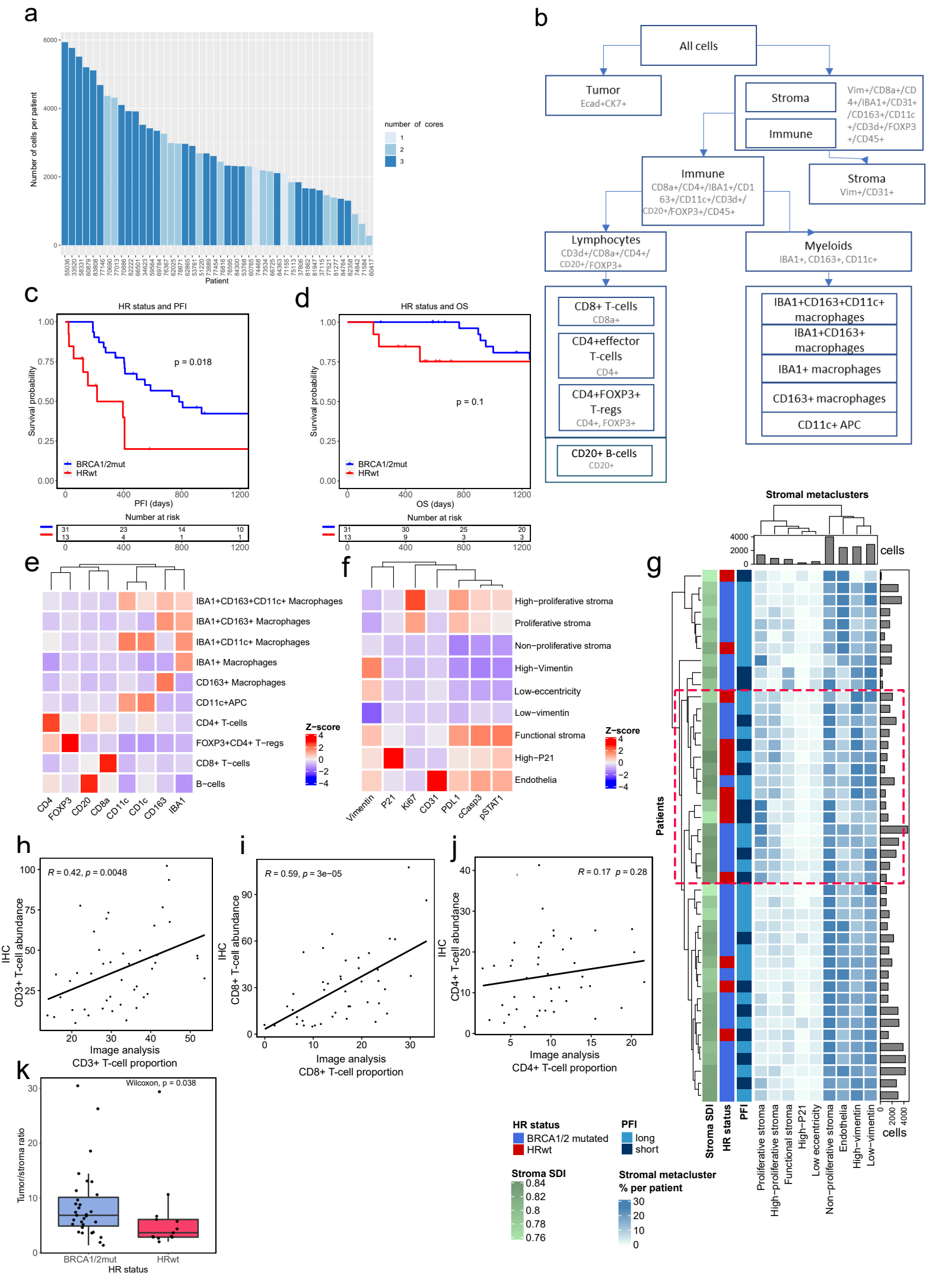
