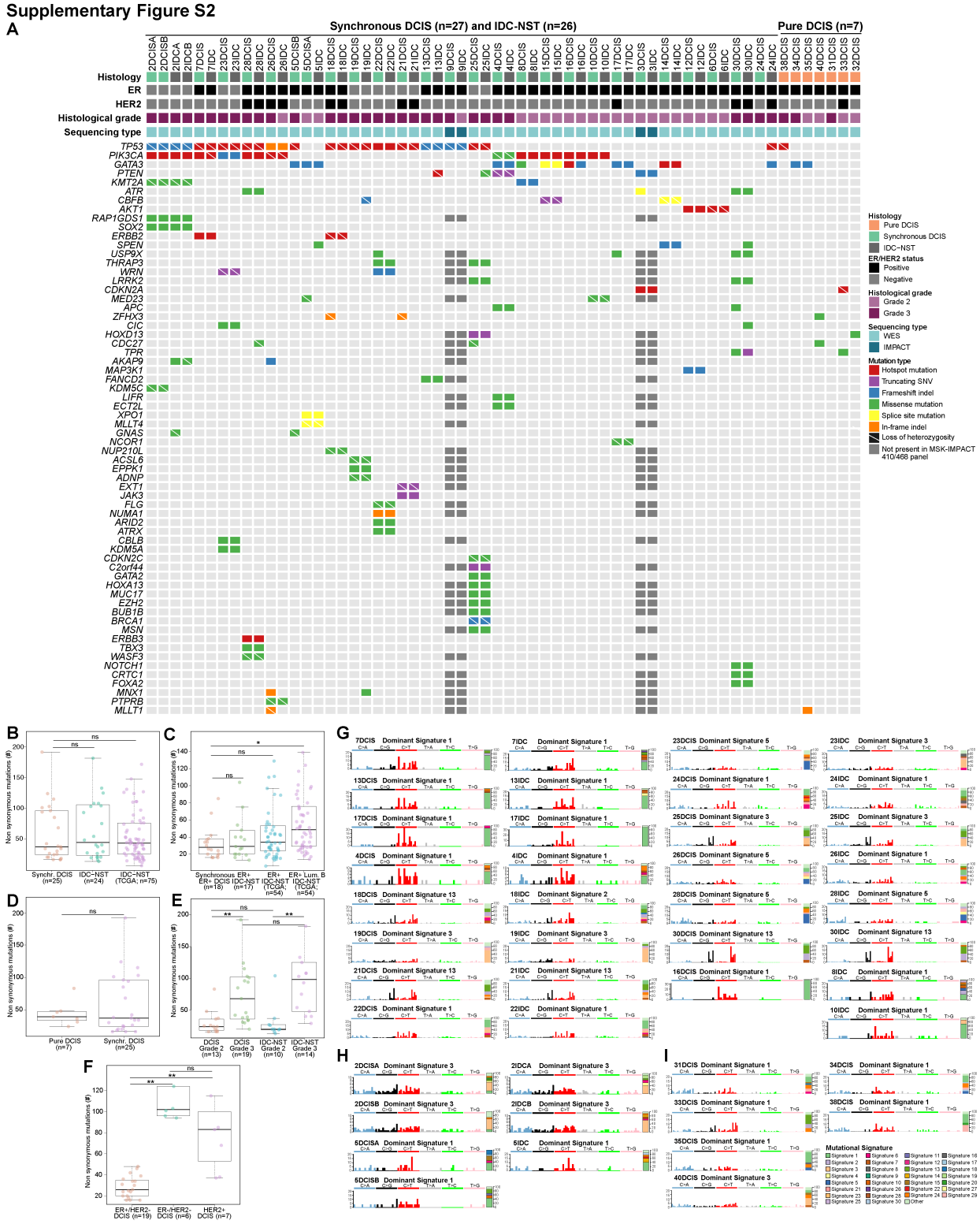

Supplementary Figure S2. Repertoire and number of non-synonymous somatic mutations and mutational signatures in synchronously diagnosed ductal carcinoma *in situ* and invasive ductal carcinoma of no special type and in pure ductal carcinoma in *situ*.

(**A**) Heatmap depicting recurrent non-synonymous somatic mutations affecting cancer genes identified in synchronously identified ductal carcinoma *in situ* (DCIS; n=27) and IDC-NSTs (n=26) and in pure

DCIS (n=7) subjected to WES or targeted sequencing using MSK-IMPACT. Cases are shown in columns and genes in rows. Clinicopathologic characteristics are shown in the phenotype bars (top). Mutations are color-coded according to the legend, and loss of heterozygosity is represented by a diagonal bar. (**B-F**) Boxplots depicting the number of non-synonymous mutations (**B**) in synchronous DCIS (n=25) and invasive ductal carcinoma of no special type from this study (IDC-NST; n=24) identified by whole-exome sequencing (WES) and in IDC-NSTs from The Cancer Genome Atlas (TCGA) matched to DCIS from this study according to age, menopausal status and estrogen receptor (ER) and HER2 status at a 3:1 ratio (n=75), (**C**) in synchronous ER-positive DCIS from this study (n=18) and ER-positive IDC-NST from this study (n=17) identified by WES, and ER-positive IDC-NST (n=54) and ER-positive luminal B IDC-NST (n=54) from TCGA matched to the DCIS from this study by age, menopausal status and HER2 status at a 3:1 ratio, (**D**) in pure DCIS (n=7) and synchronous DCIS (n=25) from this study, (**E**) in grade 2 DCIS (n=13), grade 3 DCIS (n=19), IDC-NST of histologic grade 2 (n=10) and IDC-NST of histologic grade 3 (n=14) from this study, (**F**) in ER-positive/HER2-negative DCIS (n=19), ER-negative/HER2-negative DCIS (n=6) and HER2-positive DCIS (n=7) from this study identified by WES. Statistical significance was evaluated by the Mann-Whitney *U* test. Two-sided *P* values for the comparisons performed are shown. *, $P<0.05$; **, $P<0.01$; ns, not significant. (**G-I**) Mutational signatures identified in (**G**) ductal carcinoma *in situ* (DCIS) and synchronously diagnosed invasive ductal carcinoma of no special type (IDC-NST), in (**H**) multifocal/ multicentric synchronously diagnosed DCIS and IDC-NSTs, and in (**I**) pure DCIS subjected to WES with at least 40 single nucleotide variants (SNVs). Bar plots show the proportion of the mutational signatures identified in each lesion (right).