**SUPPLEMENTARY MATERIAL**

**Figure S1.** FGFR2 decreases DNA double-strand break repair by decreasing Mre11 expression. Schematics show the substrate plasmids used to detect homologous recombination repair (HRR; A) and non-homologous end joining (NHEJ; B). (C) Knockdown of endogenous FGFR2 increased Mre11 expression.

FGFR2-overexpressing gastric carcinoma cells, KATO III, were transfected with si-FGFR2 or control siRNA. The protein for immunoblotting was extracted 2 days after transfection. Quantification of Mre11 band intensities was determined by ImageJ (NIH) and is indicated below individual bands. (D) and (E) The mRNA expression data for breast cancer tissues from the Cancer Genome Atlas ([http://cancergenome.nih.gov](http://cancergenome.nih.gov)) (D) and METABRIC (E; ref. 28) revealed an inverse correlation between FGFR2 and Mre11. (F) NHEJ activity was restored by co-transfection with FGFR2- and Mre11-expressing plasmids. Values were normalized to the vector control (Cont) and are presented as the mean ± SD, n = 6. *P < 0.05 for the difference between FGFR2-overexpressing and Cont cells in the precise and overall NHEJ assay.

**Figure S2.** FGFR2 inhibits Mre11 expression through transcription factor POU1F1.

(A) Band intensities of Mre11 in Fig. 2A were quantified by ImageJ, and are presented as the mean ± SD, n = 2. Immunoblotting (B, left panel) and quantitative reverse transcription-PCR (B, right panel) showed that T-47D breast cancer cells were transfected with plasmids expressing either FGFR2, FGFR2<sup>DM</sup>, or empty vector. For FGF7 treatment, the cells were transfected with either empty vector or FGFR2<sup>DM</sup>, and the medium was replaced with FGF7-containing medium post-transfection. (B, right panel) The relative expression values (2<sup>-ΔΔCt</sup>) of Mre11 mRNA are presented as the mean ± SD, n = 6. (C) Knockdown of endogenous FGFR2 increased Mre11
expression. FGFR2-overexpressing KATO III cells were transfected with si-FGFR2 or control siRNA. The RNA for quantitative reverse transcription-PCR was extracted 2 days after transfection. The relative expression values ($2^{\Delta\Delta Ct}$) of Mre11 mRNA are presented as the mean ± SD, $n = 4$. *$P < 0.05$ for the difference between si-FGFR2 and si-Control. (D) Truncation of predicted transcription factor (TF) binding sites within the Mre11 promoter is indicated in the figure. Deletion of specific regions of the Mre11 promoter reveals that the predicted POU1F1-binding region (nt 52–58) regulates FGFR2-attenuated Mre11 promoter-driven luciferase activity. Relative luminescence units (RLUs) were normalized to the vector control (Cont) and are presented as the mean ± SD, $n = 6$. (E) Quantitative reverse transcription-PCR showed that FGFR2-reduced Mre11 expression was restored when knocking-down of POU1F1 in T-47D cells. The relative expression values ($2^{\Delta\Delta Ct}$) of Mre11 mRNA are presented as the mean ± SD, $n = 6$. All the vector and vehicle control in the above experiments are presented as Cont. *$P < 0.05$ for the difference between each indicated groups and Cont.

**Figure S3.** Mre11 expression and DNA non-homologous end joining activity are affected by FGFR2 via MEK/ERK signaling. (A) Immunoblotting showed that expression of Mre11 decreased with overexpression of FGFR2, and this was restored due to the treatment of MEK inhibitor (U0126, 1 μM) but not by the treatment of PI3K inhibitor (LY294002, 2 μM). Inhibitors were treated at 2 days post-transfection for 6 h. Transfection of empty vector and following treatment of DMSO as vehicle control is presented as Cont. (B) DNA non-homologous end joining (NHEJ) activity was unaffected by FGFR2 in the presence of U0126 or co-transfection with dominant-negative MEK ($MEK^{DN}$). MCF-7 cells transfected with the indicated plasmid and/or subjected to U0126 treatment were used to examine precise and
overall NHEJ activity. Values were normalized to the vector and vehicle control (Cont) and are presented as the mean ± SD, n = 6. *P < 0.05 for the difference between Cont and FGFR2-overexpressing cells in the precise and overall NHEJ assay.

**Figure S4.** ERK interacts with POU1F1 and further phosphorylates POU1F1 at Thr75 to regulate Mre11 expression. (A) The interaction between POU1F1 and ERK was detected by co-IP in MCF-7 cells. Myc-tagged POU1F1 protein was immunoprecipitated with anti-Myc and resolved by SDS-PAGE and immunoblotted with anti-ERK. Immunoblotting (B) and quantitative reverse transcription-PCR (C) showed that Mre11 expression was downregulated by overexpression of POU1F1WT and POU1F1T75E in T-47D cells. In contrast, transfection of POU1F1T75A did not decrease Mre11 expression. (C) The relative expression values (2^\(-\Delta\Delta Ct\)) of Mre11 mRNA are presented as the mean ± SD, n = 6. *P < 0.05 for the difference between each indicated groups and vector control (Cont).

**Figure S5.** Higher FGFR2 expression correlates with better prognosis for breast cancer patients receiving chemotherapy. (A) Relapse-free survival of breast cancer patients who received chemotherapy (left panel) or who did not receive chemotherapy (right panel), as stratified by median expression of FGFR2. Log-rank-test P values are displayed. Data were collected from KM plotter (ref. 34). (B) Disease-free survival of breast cancer patients who received chemotherapy (left panel) or who did not receive chemotherapy (right panel), as stratified by median expression of FGFR2. Log-rank-test P values are displayed. Data were collected from METABRIC (ref. 28).

**Figure S6.** FGFR2 overexpression sensitizes breast cancer cells to PARP inhibitor. MCF-7 stable clones expressing either FGFR2 or vector control (VC; pLX-301-3×Flag) were treated with the PARP inhibitor ABT-888 for 24 h. The MTT
assay was performed 5 days post-treatment.
Fig. S2

A

Mean pixel density (relative to Cont)

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B

Mre11 mRNA expression (relative to Cont)

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p-ERK1/2

Tubulin

C

Mre11 mRNA expression (relative to si-Control)

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D

Putative TF

Mre11 promoter

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E

Mre11 mRNA expression (relative to Cont)

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Deletion of putative transcription factor (TF) binding site
**Fig. S5**

**A**

Receiving chemotherapy (n=417)

- Survival Probability
- Log rank P value = 0.02
- HR = 0.71 (0.51-0.98)

No chemotherapy (n=1554)

- Survival Probability
- