

Supplementary figures' legends

Figure S1: Characteristics of NLS subtypes. NLSs were classified according to their type as described in the Methods. The number of NLSs of different subtype with the indicated characteristics are shown.

Figure S2: Heatmap representing the level of motif inclusion for alternative NLSs. The GSE45419 RNA-seq datasets consisting of benign breast lesions, ER positive, triple negative and HER2 positive primary breast tumors (32 samples in total) were analyzed to quantify the NLS MII in each tissue considered. MII values are represented using the color scheme depicted in the legend. Genes which were detected below a threshold of 1 TPM were not further considered and are represented by grey cells in the heatmap. Only motifs present in at least 17 of the 32 samples are shown. The sample type is indicated using a color-coded bar at the top of the heatmap. While some NLSs display generally uniform MII values across the samples regardless of type, a subset show specificity for a certain sample type. In particular, the benign breast lesions cluster together and display different MII values for some NLSs, suggesting a differential regulation of the presence of the NLS in these samples.

Figure S3: Heatmap representing the level of motif inclusion for alternative NESs. As for figure S2, the GSE45419 RNA-seq datasets were analyzed to quantify the NES MII in each tissue considered. The heatmap is as described for figure S2. Motifs of same type present in the same gene and displaying the exact same MII profile across all tissues were collapsed into one entry (for example, CDC7 has two annotated NESs with the same MII profile across all tissues. These motifs were collapsed into one entry labelled CDC7(1;2)).

Additional Table 1: Regulation analysis of subclasses of NLSs

	Monopartite	Bipartite	PY-NLS	Non-classified
Total	45	30	24	76
Constitutive motifs	16	12	8	32
Alternative motifs	29	18	16	44
Encoded in 1 exon	39	23	15	51
Encoded in 2 exons	6	7	9	22
Encoded in 3 exons	0	0	0	3
Regulated by splicing	6	3	6	12
Regulated by alternative 5'	21	8	6	24
Regulated by alternative 3'	15	12	7	32
Regulated by frameshift	1	0	1	0

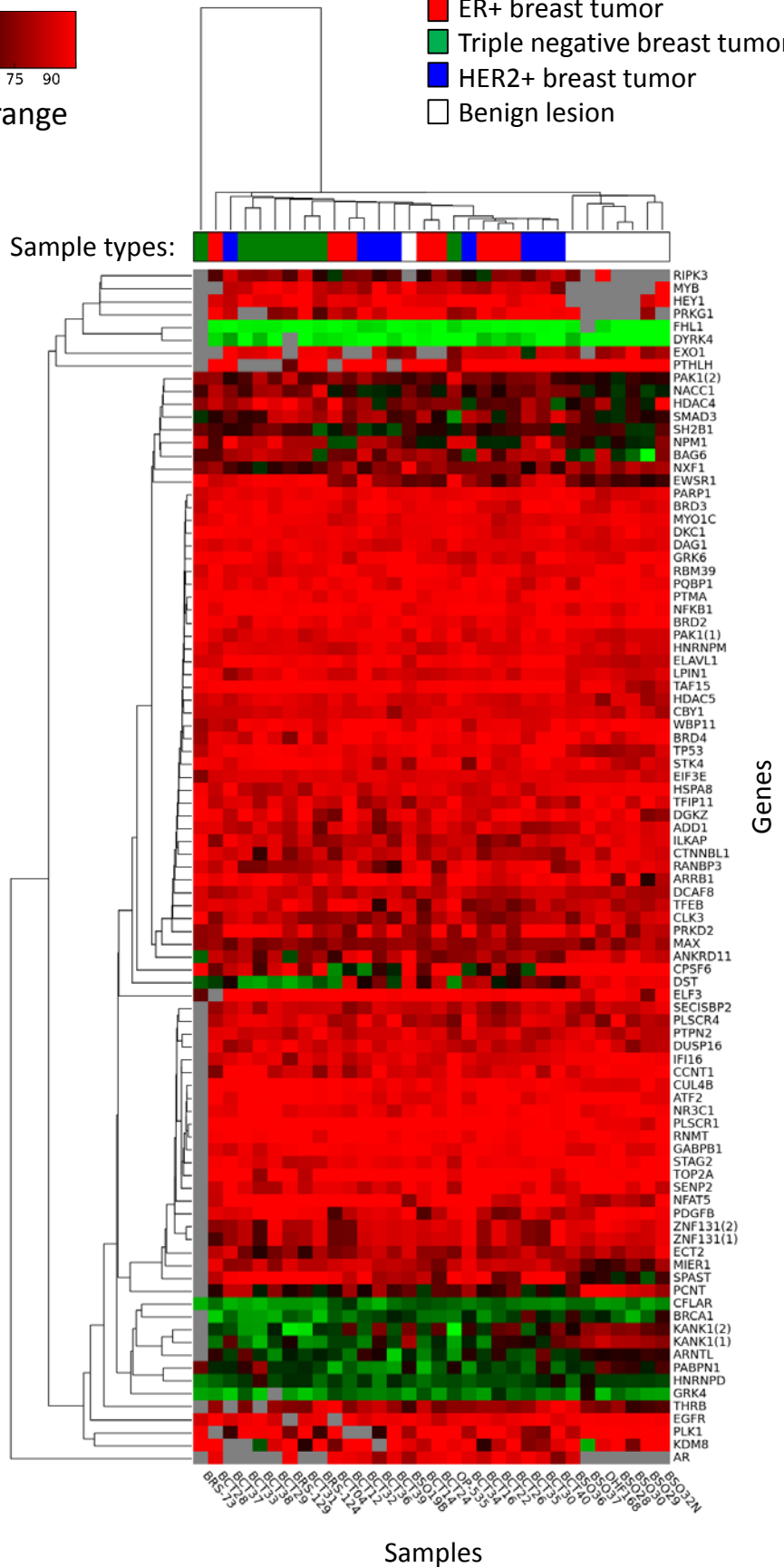
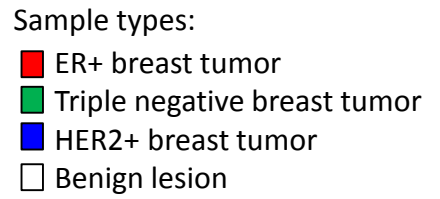
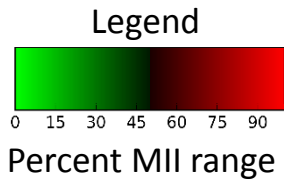
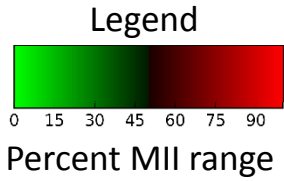


