Supplementary Figures
Van Dyck et al.

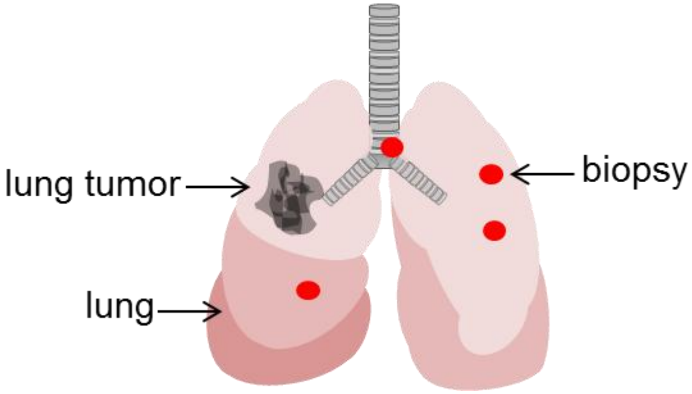


Figure S1. Scheme illustrating the sites where benign lung biopsies were taken for the analysis of the smoking-related molecular field of injury of the lung and airway in patients with NSCLC. See text for additional details.

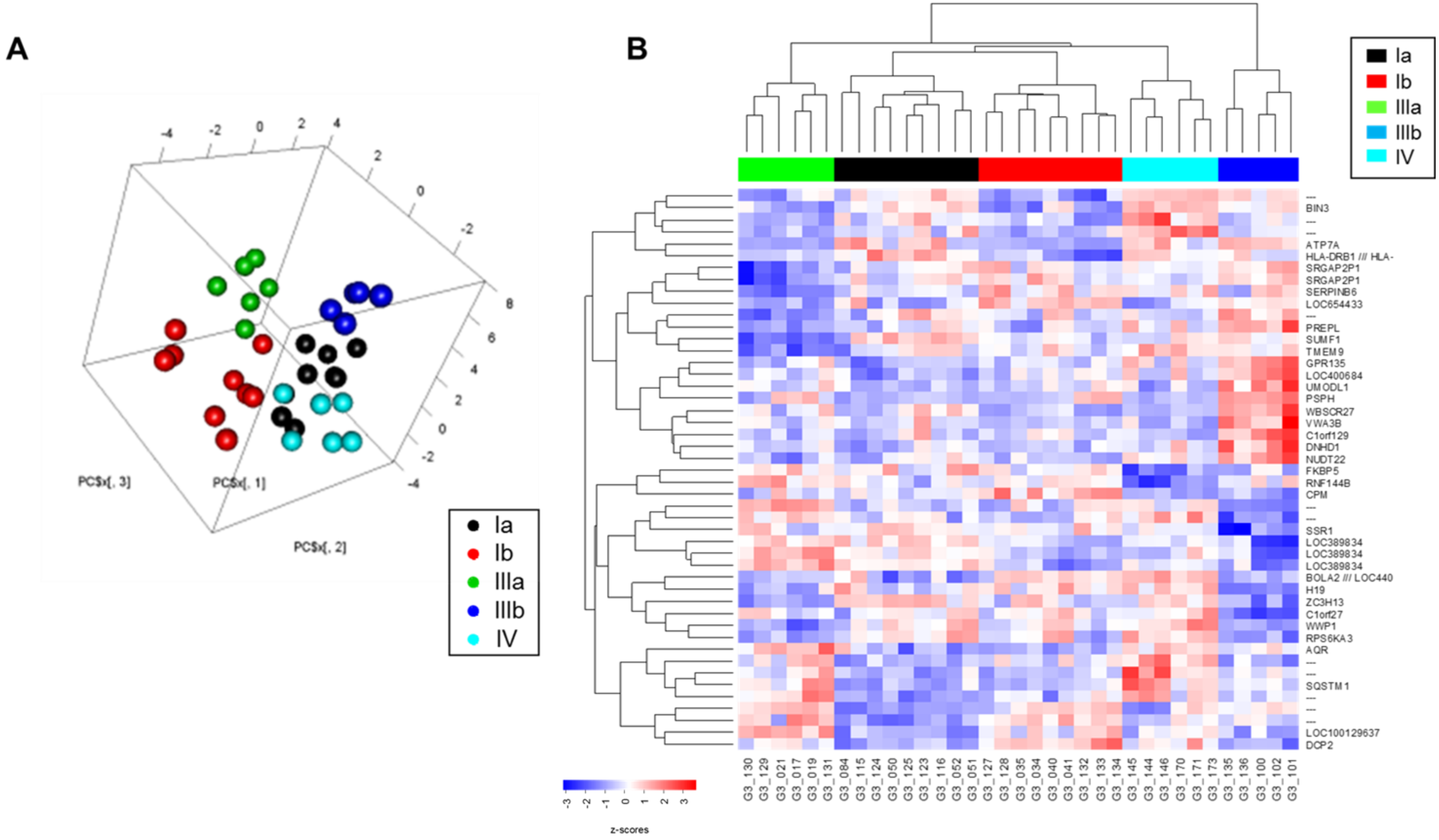
