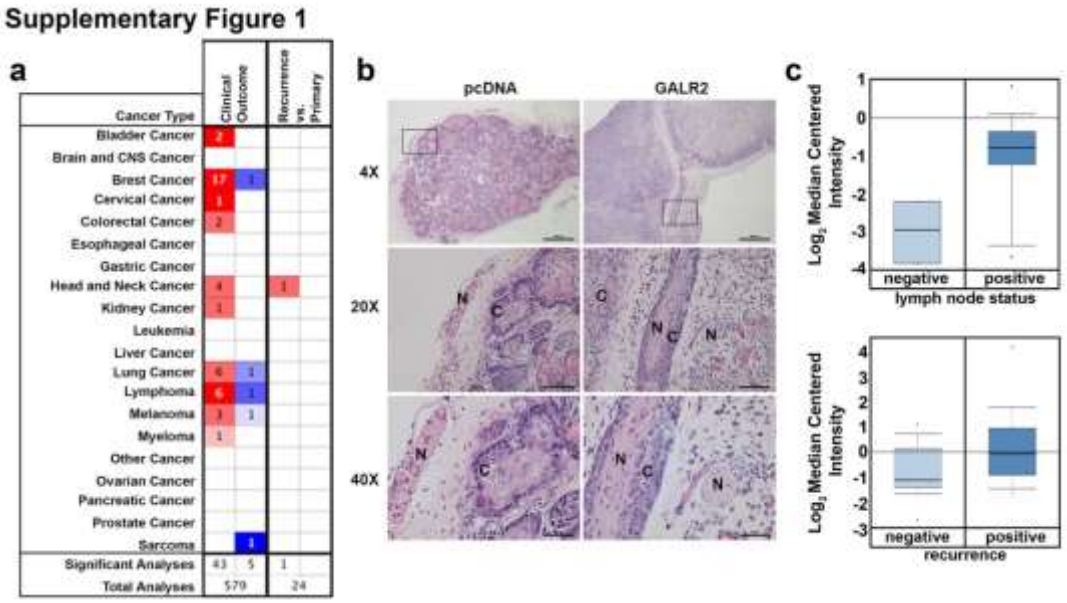
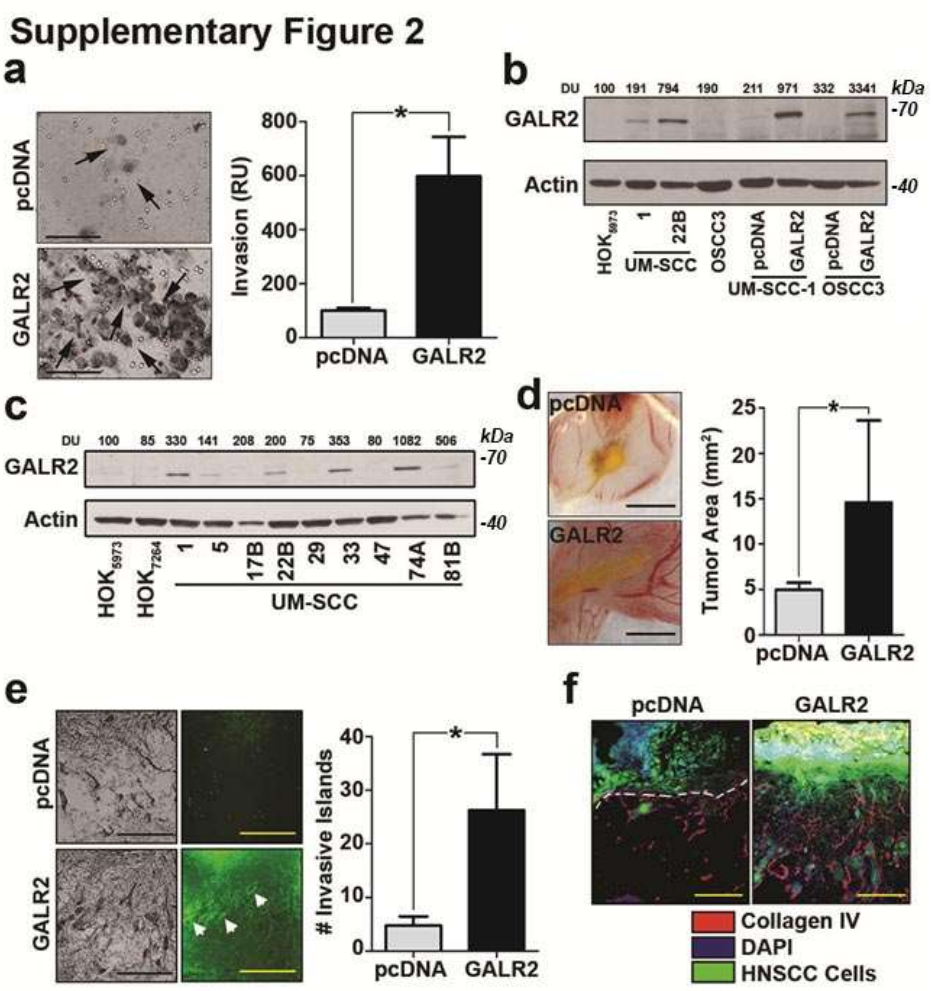
Supplementary Information

