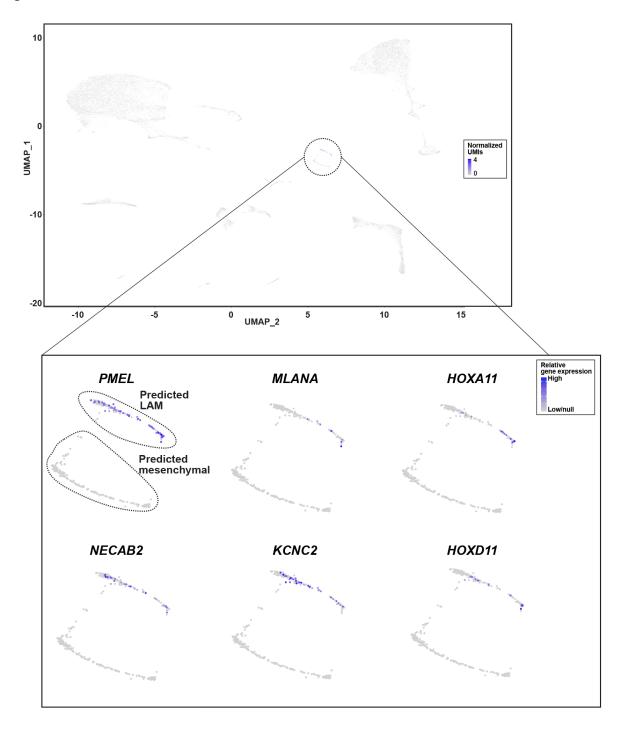
## **Supplementary Figures**

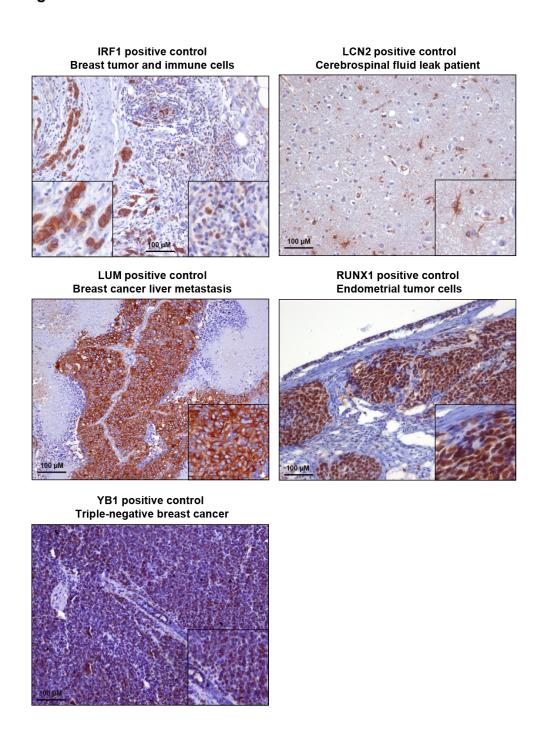
**Figure S1**. Top panel, UMAP projection of LAM lung tissue scRNA-seq data (6). Bottom panels, zoom-in image of the LAM and lung mesenchymal cell cluster, and expression of defined LAM cell markers (6).

Figure S1

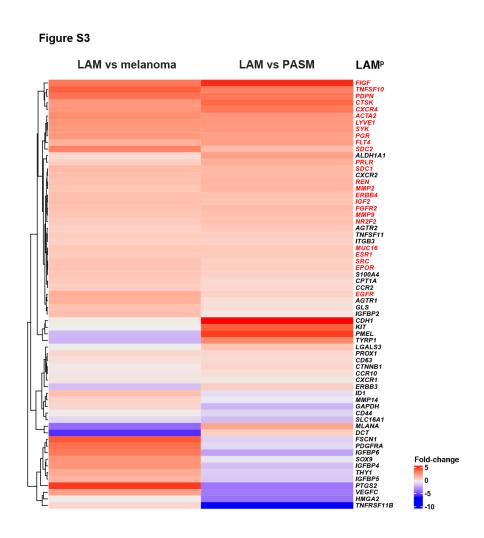


**Figure S2**. Positive controls of immunohistochemical assays. IRF1, cytoplasmic expression in breast cancer cells and nuclear expression in immune cells; LCN2, cytoplasmic expression in astrocytes of a brain of a patient diagnosed with cerebrospinal fluid leak; LUM, cytoplasmic expression in metastatic breast cancer cells in liver; RUNX1, nuclear expression in endometrial cancer cells; and YB1 nuclear and cytoplasmic expression in triple-negative breast cancer.

Figure S2



**Figure S3**. Unsupervised hierarchical clustering of expression differences (fold change) of LAMP genes between LAM lung nodules and melanoma (Malme-3M) or pulmonary arterial smooth muscle (PASM) cells. Data from the GEO GSE12027 study (28). The genes marked in red were found to be significantly (Kruskal–Wallis test P < 0.05) overexpressed in LAM lung nodules relative to both cell lines.