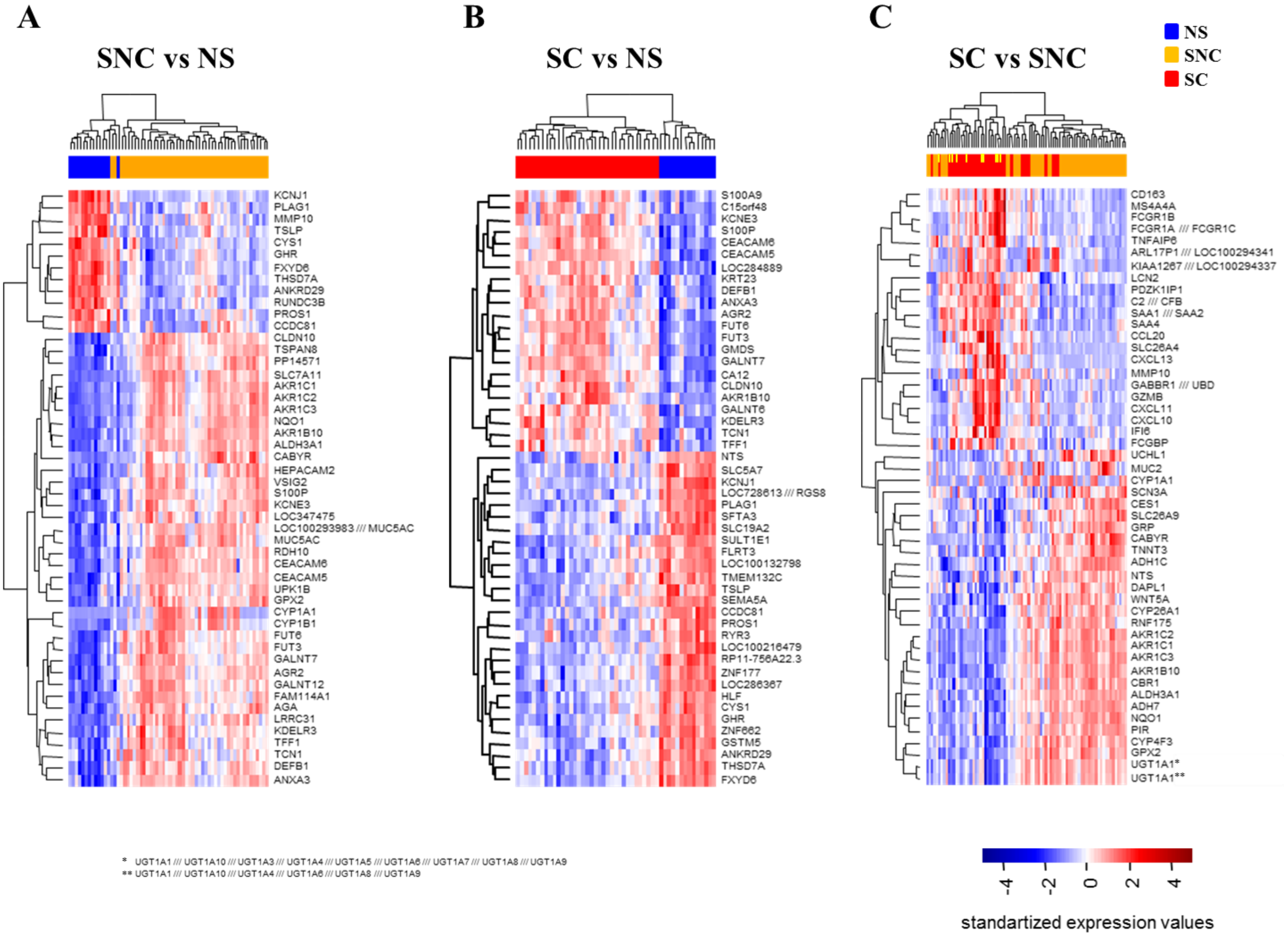


Figure S2. Genes differentially expressed amongst the 5 cancer stages of the SC biopsies. (**A**) 3-dimensional representation of the principal component analysis showing segregation of the 37 SC biopsies based on the 47 DEGs. (**B**) Hierarchical clustering of SC biopsies based on the 47 DEGs. See text for details.