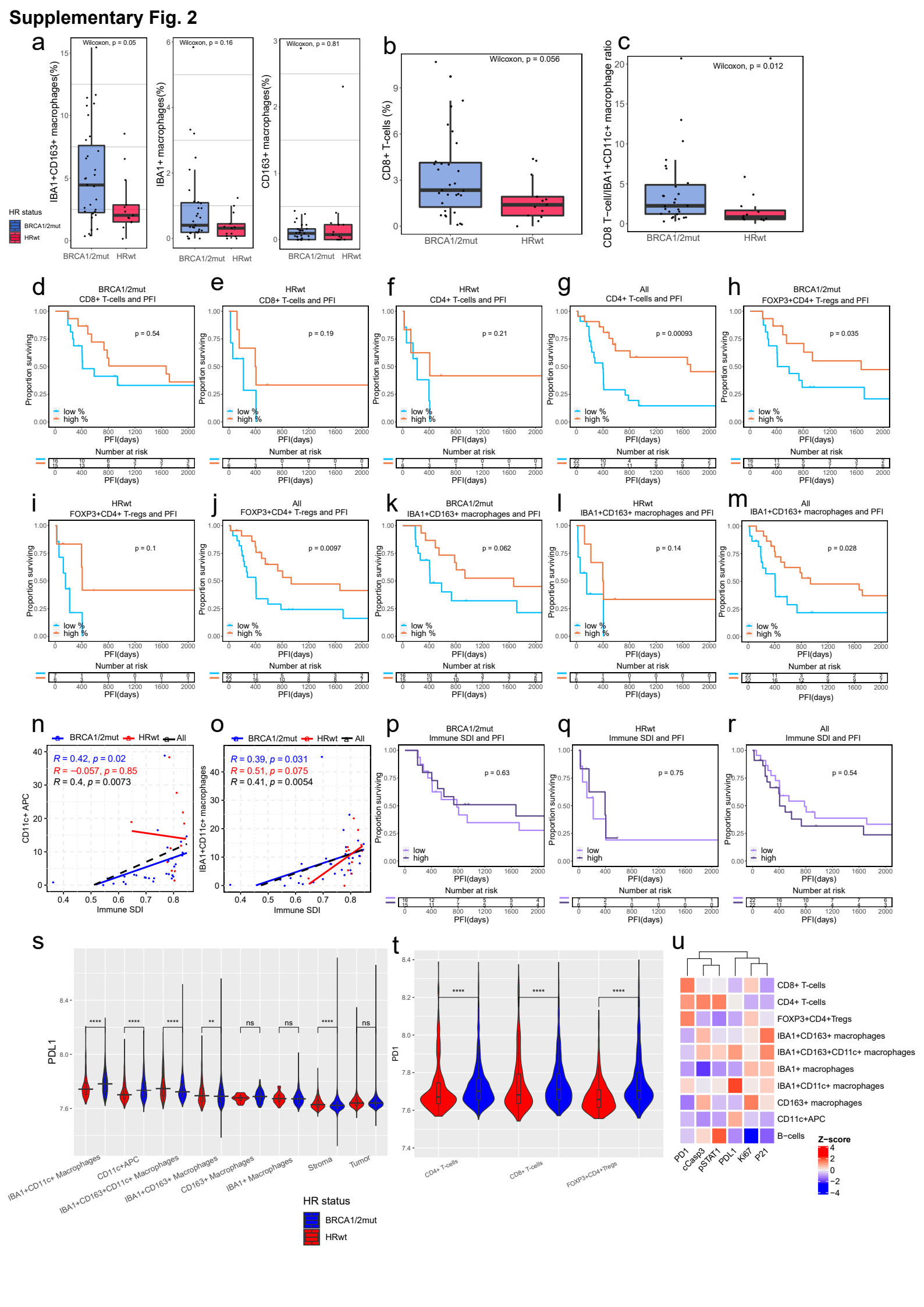
Supplementary Fig. 1



Supplementary Fig 1. Single-cell cell type annotations show distinct marker expression profiles and correlate with conventional pathological scoring

a Barplot of the number of TMA cores and single cells by patient. The color of the bars represents the number of cores per patient. **b** Using sequential annotation, we first identified tumor, immune and stromal cells, after which we annotated the immune cell subpopulations. Markers used for annotation are shown in the flowchart. **c** Kaplan-Meier graph for PFI and **d** for OS grouped by the HR status. Number of patients at risk is shown at the bottom of each Kaplan-Meier graph. P-values were calculated by the log-rank test. **e** Heatmap of the Z-score of marker expressions across the annotated immune subtypes shows distinct expression profiles of the cell type markers and **f** a heatmap across the annotated stromal metaclusters shows distinct expression profiles of the cell type and functional state markers. Hierarchical clustering was performed for the columns. **g** A hierarchical clustering heatmap of stromal metacluster proportions out of all stromal cells, annotated with stromal diversity (stromal SDI), and clinical data including HR status and PFI. The barplot annotations for the columns and rows represent the total number of cells of each stromal metacluster and the number of stromal cells in total per patient, respectively. **h** Linear correlation of imaging-based CD3+ lymphocyte annotations (CD8+T-cells, CD4+T-cells and FOXP3+CD4+T-regulatory cells) and pathological score of the count of lymphocytes from conventional immunohistochemistry (IHC). **i** Linear correlations of imaging-based CD8+T-cell annotations and **j** of CD4+T-cell annotations and pathological scores from conventional immunohistochemistry. The imaging-based annotations were calculated as a proportion out of immune cells. All counts from conventional immunohistochemistry were performed from selected fields enriched for CD3+ immune cells. Spearman correlation coefficients and p-values are shown. **k** Boxplot showing an increased ratio of tumor to stromal cells in *BRCA1/2*mut as compared to HRwt tumors. The difference between the groups was calculated by Wilcoxon signed-rank test. Boxplot visualizes sample medians, first to third quartiles and whiskers indicate values at 1.5 times the interquartile range**.** Individual dots represent values per tumor.

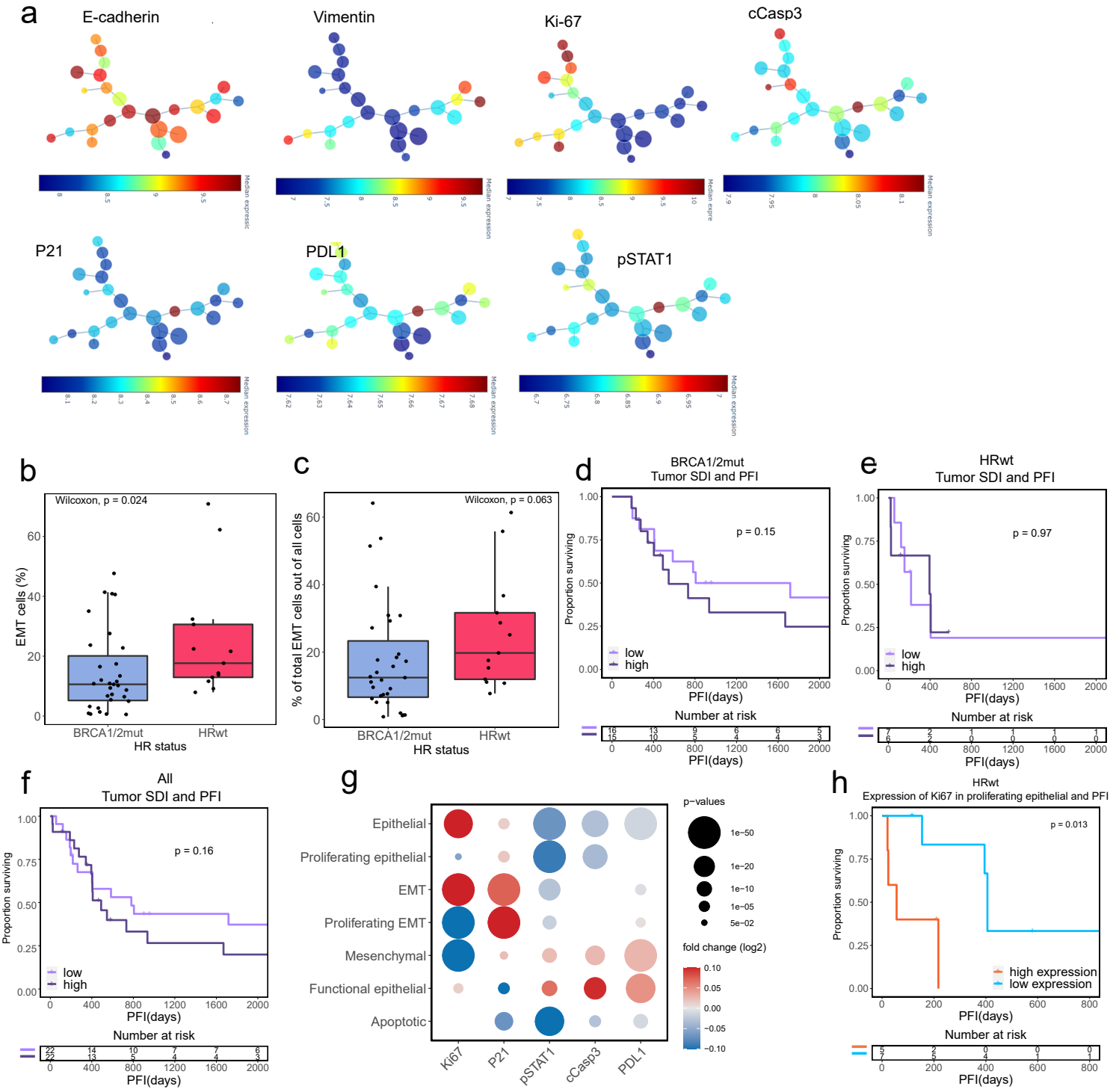
Supplementary Fig. 2



Supplementary Fig. 2 Various immune cell subpopulations associate with PFI and immune diversity

a Boxplots showing the proportions of IBA1+CD163+, IBA1+ and CD163+ macrophages as well as **b** the proportion of CD8+T-cells as a proportion of all cells, stratified by HR status and **c** boxplot showing the ratio of CD8+T-cells to IBA1+CD11c+ macrophages as a proportion of immune cells, stratified by HR status. The difference between the groups was calculated by Wilcoxon signed-rank test. Boxplots visualize sample medians, first to third quartile and whiskers indicate values at 1.5 times the interquartile range**.** Individual dots represent values per tumor. **d** Kaplan-Meier graphs for PFI for the proportion of CD8+T-cells out of all cells in patients with *BRCA1/2*mut tumors and **e** in patients with HRwt tumors. **f** Kaplan-Meier graphs for PFI for the proportion of CD4+T-cells in all patients and **g** in patients with HRwt tumors. **h** Kaplan Meier graph for PFI for FOXP3+CD4+T-regulatory cells in all patients and **i** in patients with *BRCA1/2*mut tumors as well as **j** in patients with HRwt tumors. **k** Kaplan Meier graphs for PFI for IBA1+CD163+ macrophages in all patients and **l** in patients with *BRCA1/2*mut tumors as well as **m** in patients with HRwt tumors. **n** Linear correlation of immune diversity (immune SDI) and the proportion of CD11c+ APCs out of all immune cells as well as **o** the proportion of IBA1+CD11c+ macrophages out of immune cells, stratified by HR status. Blue line represents *BRCA1/2*mut tumors, red line HRwt tumors and black dashed line all tumors pooled. Spearman correlation coefficients and their p-values are shown. **p** Kaplan-Meier graph for PFI for immune diversity in all patients, **q** in patients with *BRCA1/2*mut tumors as well as **r** in patients with HRwt tumors. The median was used as cutoff for the proportions of immune cells and immune diversity. Number of patients at risk is shown at the bottom of each Kaplan-Meier graph. P-values were calculated using the log-rank test. **s** Violin plots showing the probability density of macrophage - and antigen presenting cell subtypes, tumor, and stromal cells and their PDL1 expression and **t** CD4+T-cells, CD8+T-cells, and FOXP3+CD4+T-regulatory cells and their PD1 expression, stratified by HR status. Boxplots inside violin plots show the sample medians, and the first and third quartiles. P-values: <0.05 = *, < 0.005 = **, <0.0005 = ***, <0.00005 = ****. **u** Heatmap of the Z-score of functional marker expressions across the annotated immune subtypes. Hierarchical clustering was performed for the columns.