Supplementary Figures

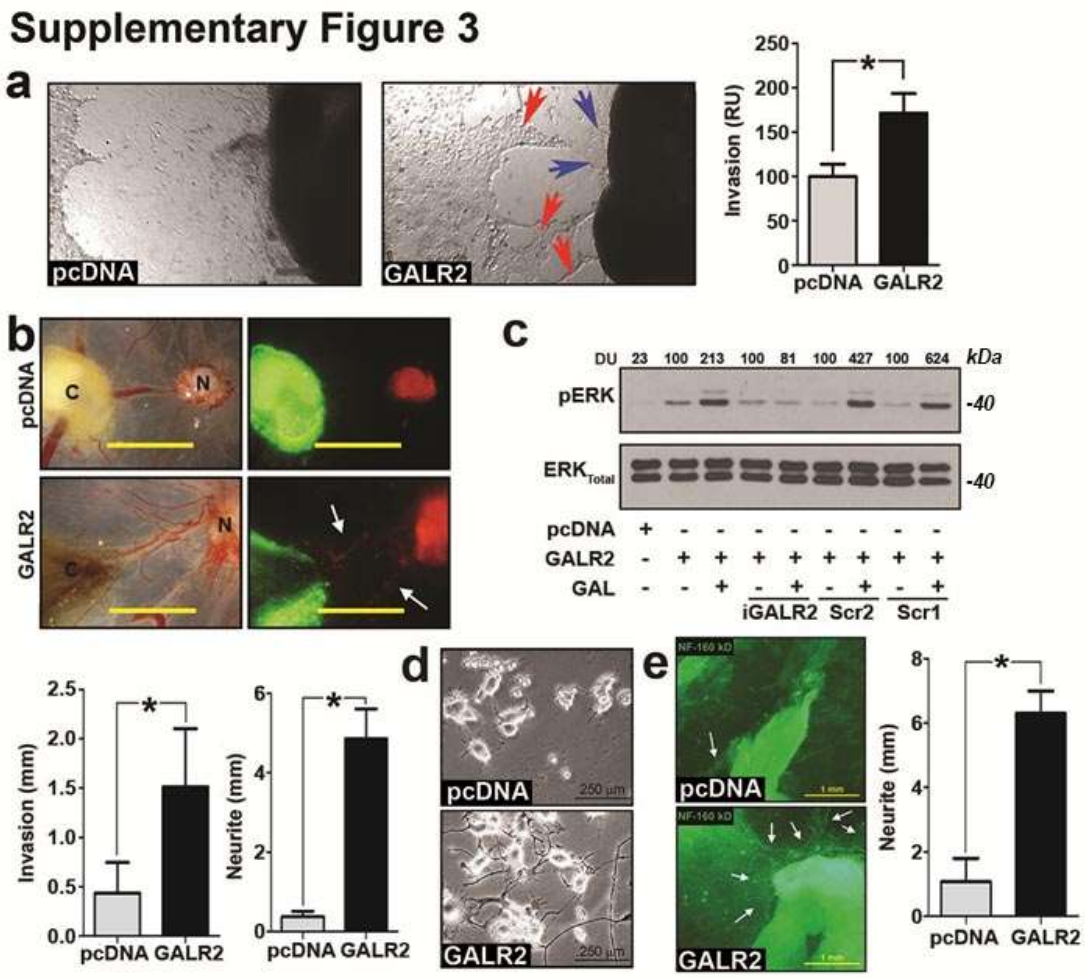


Supplementary Figure 1. GAL predicts clinical outcome in multiple cancer types. (a) Overexpression of GAL was correlated with poor clinical outcome in 43 analyses across multiple cancer types in the Oncomine™ database and in recurrent tumours versus primary HNSCC (Red = high expression, blue = low expression. Relative intensity indicates degree of over- or underexpression). Some of the analyses represent the same patients at different time points (e.g. 1, 3 and 5 years). (*$P < 0.05$, two sample t-test and a fold-change threshold of 1.5 were used). **(b)** Low and high power photomicrographs of Fig. 1a showing PNI (N=nerve, C=cancer). (scale bars: 4X = 500µm, 20X = 100µm, 40X = 50µm). **(c)** GAL overexpression is significantly correlated with positive lymph node status (top graph, from TCGA, National Cancer Institute) and recurrence (lower graph, from the Ginos Head-Neck study) of HNSCC. http://cancerres.aacrjournals.org/content/64/1/55.long

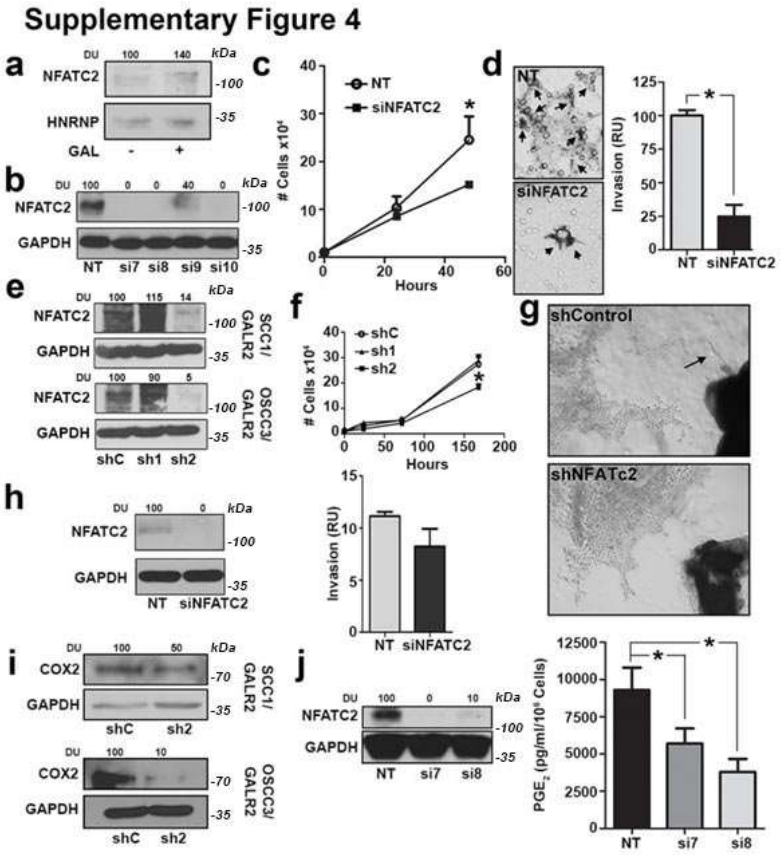
Description of Ginos study (from Oncomine): Forty one (41) HNSCC and 13 buccal mucosa samples were analysed on Affymetrix U133A microarrays. Sample data includes type, age, angiolymphatic invasion, differentiation, lymph node status, N-stage, perineural invasion, primary/recurrent, sex, site, stage and T-stage. Array Type: Human Genome U133A Array, measured 12,624 genes, 22283 reporters.



