SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure S1. Mutational signatures and survival of primary endometrioid and serous endometrial cancers stratified according to molecular subtype.

A) Mutational signatures of 232 endometrioid and serous endometrial carcinomas from The Cancer Genome Atlas (TCGA) stratified according to molecular subtype, sorted according to the proportion of the most recurrent dominant mutational signature within a given molecular subtype. Mutational signatures are color-coded according to the legend on the right. Information on the total number of non-synonymous somatic mutations, patient age, tumor stage, FIGO tumor grade, presence of *POLE* exonuclease domain mutations, MSIsensor score and *MLH1* promoter methylation status are provided for each case below the mutational signatures. EDM, exonuclease domain mutation; HRD, homologous recombination DNA repair deficiency; MMR, DNA mismatch repair; MSI, microsatellite instability. **B)** Kaplan–Meier progression-free survival curves for endometrial cancer patients stratified according to molecular subtype (left) and dominant molecular signature (right). P-values of the log-rank test are shown.

Supplementary Fig. S2. Mutational signatures of endometrial cancers of MSI (hypermutated) molecular subtype.

Mutational signatures of 65 endometrioid endometrial carcinomas of MSI (hypermutated) molecular subtype from The Cancer Genome Atlas (TCGA), sorted according to the proportion of DNA MMR-related mutational signatures 6, 15, 20 and 26. Mutational signatures are color-coded according to the legend on the right. Information on the primary and secondary signatures, percentage of MSI signatures, total number of non-synonymous somatic mutations, somatic single nucleotide variants (SNVs), percentage of small insertions and deletions (indels), MSIsensor score and *MLH1* promoter methylation status are provided for each case on the right of the mutational signatures. HRD, homologous recombination DNA repair deficiency; MMR, DNA mismatch repair; MSI, microsatellite instability.

Supplementary Fig. S3. Mutational signatures of endometrial cancers of copy number-low (endometrioid) molecular subtype.

Mutational signatures of 90 endometrioid endometrial carcinomas of copy number-low (endometrioid) molecular subtype from The Cancer Genome Atlas (TCGA), sorted according to the proportion of mutational signature 1. Mutational signatures are color-coded according to the legend on the right. Information on the primary and secondary signatures, total number of non-synonymous somatic mutations, somatic single nucleotide variants (SNVs), percentage of small insertions and deletions (indels), MSIsensor score and *MLH1* promoter methylation status are provided for each case on the right of the mutational signatures. HRD, homologous recombination DNA repair deficiency; MMR, DNA mismatch repair; MSI, microsatellite instability.

Supplementary Fig. S4. Features associated with defective homologous recombination DNA repair in copy-number high (serous-like) endometrial cancers, high-grade serous ovarian cancers and basal-like breast cancers.

A) Large-scale state transitions (LST) scores in copy-number high (serous-like) endometrial cancers, high-grade serous ovarian cancers and basal-like breast cancers from The Cancer Genome Atlas (TCGA). n.s., not significant. Mann-Whitney U test. Dashed line indicates the cut-off (≥15) for high LST scores. **B)** Average deletion length (nucleotides) in copy-number high (serous-like) endometrial cancers, high-grade serous ovarian cancers and basal-like breast cancers from TCGA. n.s., not significant. Mann-Whitney U test. Dashed line indicates 5 bp, the cut-off for small deletion length found in tumors with defective homologous recombination DNA repair. **C)** Percentage of cases with bi-allelic germline or somatic genetic alterations in 102 homologous recombination (HR) genes in copy-number high (serous-like) endometrial cancers, high-grade serous ovarian cancers and basal-like breast cancers from TCGA.

Supplementary Fig. S5. Mutational signatures of shared and private mutations identified in primary endometrial cancers and matched metastases.

Cancer cell fractions of non-synonymous somatic mutations identified in primary endometrial cancers and metastases using ABSOLUTE [26], color-coded according to the legend. The number of non-synonymous somatic mutations identified in a given lesion is shown in parentheses on the right. Pie charts represent the mutational signatures identified in mutations shared between primary tumors and metastases (root, R) in mutations private to the primary lesion (P) and in mutations private to the metastases (M), color-coded according to the legend. The length of the branches is proportional to the number of somatic mutations that are shared/ unique to a given lesion, and the number of mutations is shown alongside the branches. The percentage of small insertions and deletions (indels, I) are included within parentheses next the R, P or M labels. Selected pathogenic somatic mutations are shown along their corresponding branches. EC, endometrial cancer; M, metastasis; P, primary tumor; R, root.