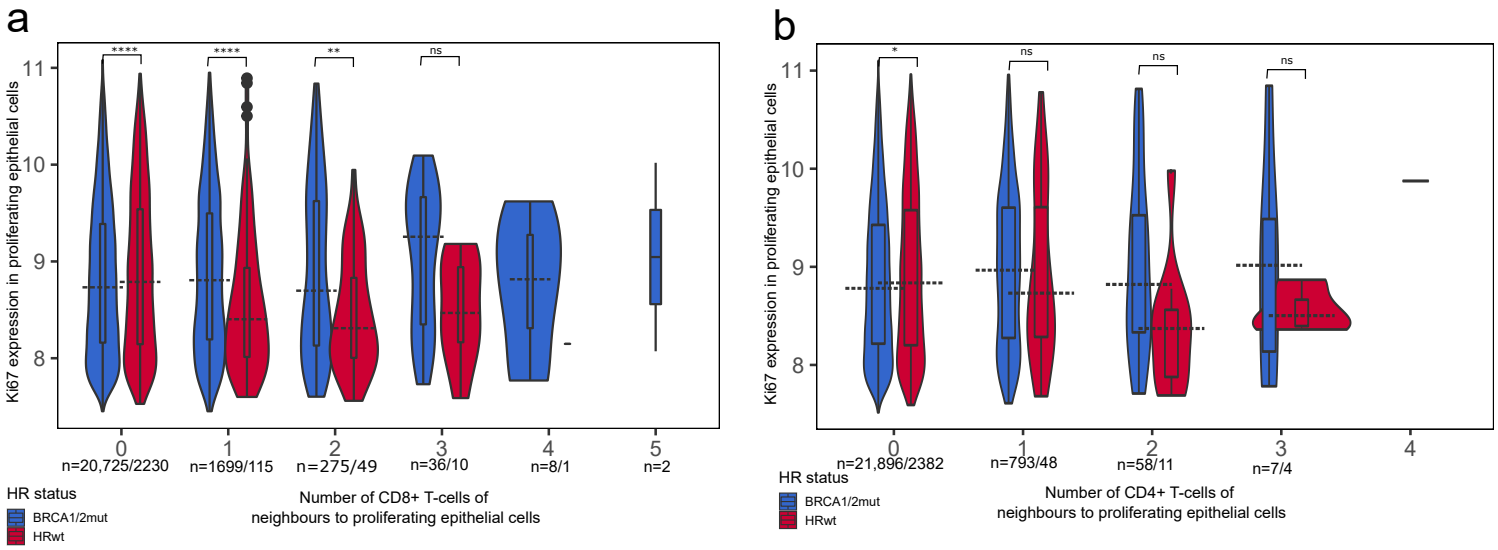
Supplementary Fig. 3



Supplementary Fig. 3 Tumor cell metaclusters show distinct marker expression profiles and associations to the HR-genotypes