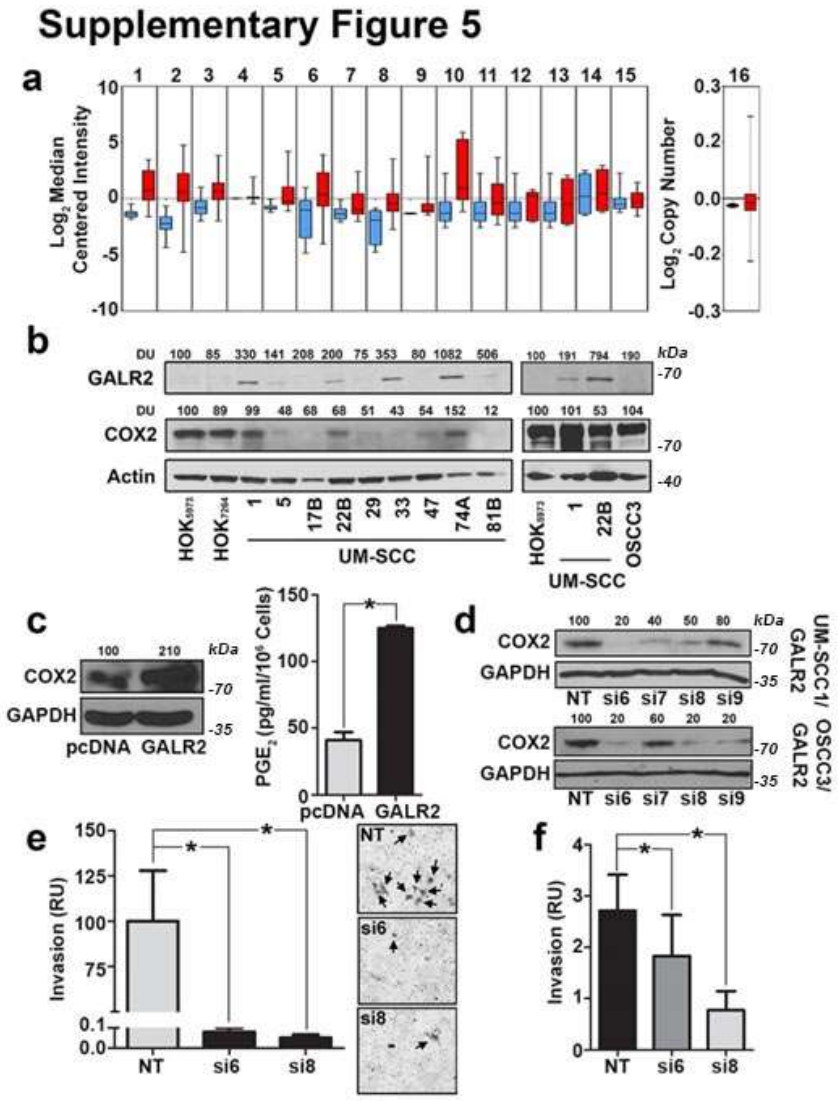
Supplementary Figure 2. GALR2 promotes tumour invasion and metastasis. (a) OSCC3-GALR2 cells are more invasive than control cells (OSCC3-pcDNA) in a Boyden chamber chemoinvasion assay with GAL as the chemoattractant (scale bar = 100μm, **P* < 0.05, two sample t-test; data represent mean + SD). **(b)** UM-SCC-1 and OSCC3 cells were transfected with control (pcDNA) or GALR2 constructs. Whole cell lysates from these cell lines, normal keratinocytes (HOK), UM-SCC1, UM-SCC-22B and OSCC3 were electrophoresed and immunoblotted with anti-GALR2 and actin, as a loading control. **(c)** Whole cell lysates from normal keratinocytes (HOK) and HNSCC cell lines (UM-SCC) were immunoblotted with anti-GALR2 and actin, as a loading control. When seeded on a CAM, OSCC3-GALR2 tumours were **(d)** larger (scale bar = 5 mm, **P* < 0.05 two sample t-test; data represent mean + SD), **(e)** more invasive (cancer cells are labelled green, scale bar = 200μm), and **(f)** more destructive of the basement membrane (labelled with Collagen IV, scale bar = 100μm) than control tumours. For CAM experiments, n = 6 per group. In vitro data are representative of three independent experiments with three replicates.



Supplementary Figure 3. GALR2 promotes PNI. (a) OSCC3-GALR2 cells are more invasive (red arrows) toward nerves than control cells and induce neurite outgrowth (blue arrows). (*P < 0.05, two sample t-test; data represent mean + SD). **(b)** On the CAM, OSCC3-GALR2 tumours (green) are more invasive and induce neurite outgrowth (red, identified with arrows, scale bar = 5mm). **(c)** UM-SCC-1-GALR2 cells were stimulated with Galanin (GAL) in the presence or absence of the GALR2 inhibitor, M871 (iGALR2), or a scrambled peptide. UM-SCC-1-pcDNA was used as a control. Whole cell lysates were immunoblotted with phospho-ERK and total ERK, as a loading control. **(d)** DRG treated with CM from OSCC3-GALR2 cells generated more neurite outgrowth than DRG treated with CM from control cells (scale bar = 250µm, *P < 0.05, two sample t-test; data represent mean + SD). **(e)** SH-SY5Y neuroblastoma cells treated with CM from OSCC3-GALR2 cells differentiated and exhibited more neurite outgrowth compared to CM from control cells (scale bar = 1mm, *P < 0.05 two sample t-test; data represent mean + SD). For CAM experiments, n = 6 for each group, and in vitro and nerve explant data are representative of three independent experiments with three replicates each.