* UGT1A1 /// UGT1A10 /// UGT1A3 /// UGT1A4 /// UGT1A5 /// UGT1A6 /// UGT1A7 /// UGT1A8 /// UGT1A9
** UGT1A1 /// UGT1A10 /// UGT1A4 /// UGT1A6 /// UGT1A8 /// UGT1A9

Figure S3. Hierarchical clustering and heatmap representation of the top 50 genes differentially expressed in the indicated comparisons of SNC vs NS, SC vs NS and SC vs SNC. The color codes for the groups and the color-coded scale (blue = downregulation, red=upregulation) for the standardised expression values are indicated, respectively, at the top and the bottom of the figure. HNC biopsies on the rightmost heatmap are indicated by bars.

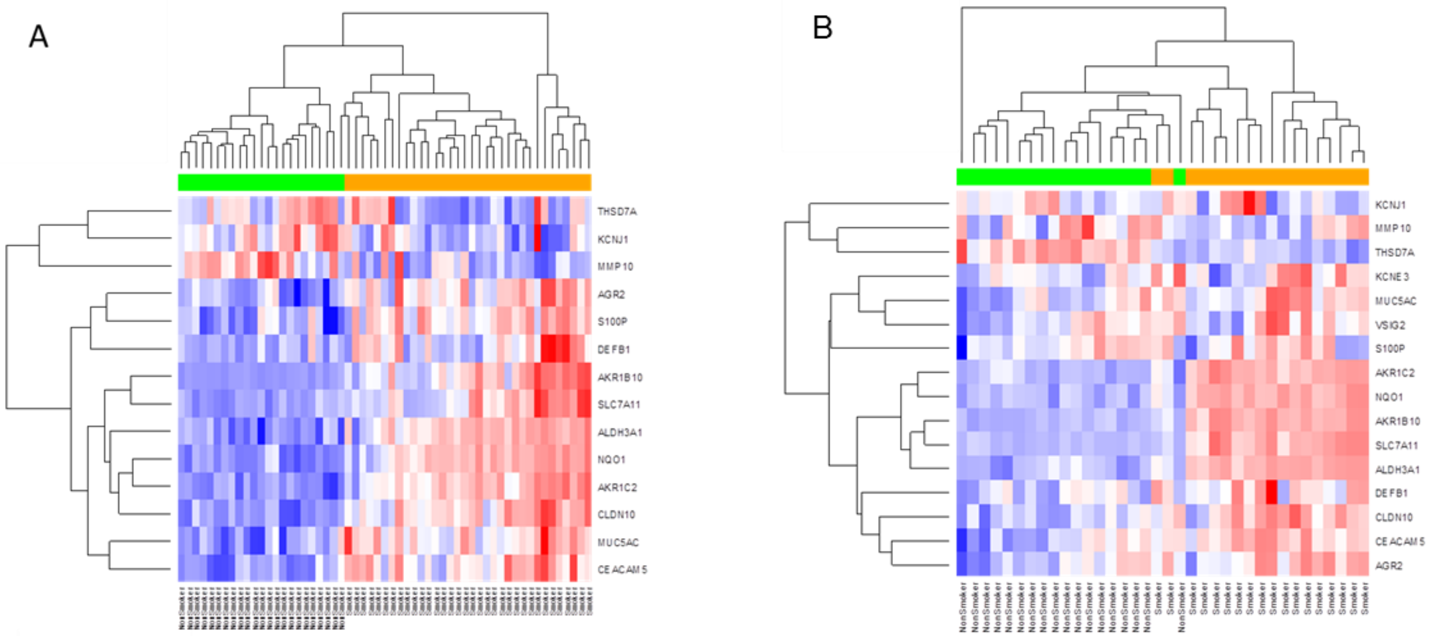
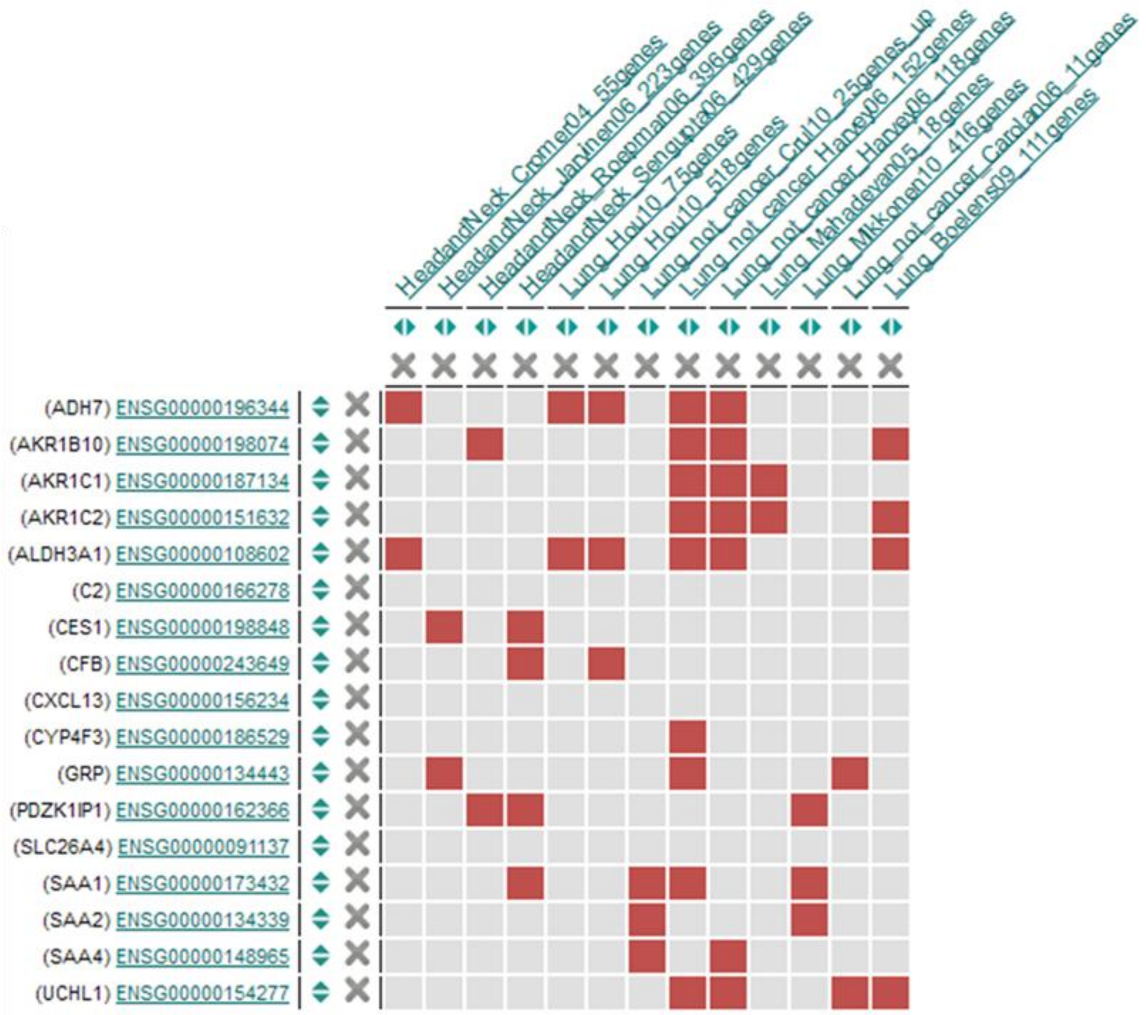


Figure S4. Validation of the 16-gene signature that distinguishes SNC and NS, on two independent datasets. Heatmaps for the signature on the datasets of (**A**) Spira et al. [10] and (**B**) Amous et al. [28]. See text for details.