a Minimum spanning trees of tumor cell clusters, showing differential median marker expression patterns in the tumor clusters. **b** Boxplot showing the proportion of EMT cells as a proportion of all cells and **c** the total proportion of EMT cells and proliferating EMT cells as a proportion of all cells, stratified by HR status. The difference between the groups was calculated by Wilcoxon signed-rank test. The black horizontal lines represent the sample medians, the boxes extend from first to third quartile and whiskers indicate the values at 1.5 times the interquartile range**.** Individual dots represent values per each tumor. **d** Kaplan-Meier graphs show no association for PFI for tumor diversity index in patients with *BRCA1/2*mut tumors, **e** with HRwt tumors or **f** in all patients. **g** Dot plot of fold changes (log2) of functional marker expression between tumor metaclusters in *BRCA1/2*mut and HRwt tumors. The color of the dots represent the fold change and their size the significance of the p-value. Fold changes with p-values <0.05 are shown. **h** Kaplan-Meier graph showing low median Ki67 expression associates with an improved PFI in patients with HRwt tumors. Number of patients at risk is shown at the bottom of each Kaplan-Meier graph. P-values were calculated using the log-rank test. Median values were used as a cut-off for high and low tumor diversity.

Supplementary Fig. 4



Supplementary Fig. 4 Ki67 expression in proliferating epithelial cells varies according to cellular neighborhoods

a Violin plots showing the probability density of proliferating epithelial cells and their Ki67 expression, stratified by HR status and the number of CD8+T-cells in the neighborhood and **b** showing the probability density of proliferating epithelial cells and their Ki67 expression, stratified by HR status and the number of CD4+T-cells in the neighborhood.

Supplementary table 1. Antibodies used in t-Cycif protocol

Antibody	Fluorochrome	Company	Cat number	Purpose
Rabbit 488	488	Thermo Fisher	A11034	Background
Rat 555	555	Thermo Fisher	A-21432	Background
Mouse 647	647	Thermo Fisher	A32728	Background
CD11c	Rabbit	CST	45581S	Dendritic cells
CD1c	Mouse	abcam	ab156708	Dendritic cells
CD4	488	R&D	fab8165g	T-cells
CD3d	555	Abcam	ab208514	T-cells
CD20	647	eBioscience	50-0202-80	B-cells
CD163	488	Abcam	ab218293	M2 macrophages
CD8a	eFluor 660	eBioscience	50-0008-80	T-cells
cCasp3	488	CST	9969S	Apoptosis
pSTAT1	555	CST	8183S	Interferon signalling
Ki67	555	eBioscience	41-5699-80	Proliferation
PD-L1	647	CST	CST 15005S	ICP
IBA1	488	Abcam	ab195031	Macrophages/myeloid cells
FOXP3	555	EbioSciences	41-477782	T-regulatory cells
PD1	647	Abcam	ab201825	ICP
E-cadherin	488	CST	3199	Tumor cells
Vimentin	555	CST	9855	Stroma
CD31	647	Abcam	218582	Stroma and endothelia
P21	488	CST	5487	Cell cycle
CK7	555	Abcam	ab209601	Tumor cells
CD45	647	Biolegend	304020	Immune cells

Supplementary table 2. Multivariate Cox regression analysis for immune cell subtypes

	Variable	HR	95% CI	Z-score	p-value
All patients	CD4+T-cells	0.419	0.181 - 0.973	-2.02	0.043*
	CD8+T-cells	0.675	0.302 - 1.151	-0.957	0.339
	FOXP3+CD4+ T-regulatory cells	0.676	0.293 - 1.56	-0.919	0.358
	IBA1+CD163+ macrophages	0.693	0.299 - 1.60	-0.857	0.391
Patients with *BRCA1/2*mut tumors	CD4+T-cells	0.316	0.114-0.877	-2.213	0.027*
	FOXP3+CD4+ T-regulatory cells	0.667	0.250-1.78	-0.809	0.418