynthesis	↓	1	KEGG	hsa00120	16	Y
Propanoate metabolism	↓	2	KEGG	hsa00640	33	Y
protein tyrosine kinase activator activity	↓	1	GO-MF	GO:0030296	4	Y
protein-glutamine gamma-glutamyltransferase activity	↓	2	GO-MF	GO:0003810	9	Y
Retinol metabolism	↓	2	KEGG	hsa00830	64	Y
serine-type peptidase activity	↓	1	GO-MF	GO:0008236	22	Y
structural constituent of myelin sheath	↓	2	GO-MF	GO:0019911	4	Y
Sulfur metabolism	↓	1	KEGG	hsa00920	13	Y
Tropane, piperidine and pyridine alkaloid biosynthesis	↓	2	KEGG	hsa00960	9	Y
Tyrosine metabolism	↓	2	KEGG	hsa00350	47	Y
Valine, leucine and isoleucine degradation	↓	2	KEGG	hsa00280	44	Y