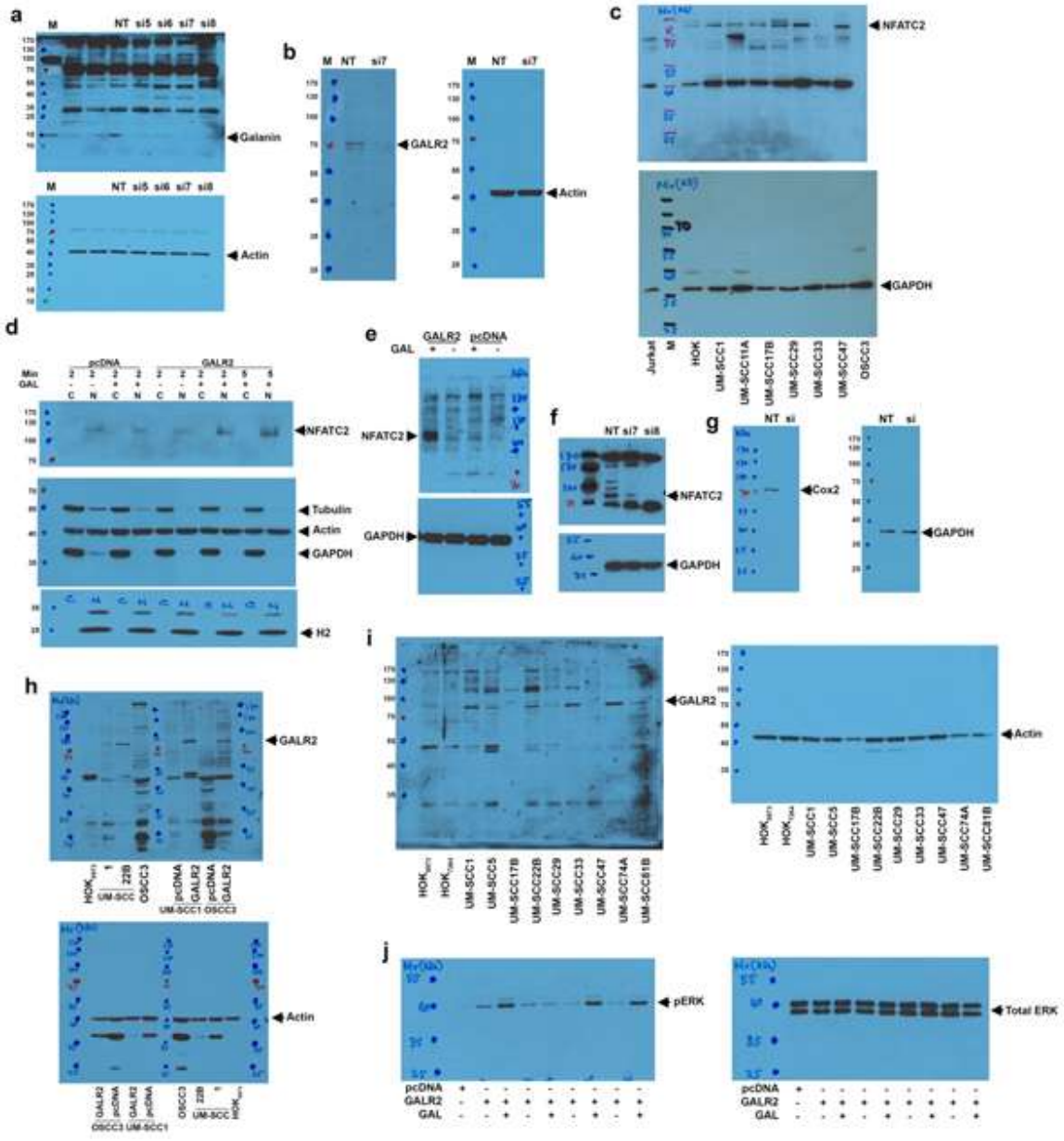


Supplementary Figure 4. GALR2 promotes tumour progression and PNI via NFATC2. (a) GAL treatment induces nuclear translocation of NFATC2 in OSCC3-GALR2 cells. **(b)** Four individual siRNAs were tested to downregulate NFATC2; si7 and si8 were selected for functional studies. OSCC3-GALR2 cells exhibit reduced **(c)** proliferation and **(d)** invasion when NFATC2 is downregulated using siRNA. (For **(c)** and **(d)** **P* < 0.05 two sample t-test; data represent mean + SD). **(e)** shRNAs were tested to use for constitutive downregulation of NFATC2 in UM-SCC-1-GALR2 and OSCC3-GALR2; sh2 was selected. **(f)** OSCC3-GALR2-shNFATc2-2 (sh2) cells exhibit reduced proliferation whereas OSCC3-GALR2-shNFATc2-1 (sh1) with no downregulation of NFATc2 exhibited the same proliferation as OSCC3-GALR2. (**P* < 0.05 two sample t-test; data represent mean + SD). **(g)** OSCC3-GALR2 cells with NFATC2 knockdown exhibit less PNI in vitro than control cells (arrow identifies neurite outgrowth in control group). **(h)** UM-SCC-1-pcDNA cells transfected with siNFATc2 exhibited no significant difference in invasion towards DRG than control cells. (**P* < 0.05 two sample t-test; data represent mean + SD). **(i)** COX2 expression is decreased in UM-SCC-1-GALR2 and OSCC3-GALR2 cells with constitutive knockdown of NFATC2. **(j)** When NFATC2 is downregulated with siRNA in OSCC3-GALR2 cells, PGE_2 secretion decreases. (**P* < 0.05 two sample t-test; data represent mean + SD). For CAM experiments, n = 6 per group. In vitro and DRG explant data are representative of three independent experiments with three replicates each.

