Supplementary Figure Legends and Figures

Supplementary Figure S1. Similarity of metastatic signatures reported for HNSCC. The HNSCC metastatic signature generated in this paper, derived by direct comparison of primary tumors with matching metastases, was compared with metastatic signatures from six other publications, five of which are derived from supervised analyses of primary tumors and one of which is a supervised comparison of immortal vs. mortal HNSCCs.[1-6] Gene lists were compared using Ingenuity Pathway Analysis (Ingenuity® Systems, www.ingenuity.com). While individual genes were only infrequently identified in multiple studies (Supplementary Figure S2), the agreement in over-representation of genes involved in the same higher-order cellular functions (e.g., cell cycle, cell-to-cell signaling and interaction) was very good, as indicated by similarly significant *p*-values. The *p*-values are plotted as a bar graph for the individual higher-order functions labeled on the x-axis. The higher-order functions shown here are the ones with the highest *p*-values and the most relevance to processes involved in HNSCC formation and progression.

Supplementary Figure S2. Genes shared in common between HNSCC metastatic signatures from different studies. Metastatic signatures from six studies[1-6] were compared with ours after gene names were standardized using Entrez Gene and UCSC Genome Database. Fifty-five genes are shown that are shared between at least two metastatic signatures (genes highlighted in red are shared between three signatures). Up or down arrows indicate the direction of the change in gene expression in the metastatic signature. Genes regulated in opposite directions in two or three studies are labeled discordant (disc.) and shown in the bottom rows of the table. Numbers at the bottom of each column tally the total number of shared genes in each metastatic signature followed by the total number of genes with standardized names that were compared. The resulting percentage is the fraction of genes in each signature that is shared with at least one other study.

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