**Supplementary materials: Details of methods**

*Immune abundance quantification of samples in Pan-MET dataset*

Total immune score and tumor purity were calculated using R package ESTIMATE [1]. Abundance of each immune cell population were calculated by R package GSVA [2] based on two sets of immune gene signatures, Davoli signatures [3] and Tamborero signatures [4]. We also applied two deconvolution methods, CIBERSORT [5] and TIMER [6]. All four methods were tested on a single cell RNA-seq dataset of 11 breast cancer tumors [7].

*M2-like macrophages quantification of normal tissues*

RNA-seq data (TPM) from normal brain, breast, ovary and small intestine tissues were downloaded from The Genotype-Tissue Expression (GTEx) Project. We randomly selected 100 samples from each tissue and calculated the percentages of M2-like macrophages using CIBERSORT.

*Differential expression (DE) test and pathway enrichment analysis*

DE genes in ER+ BRMs versus PBTs were tested using R package DESeq2 [8]. Significantly up- or down-regulated genes were further used for pathway enrichment analyses. We obtained 2531 pathways, contributed by BioCarta, GO, KEGG, Reactome, containing 5–2000 genes, from Molecular Signature Database (MSigDB Version 5.1. Broad Institute, Cambridge, MA, USA). Fisher’s exact test was performed with false discovery rate (FDR) 0.05 as cutoff.

*Multiplex staining experiment of selective pairs in Pan-MET dataset*

FFPE tissue sections (5micron) were mounted on slides and deparaffinized. Briefly, tissues were subjected to cycles of antigen retrieval, blocking, primary antibody followed by secondary-HRP antibody. Separate Opal detection and signal amplification antibodies were used for each marker. The panel of markers used included CD8, CD20, CD68, Foxp3, PD-L1, pan-CK and DAPI. Imaging, analysis and quantification was performed using the Perkin Elmer Vectra platform and Inform software [9]. The list of antibodies with catalog numbers and dilutions used provided in supplementary Table S8.

*Evaluation of stromal tumor infiltrating lymphocytes (sTILs) in BRM-sTIL dataset samples.*

H&E stained sections were manually counted for percent sTILs using standard criteria developed by the international TILs working group [10]. sTILs were rounded to the nearest 5% increment. Only the stromal compartment within the borders of invasive tumor was evaluated. TILs in zones of necrosis, crushed artifacts, or normal tissue were excluded. Only mononuclear infiltrate was counted. Full tumor sections were preferentially examined over needle biopsies whenever possible; core biopsies were analyzed when full sections were unavailable. Each slide was independently reviewed by two study personnel (JLN and CL) to minimize inter-observer variability. When the sTILs differed by 10% or more, the study pathologist (AH) made the final determination. If multiple BRMs or PBTs were available for the same patient, average sTILs percentage was used for all comparisons.

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