A

Gene Signature*	Signature Name	Description	Reference	Size	Overlap	P-value
17115125-SuppTable2	Lung_not_cancer_Harvey06_152genes	Genes differentially expressed in the small airway epithelium of 6 healthy smokers vs 5 healthy non-smokers	1	125	9	0
17115125-SuppTable4	Lung_not_cancer_Harvey06_118genes	Genes differentially expressed in the small airway epithelium of 10 healthy smokers vs 12 healthy non-smokers	1	91	7	0
16912175-SuppTable3b	HeadandNeck_Sengupta06_429genes	Genes whose expression is down-regulated in nasopharyngeal carcinoma tumors vs normal tissues	2	356	4	0
19334046-TableS3a	Lung_Boelens09_111genes	Up-regulated genes in normal bronchial epithelium as compared to ex-smokers	3	97	4	0
20332630-Table4	Lung_not_cancer_Crul10_25genes_up	Top 25 of the most highly up-regulated genes between COPD patients with acute exacerbation vs stable COPD patients	4	23	3	0
15735009-Table1	Lung_Mahadevan05_18genes	Altered gene expression patterns in MCF-7 cells induced by the urban dust particulate complex mixture standard reference material 1649a.	5	18	2	0
17108109-Table2a	Lung_not_cancer_Carolan06_11genes	Microarray assessment of neuroendocrine cell-specific genes in normal nonsmokers normal smokers, smokers with early COPD and smokers with established COPD	6	10	2	0
14676830-Table3	HeadandNeck_Cromer04_55genes	Sequences decreased in tumours of the hypopharynx (55 genes, 12 of which were decreased sequences in common with previous studies)	7	51	2	0.0001
20421987-TableS5	Lung_Hou10_75genes	NSCLC histology signature (short)	8	58	2	0.0001
20035825-TableS7a	Lung_Mikkonen10_416genes	Up-regulated genes in A549 cells treated with 1 μM Dexamethasone or vehicle for 24h.	9	325	3	0.0003
20421987-TableS4	Lung_Hou10_518genes	NSCLC histology signature (long)	8	404	3	0.0006
16715129-SuppTable5	HeadandNeck_Jarvinen06_223genes	Statistically identified genes whose expression was decreased due to copy number losses in the primary tumors.	10	213	2	0.0031
16489042-SuppTable1a	HeadandNeck_Roepman06_396genes	Predictive genes showing negative correlation with lymph node metastasis	11	318	2	0.0109

B



	HeadandNeck_Cromer04_55genes	HeadandNeck_Jarvinen06_223genes	HeadandNeck_Roepman06_396genes	HeadandNeck_Sengupta06_429genes	Lung_Hou10_75genes	Lung_Hou10_518genes	Lung_not_cancer_Crul10_25genes_up	Lung_not_cancer_Harvey06_152genes	Lung_not_cancer_Harvey06_118genes	Lung_Mahadevan05_18genes	Lung_Mkkonen10_416genes	Lung_not_cancer_Carolan06_11genes	Lung_Boelens09_111genes
(ADH7) ENSG00000196344	🟥				🟥	🟥		🟥	🟥				
(AKR1B10) ENSG00000198074			🟥					🟥	🟥				🟥
(AKR1C1) ENSG00000187134								🟥	🟥	🟥			
(AKR1C2) ENSG00000151632								🟥	🟥	🟥			🟥
(ALDH3A1) ENSG00000108602	🟥				🟥	🟥		🟥	🟥				🟥
(C2) ENSG00000166278													
(CES1) ENSG00000198848		🟥		🟥									
(CFB) ENSG00000243649				🟥		🟥							
(CXCL13) ENSG00000156234													
(CYP4F3) ENSG00000186529								🟥					
(GRP) ENSG00000134443		🟥						🟥				🟥	
(PDZK1IP1) ENSG00000162366			🟥	🟥							🟥		
(SLC26A4) ENSG00000091137													
(SAA1) ENSG00000173432				🟥			🟥	🟥			🟥		
(SAA2) ENSG00000134339							🟥				🟥		
(SAA4) ENSG00000148965							🟥		🟥				
(UCHL1) ENSG00000154277								🟥	🟥			🟥	🟥

Figure S5. (**A**) The 13 published lung and head and neck gene-signatures displaying a significant enrichment in the genes composing the 15-gene signature that distinguishes between SC and SNC. Analysis was carried out using the GeneSigDB interface: Results of the enrichment test were filtered based on the corrected P-value (<0.05), gene overlap >1 (number of genes shared by each signature and the signature identified in this study) and relevance to lung and head and neck. The size of each gene-signature is indicated, as well as the gene overlap. Note that the numbers in the gene-signature column refer to the PubMed index of each reference. (**B**). Heatmap representation of the presence (red square) or absence (grey square) of each gene composing the signature identified in this study, within the 18 gene-signatures identified in (A). See text for discussion.

References:

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