**Figure S4**. LAM<sup>core</sup> correlation with ER-target and PR/ER-target signatures in LAM cells with low (left panel) and high (right panel) LAM<sup>core</sup> scores. The  $r_s$  are indicated; n.s., not significant.

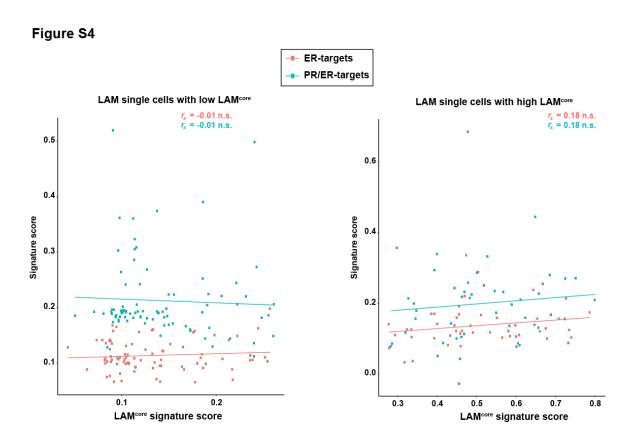
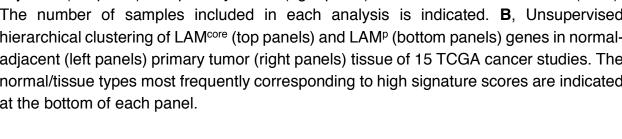
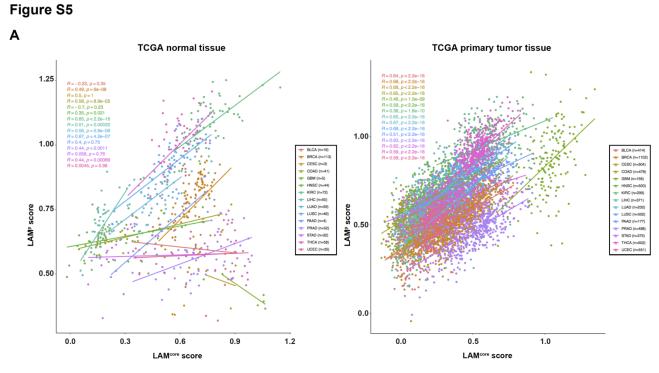
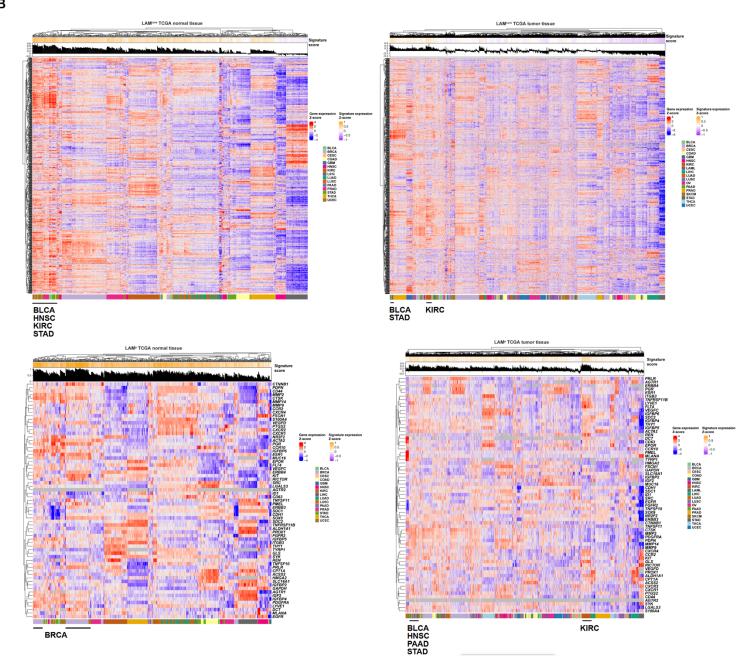


Figure S5. A, LAMP-LAMcore score correlations (rs and P value are indicated) in normaladjacent (left panel) and primary tissue (right panel) of 15 TCGA cancer studies (inset). The number of samples included in each analysis is indicated. B, Unsupervised hierarchical clustering of LAMcore (top panels) and LAMp (bottom panels) genes in normaladjacent (left panels) primary tumor (right panels) tissue of 15 TCGA cancer studies. The normal/tissue types most frequently corresponding to high signature scores are indicated at the bottom of each panel.







**Figure S6**. Graphs showing the *IRF1* (left) and *RUNX1* (right) loci (genome hg19, other genes in these regions are not depicted) association results (-log10 P value, Y-axis) with spirometry measures (FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC, and PEF). The data corresponds to the summary statistics of the genome-wide association study of the UK Biobank and SpiroMeta consortium.