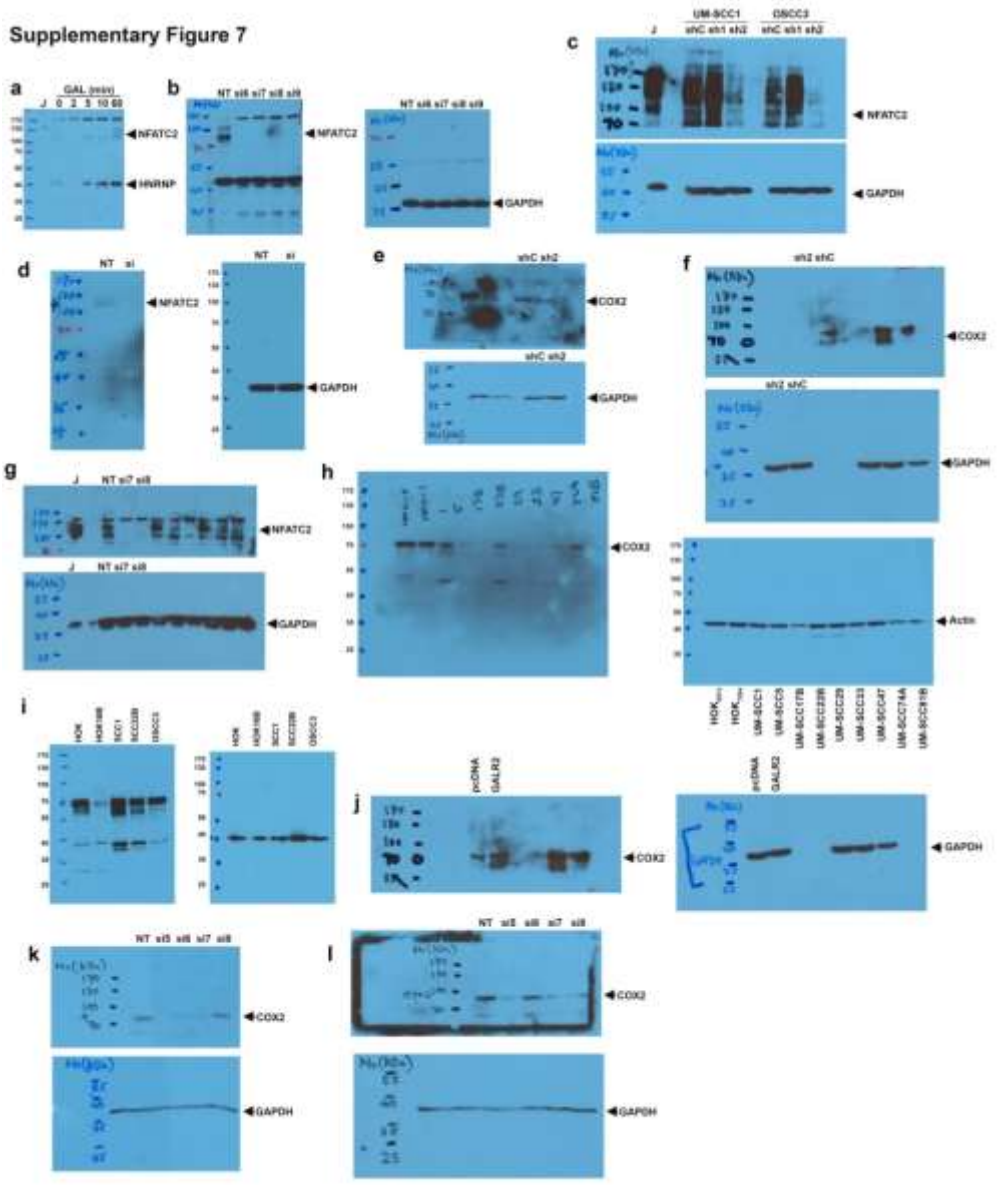


Supplementary Figure 5. COX2 is highly expressed in HNSCC and mediates GALR2-induced invasion. (a) A meta-analysis of HNSCC studies on Oncomine™ shows that COX2 is highly expressed in cancer versus normal (non-cancer) samples (one sample t-test of dichotomized results against the hypothetical mean of 0.05, $P< 0.0001$). **(b)** COX2 does not correlate with GALR2 in normal keratinocytes and HNSCC cell lines. The actin and GALR2 panels from Supplementary Fig. 2c are shown again for normalization and comparison, respectively. **(c)** OSCC3-GALR2 cells express more COX2 and secrete more PGE_2 than control cells (left, immunoblot of whole cell lysates; right, ELISA of CM). (*$P <$ 0.05 two sample t-test; data represent mean + SD). **(d)** Four individual siRNAs were tested in UM-SCC-1-GALR2 and OSCC3-GALR2 cells; si6 and si8 were selected. **(e and f)** Downregulation of COX2 in OSCC3-GALR2 cells using siRNA decreases invasion in a Boyden chamber assay **(e)** and also decreases invasion toward nerves in co-culture **(f)**. (*$P < 0.05$ two sample t-test; data represent mean + SD). In vitro and nerve explant data are representative of three independent experiments each with three replicates.