Figure S2



Sample types:

- ER+ breast tumor
- Triple negative breast tumor
- HER2+ breast tumor
- Benign lesion

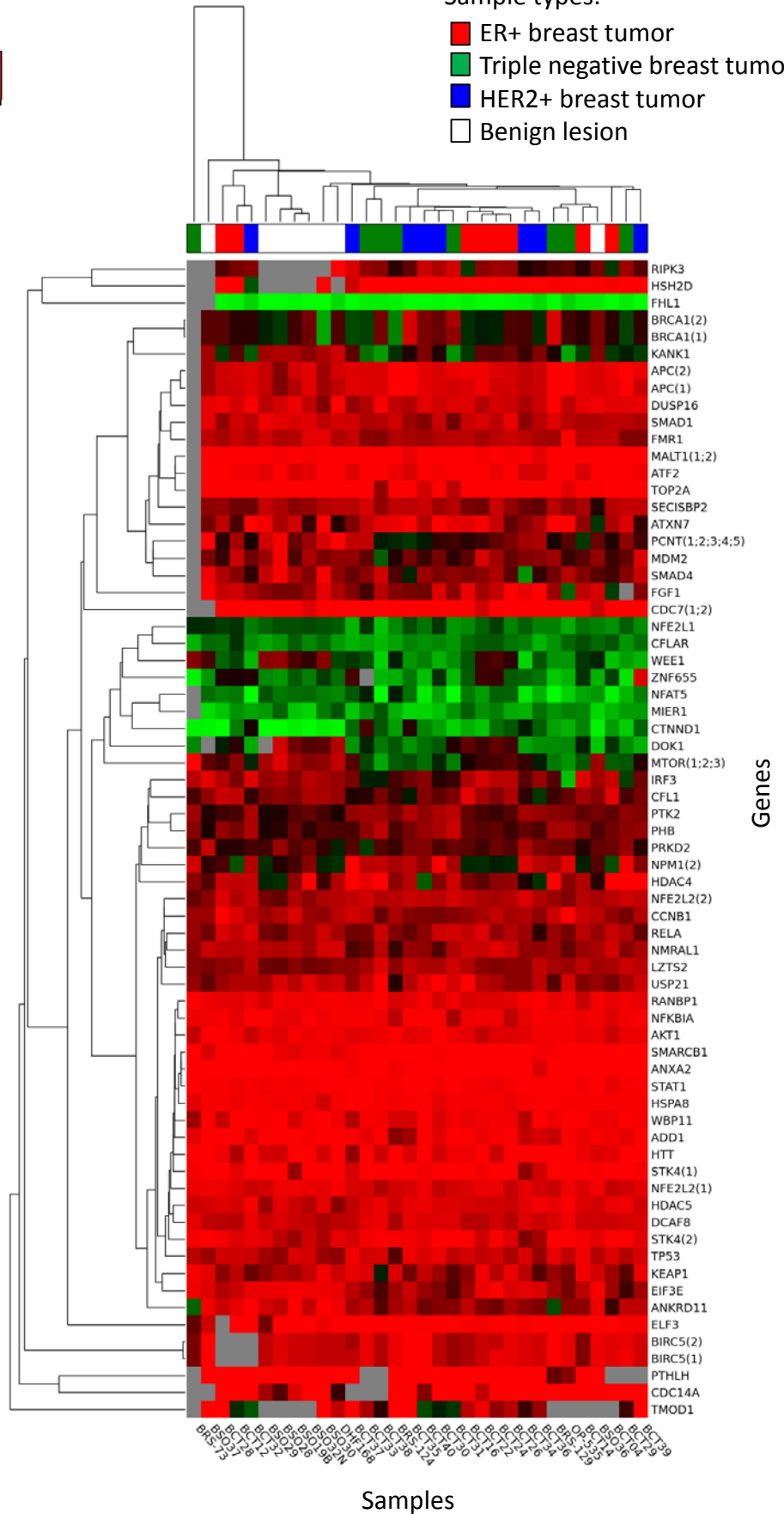


Figure S3