**Supplementary Methods.**

**Immune Cell Composition of Human Tumors** – The percentage of tumor infiltrating lymphocytes (TILs) was determined by a pathologist using H&E tumor sections according to the 2014 guidelines by the International Working Group for TILs in breast cancer (1). Multiplex immune fluorescence was performed on tumor material of a selection of patients (n=15), selected on the basis of having the largest difference in TIL before and after Tamoxifen treatment. Staining and imaging was performed as described before (2) and analyzed with Halo Highplex software.

**Supplementary Figure Legends**

**Supplementary Figure 1.** Tamoxifen treatment induces expression of NFκB-related genes. Boxplots representing a selection of genes from the GSEA geneset “TNFα signaling via NFκB” that were found significantly differentially expressed (FC<-1/FC>1 and adj.P.Val < 0.005) between tamoxifen treated and pre-treatment patient material. All genes included have been reported to be targets of NFκB (3-10).

**Supplementary Figure 2.** Immune cell composition and numbers in the tumor microenvironment do not significantly change upon tamoxifen treatment. A. The percentage of tumor infiltrating lymphocytes (TILs) as determined by pathologist using H&E tumor sections before (pre) (n=64) and after tamoxifen treatment (Tam) (n=39). A one-sided, two-sample T-test was used to test for significance. B. Multiplex immunofluorescence was performed for immune cell subsets expressing CD4, CD8 and CD68 on paired tumor material (n=13) from the same patient before (pre) and after Tamoxifen treatment (Tam). One-sided, paired T-tests were used to test for significance.

**Supplementary Figure 3**. NFκB pathway and EMT/stemness factors in tamoxifen-tolerant persisters in T47D cells. **A,** T47D cells were seeded in clonogenic density and treated in estrogenized growth media (GM) -/+ 1µM 4OHT for 2 weeks. NFκB-target genes were measured by RT-QPCR. **B**, DMF 20µM and IKK7 1µM were added to T47D cells treated as described above. Colonies were fixed and stained with crystal violet, and representative pictures are shown. **C**, Nuclear proteins were examined by Western Blotting. TBP served as a loading control. **D**, Expression of stem and EMT factors was measured by RT-QPCR in T47D clonogenic cells treated with GM-/+ 1µM 4OHT for 2 weeks. \**P*<0.01, \*\**P*<0.005, \*\*\**P*<0.001.

**Supplementary Figure 4.** Expression of p65 and p50 proteins in MCF-7 CRISPR/Cas9 knock out clones. Western blot analysis for p65 and p50 was performed. β-actin served as a loading control.

**Supplementary Figure 5.** NFκB pathway is not directly activated by tamoxifen. **A**, MCF-7 cells were treated with 1µM 4OHT for 24 hrs in clonogenic conditions and ER-target genes (PR, pS2, SDF-1) or NFκB-target genes (ICAM1, TNF, CCL2, and PHLDA1) were measured by RT-QPCR. **B**, MCF-7-κB-RE-GFP reporter cells were treated with 1µM 4OHT for 2, 4, 8, 24, and 48 hrs. TNFα (10 ng/ml) for 4 hrs was used as a positive control. GFP (left panel) and ICAM1 (right panel) levels were measured by RT-QPCR. \**P*<0.01, \*\**P*<0.005, \*\*\**P*<0.001. *NS*, not significant.

**Supplementary Figure 6**. Sorted NFκB+ vs NFκB− or unsorted tamoxifen-tolerant cells based on GFP expression were reseeded for another round of clonogenic assay and the %GFP+ population was quantified in the second round. \*\*P<0.005, \*\*\*P<0.001.

**Supplementary References**

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