Supplementary Figure 6



Supplementary Figure 6: Scanned films for: **(a)** Fig. 2b. **(b)** Fig. 3c. **(c)** Fig. 5a-upper left panel. **(d)** Fig. 5a-upper right panel. **(e)** Fig. 5a-lower left panel (Note: flipped in Fig. 5a-lower panel to put pcDNA control on left). **(f)** Fig. 5i. **(g)** Fig. 6e. **(h)** Supplementary Fig. 2b (Note: actin inverted in Supplementary Fig. 2b to correspond with samples). **(i)** Supplementary Fig. 2c. **(j)** Used for Supplementary Fig. 3c



Supplementary Figure 7: Scanned films for: **(a)** Supplementary Fig. 4a. **(b)** Supplementary Fig. 4b. **(c)** Supplementary Fig. 4. **(d)** Supplementary Fig. 4h. **(e)** Supplementary Fig. 4i-upper panel **(f)** Supplementary Fig. 4i-lower panel **(g)** Supplementary Fig. 4j. **(h)** Supplementary Fig. 5b. (Note: the actin and GALR2 in Supplementary Fig. 5b left panel are from blots in Figs. 6h and 6i since these two panels were shown initially in Fig. 2b and 2c and again in Fig. 5b for comparison to COX2). **(i)** Supplemental Fig. 5b, right panel. **(j)** Supplementary Fig. 5c. **(k)** Supplementary Fig. 5d-upper panel. **(l)** Supplementary Fig. 5d-lower panel.

Supplementary Tables

Supplementary Table 1:

Study Number	Accession Number	Name	Link to Data	Reference	Normal Tissues
1	GSE12452	Sengupta Head Neck	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE12452	Sengupta, S., den Boon, J. A., Chen, I. H., Newton, M. A., Dahl, D. B., Chen, M., et al. (2006). Genome-wide expression profiling reveals EBV-associated inhibition of MHC class I expression in nasopharyngeal carcinoma. *Cancer Research,66*(16), 7999-8006.	Nasopharyngeal
2	No Accession Number	Ginos Head Neck	http://cancerres.aacrjournals.org/content/64/1/55.long	Ginos, M. A., Page, G. P., Michalowicz, B. S., Patel, K. J., Volker, S. E., Pambuccian, S. E., et al. (2004). Identification of a gene expression signature associated with recurrent disease in squamous cell carcinoma of the head and neck. *Cancer Research, 64*(1), 55-63.	Buccal mucosa
3	GSE25099	Peng Head Neck	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE25099	Peng, C., Liao, C., Peng, S., Chen, Y., Cheng, A., Juang, J., et al. (2011). A novel molecular signature identified by systems genetics approach predicts prognosis in oral squamous cell carcinoma. *PloS One, 6*(8), e23452.	Oral Cavity
4	GSE55543	TCGA Head Neck	http://tcga-data.nci.nih.gov/tcga/ http://gdac.broadinstitute.org/runs/stddata__2013_09_23/data/	No associated paper – see: https://tcga-data.nci.nih.gov/tcga/ .	Blood and Head and Neck Parts
5	GSE9844	Ye Head Neck	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE9844	Ye, H., Yu, T., Temam, S., Ziober, B. L., Wang, J., Schwartz, J. L., et al. (2008). Transcriptomic dissection of tongue squamous cell carcinoma. *BMC Genomics, 9*, 69-2164-9-69.	Tongue squamous cells
6	GSE13601	Estilo Head Neck	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE13601	Estilo, C. L., Pornchai, O., Talbot, S., Socci, N. D., Carlson, D. L., Ghossein, R., et al. (2009). Oral tongue cancer gene expression profiling: Identification of novel potential prognosticators by oligonucleotide microarray analysis.*BMC Cancer, 9*(1), 11.	Paired normal tongue
7	GSE3524	Talbot Lung (Head and neck dataset)	http://www.ncbi.nlm.nih.gov/pubmed/15833835?dopt=Abstract	Talbot, S. G., Estilo, C., Maghami, E., Sarkaria, I. S., Pham, D. K., O-charoenrat, P., et al. (2005). Gene expression profiling allows distinction between primary and metastatic squamous cell carcinomas in the lung. *Cancer Research, 65*(8), 3063-3071.	Lung and Tongue
8	GSE2379	Cromer Head Neck	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE2379	Cromer, A., Carles, A., Millon, R., Ganguli, G., Chalmel, F., Lemaire, F., et al. (2004). Identification of genes associated with tumorigenesis and metastatic potential of hypopharyngeal cancer by microarray analysis. *Oncogene, 23*(14), 2484-2498.	Uvula

9	GSE3524	Toruner Head Neck	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE3524	Toruner, G. A., Ulger, C., Alkan, M., Galante, A. T., Rinaggio, J., Wilk, R., et al. (2004). Association between gene expression profile and tumor invasion in oral squamous cell carcinoma. *Cancer Genetics and Cytogenetics,154*(1), 27-35.	Normal squamous cells
10	GSE6791	Pyeon Multi-Cancer: Oropharyngeal Carcinoma	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE6791	Pyeon, D., Newton, M. A., Lambert, P. F., den Boon, J. A., Sengupta, S., Marsit, C. J., et al. (2007). Fundamental differences in cell cycle deregulation in human papillomavirus-positive and human papillomavirus-negative head/neck and cervical cancers. *Cancer Research, 67*(10), 4605-4619.	Oral Tissues
11	GSE6791	Pyeon Multi-Cancer: Tongue Carcinoma	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE6791	Pyeon, D., Newton, M. A., Lambert, P. F., den Boon, J. A., Sengupta, S., Marsit, C. J., et al. (2007). Fundamental differences in cell cycle deregulation in human papillomavirus-positive and human papillomavirus-negative head/neck and cervical cancers. *Cancer Research,67*(10), 4605-4619.	Oral Tissues
12	GSE6791	Pyeon Multi-Cancer: Floor of the Mouth	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE6791	Pyeon, D., Newton, M. A., Lambert, P. F., den Boon, J. A., Sengupta, S., Marsit, C. J., et al. (2007). Fundamental differences in cell cycle deregulation in human papillomavirus-positive and human papillomavirus-negative head/neck and cervical cancers. *Cancer Research, 67*(10), 4605-4619.	Oral Tissues
13	GSE6791	Pyeon Multi-Cancer: Oral Cavity Carcinoma	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE6791	Pyeon, D., Newton, M. A., Lambert, P. F., den Boon, J. A., Sengupta, S., Marsit, C. J., et al. (2007). Fundamental differences in cell cycle deregulation in human papillomavirus-positive and human papillomavirus-negative head/neck and cervical cancers. *Cancer Research, 67*(10), 4605-4619.	Oral Tissues
14	GSE1722	Schlingemann Head Neck	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE1722	Schlingemann, J., Habtemichael, N., Ittrich, C., Toedt, G., Kramer, H., Hambek, M., et al. (2005). Patient-based cross-platform comparison of oligonucleotide microarray expression profiles. *Laboratory Investigation, 85*(8), 1024-1039.	Hypopharynx and Oropharynx
15	GDS2520	Kuriakose Head Neck	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE6631	Kuriakose, M., Chen, W., He, Z., Sikora, A., Zhang, P., Zhang, Z., et al. (2004). Selection and validation of differentially expressed genes in head and neck cancer. *Cellular and Molecular Life Sciences CMLS, 61*(11), 1372-1383.	Oral Mucosa
16	GSE25103	Peng Head Neck 2	http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE25103	Peng, C., Liao, C., Peng, S., Chen, Y., Cheng, A., Juang, J., et al. (2011). A novel molecular signature identified by systems genetics approach predicts prognosis in oral squamous cell carcinoma. *PloS One, 6*(8), e23452.	Oral Cavity

