

**Supplementary Figure 1. Validation of the gene expression signature for anchorage-independent cell growth ability of cultured breast cancer cells.**

A. Self-consistence of the anchorage independence signature. We tested whether the anchorage-independence genes would generate signatures that were more self-consistent than sets of random genes. Left: The receiver-operating characteristic (ROC) curve analysis of the predicted probability of the training samples used to generate the anchorage independence (AI) signature. We plot, in red, the ROC of the ability of the 200 genes in the AI signature to partition the anchorage independent cell lines from the dependent ones. As shown, the signature is able to distinguish the samples perfectly. As a comparison, we also plot, in dashed black, the ability of 10,000 randomly selected sets of 200 genes to partition the same cell lines. Right: Histogram of the area under the curve (AUC). We compare the area under the curve (AUC) of the genes in the AI signature from the 10,000 random gene sets. The AUC of the AI signature is 1.00, greater than the AUC of the random gene sets, leading to a  $p$ -value of  $< 0.0005$ .

B. Prediction of anchorage-independent cell growth ability for breast cancer cells with intermediate capacity of colony formation. The gene signature generated in Figure 2 is applied to predict the status of breast cancer cells with an intermediate phenotype in anchorage-independent growth (20-200 colonies; HCC1143, HCC1806, HCC1428, MDA-MB-453, CAMA1, BT549 and MDA-MB-157). Using half the training samples, we predicted the status of the remaining half of the cell lines. The predicted probabilities of anchorage-independent growth ability are plotted and compared among breast cancer cells with anchorage-dependent (AD<20 colonies), an intermediate phenotype (20-200 colonies) and anchorage-independent (AI>500 colonies) growth ability by Mann-Whitney U test using GraphPad's Prism. A bar indicates the mean value for each group.

**Supplementary Figure 2. Validation of the gene expression signature for anchorage-independent cell growth in cultured ovarian cancer cells.**

A. A gene signature for anchorage-independent growth of ovarian cancer cells. Left panel; the expression pattern of genes that distinguish anchorage-independent cells (AI>500 colonies) from anchorage-dependent cells (AD<20 colonies). The expression levels for six hundred genes are shown as a heatmap (red=high and blue=low expression). Right panel; a leave-one-out cross validation of probabilities for anchorage-independent growth ability (blue=anchorage-dependent cells, red=anchorage-independent cells). The accuracy of this signature was 88.1% when we use 0.5 as a cut-off probability. B. Using half the training samples, we predicted the status of the remaining half of the cell lines. The predicted probabilities of anchorage-independent growth ability are plotted and compared between AD and AI ovarian cancer cells by Mann-Whitney U test using GraphPad's Prism. A bar indicates the mean value for each group. Both halves of the samples provided statistically significant predictive abilities.

**Supplementary Figure 3. Detection of anchorage-independent cell growth signature in *c-Myc* or *v-Src* transformed mouse embryonic fibroblasts (MEFs).**

A. Morphological appearance of transformed MEF colonies grown in methylcellulose three weeks after plating of 20,000 cells. Photographs of colonies of MEFs transformed by empty, *c-myc* or *v-src* retroviral vector (WA cells for representation) are shown. Expression of *c-Myc* or *v-Src* is equally efficient in transforming MEFs to an anchorage-independent state.

B. Prediction of anchorage-independent growth ability of transformed MEFs by the gene signature derived from human breast cancer cells. The predicted probabilities are plotted and statistically evaluated using Mann-Whitney U test using GraphPad's Prism. A bar indicates the mean value for each group.

**Supplementary Figure 4. Supervised analysis to generate a signature of mitochondrial biogenesis by overexpression of peroxisome proliferator-activated receptor-gamma co-activator 1  $\alpha$  (PGC1 $\alpha$ ).** Right panel; gene expression pattern of the PGC1 $\alpha$  signature. The

expression pattern of the top 240 genes is shown as a heatmap (red=increased and blue=decreased expression); red indicates genes predicted to localize to mitochondria. Left panel; leave-one-out cross validation of the signature. Blue and red colors indicate control and PGC1 $\alpha$  overexpression, respectively.

**Supplementary Table1. List of top 200 genes in the signature of anchorage-independent growth ability.**

**Supplementary Table 2. Gene ontology analysis for the genes in the anchorage-independent growth signature.** The significance is shown as a Bayes factor and a *p* value.

**Supplementary Table 3. Spearman correlation analysis of MYC pathway with metabolic, mitochondrial and ribosomal pathway.** The predicted probability of MYC pathway status of 19 breast cancer cells is analyzed with average ranks of metabolic, mitochondrial, ribosomal gene expression or the predicted probabilities of PGC1 $\alpha$  by Spearman correlation.