Supplementary Table 1: Information about studies in meta-analyses.

Supplementary Table 2: Meta-analysis of GAL.

Study	t-Test (df)	*P*-Value	Normal/Cancer Samples
1) Sengupta Head-Neck	2.038 (39)	0.024	10/31
2) Ginos Head-Neck	1.347 (52)	0.092	13/41
3) Peng Head-Neck	0.085 (77)	0.466	22/57
4) TCGA Head-Neck	7.889 (817)	1.61e-14	434/385
5) Ye Head-Neck	2.596 (36)	0.007	12/26
6) Estilo Head-Neck	1.66 (55)	0.051	26/31
7) Talbot Lung	-0.194 (91)	0.577	28/31
8) Cromer Head-Neck	2.258 (36)	0.048	4/34
9) Toruner Head-Neck	0.105 (18)	0.46	4/16
10) Pyeon Oropharyngeal	0.796 (26)	0.224	22/6
11) Pyeon Tongue	2.303 (35)	0.014	22/15
12) Pyeon Floor of the Mouth	1.283 (25)	0.134	22/5
13) Pyeon Oral Cavity	0.753 (24)	0.252	22/4
14) Schlingemann Head-Neck	1.601 (6)	0.08	4/4
15) Kuriakose Head-Neck	2.421 (23)	0.06	22/3
16) Peng Head-Neck 2	4.902 (120)	1.75e-6	10/112
Meta-Analysis	2.6 (15)	0.01005	NA

Supplementary Table 2: GAL expression is upregulated in HNSCC relative to normal tissue. Individual HNSCC studies examined the difference in GAL expression between normal and cancer tissues with two sample t-tests. The meta-analysis was then conducted as a one sample t-test comparing the proportion of studies that were statistically significant at the 0.05 level with the proportion of studies expected to be significant at the 0.05 level. The *P*-value resulting from this meta-analysis was 0.01, sufficiently extreme to reject the null hypothesis that there was no relationship between GAL expression and tissue cancer status.

Supplementary Table 3: Summary information about studies for Supplementary Fig. 1a.

Analysis Type by Cancer	Clinical Outcome		Recurrence	Total Number of Analyses	Number of Studies	Sample Number: Smallest study	Sample Number: Largest study	Sample Number: Mean	Total Patients across studies
Bladder Cancer	2			17	5	9	288	135.4	677
Brain and CNS Cancer				56	15	29	1531	213.13	3197
Breast Cancer	17	1		129	26	40	2136	395.10	10275
Cervical Cancer	1			4	3	66	301	155.67	467
Colorectal Cancer	2			35	10	48	1172	229.7	2297
Esophageal Cancer				2	1	40	40	40	40
Gastric Cancer				28	3	132	637	303.33	910
Head and Neck Cancer	4		1	34	4	38	1012	488.25	1953
Kidney Cancer	1			19	4	34	1463	440.5	1762
Leukemia				18	15	12	161	46.07	645
Liver Cancer				17	4	52	292	161.75	647
Lung Cancer	6	1		81	14	51	2058	304.141	4258
Lymphoma	6	1		50	11	22	414	142.09	1563
Melanoma	3	1		10	2	63	154	108.5	217
Myeloma	1			6	3	65	414	247.67	743
Other Cancer				16	9	25	1602	469.33	4224
Ovarian Cancer				25	7	50	1168	362.141	2535
Pancreatic Cancer				5	2	27	131	79	158
Prostate Cancer				18	8	54	380	192.63	1541
Sarcoma		1		10	4	14	165	58.25	233
Significant Analyses	43	5	1						
Total Analyses	579		24						

Supplementary Table 3: Summary information about studies for Supplementary Fig. 1a.

Supplementary Table 4: Meta-analysis of COX2.

Study	t-Test (df)	*P*-Value	Normal/Cancer Samples
1) Sengupta Head-Neck	8.061 (39)	4.42e-10	10/31
2) Ginos Head-Neck	8.141 (52)	2.42e-10	13/41
3) Peng Head-Neck	6.236 (77)	2.58e-8	22/57
4) TCGA Head-Neck	7.427 (817)	2.68e-13	434/385
5) Ye Head-Neck	4.093 (36)	1.56e-4	12/26
6) Estilo Head-Neck	4.826 (56)	5.97e-6	26/32
7) Talbot Lung	4.038 (57)	1.2e-4	28/31
8) Cromer Head-Neck	2.413 (36)	0.042	4/34
9) Toruner Head-Neck	2.17 (18)	0.022	4/16
10) Pyeon Oropharyngeal	2.864 (26)	0.017	22/6
11) Pyeon Tongue	2.877 (35)	0.005	22/15
12) Pyeon Floor of the Mouth	1.355 (25)	0.118	22/5
13) Pyeon Oral Cavity	0.971 (24)	0.2	22/4
14) Schlingemann Head-Neck	0.226 (6)	0.415	4/4
15) Kuriakose Head-Neck	-2.008 (23)	0.969	22/3
16) Peng Head-Neck 2	2.051 (120)	0.021	10/112
Meta-Analysis	6.261 (15)	0.0001	NA

Supplementary Table 4: COX2 expression is upregulated in HNSCC relative to normal tissue. The individual studies in Oncomine™ examined the difference with two sample t-tests comparing COX2 expression in normal and cancerous tissues. The meta-analysis was conducted as a one sample t-test comparing the proportion of studies that were statistically significant at the 0.05 level. The *P*-value from the meta-analysis was 0.0001, sufficiently extreme to reject the null hypothesis that there was no relationship between COX2 expression and tissue cancer status.

Supplementary Table 5:

Gender		
	Male	8
	Female	4
Age		
	<50 years	1
	50 years – 70 years	8
	>70 years	3
Location(s)		
	Tongue	7
	Lateral	5
	Ventral	2
	Dorsal	1
	Inferior	1
	Floor of the mouth	3
	Buccal mucosa	2
	Palate	1
Diagnoses		
	Well differentiated SCC	10
	Moderately differentiated SCC	1
	Poorly differentiated SCC	1

Supplementary Table 5: Clinical data for human HNSCC specimens.

Supplementary Table 6:

***NFATC2* (NFATC2)**	si7 – GCUUAGAAACGCCGACAUU si8 – AGACGGAGCCCACGGAUGA si9 – GCAGAAUCGUCUCUUUACA si10 – GAACCUCGCCAAUAAUGUC
***PTGS2* (COX2)**	si6 – GGACUUAUGGGUAAUGUUA si7 – GAUAAUUGAUGGAGAGAUG si8 – GUGAAACUCUGGCUAGACA si9 – CGAAAUGCAAUUAUGAGUU
GAL	si5 – AAACGAGGCUGGACCCUGA si6 – CAGAAGACAUCGAGCGGUC si7 – AGAAUGGCCUCACCAGCAA si8 –UAUCAUGCGCACAAUCAUU
GALR2	si7 – UCUCGCACCUGGUCUCCUA

Supplementary Table 6: siRNA target sequences for NFATC2 PTGS2 (COX2), Galanin (GAL) and GALR2 (Dharmacon) used in this study.

Supplementary Table 7:

***PTGS* (COX2)**	F1, 5'-GAATTTACCTTTCCCGCCTCTC-3' R1, 5'-AAGCCCGGTGGGGGCAGGGTTT-3' F2, 5'-GAAGCCAAGTGTCCTTCTGC-3' R2, 5'-GGAGAGGGAGGGATCAGAC-3' F3, 5'-AAGGCATACGTTTTGGACATTTAGC-'3 R3, 5'-CTTTATATTGGTGACCCGTGGAGCT-3'
***GAL* (GAL)**	F1, 5'-TTCGGGATTAGGGTCTCTCC-3' R1, 5'-GGTCCTCTGGGCCATCATAG-3' F2, 5'-CTATGATGGCCCAGAGGACC-3' R2, 5'-GGCGCCAGTAGTACCTTGAG-3' F3, 5'-CTATGATGGCCCAGAGGACC-3' R3, 5'-ATATGCGGCGCACCCGGGAGCC-3'
GAL (GAL)	F, 5'-GCGCACAATCATTGAGTTTC-3' R, 5'-GGCAAAGAGAACAGGAATGG-3'
GAPDH	F, 5'-GCGAGATCCCTCCAAAATCAA'3
(Expression Primers)	R, 5'-GTTCACACCCATGACGAACAT'3.

Supplementary Table 7: Primer pairs used in the ChIP Assay and PCR.

REFERENCES

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3. Ginos MA, *et al.* Identification of a gene expression signature associated with recurrent disease in squamous cell carcinoma of the head and neck. *Cancer research* **64**, 55-63 (2004).

4. Kuriakose MA, *et al.* Selection and validation of differentially expressed genes in head and neck cancer. *Cellular and molecular life sciences : CMLS* **61**, 1372-1383 (2004).

5. Peng CH, *et al.* A novel molecular signature identified by systems genetics approach predicts prognosis in oral squamous cell carcinoma. *PloS one* **6**, e23452 (2011).

6. Pyeon D, *et al.* Fundamental differences in cell cycle deregulation in human papillomavirus-positive and human papillomavirus-negative head/neck and cervical cancers. *Cancer research* **67**, 4605-4619 (2007).

7. Schlingemann J, *et al.* Patient-based cross-platform comparison of oligonucleotide microarray expression profiles. *Laboratory investigation; a journal of technical methods and pathology* **85**, 1024-1039 (2005).

8. Sengupta S, *et al.* Genome-wide expression profiling reveals EBV-associated inhibition of MHC class I expression in nasopharyngeal carcinoma. *Cancer research* **66**, 7999-8006 (2006).

9. Talbot SG, *et al.* Gene expression profiling allows distinction between primary and metastatic squamous cell carcinomas in the lung. *Cancer research* **65**, 3063-3071 (2005).

10. Toruner GA, *et al.* Association between gene expression profile and tumor invasion in oral squamous cell carcinoma. *Cancer genetics and cytogenetics* **154**, 27-35 (2004).

11. Ye H, *et al.* Transcriptomic dissection of tongue squamous cell carcinoma. *BMC genomics* **9**, 69 (2008).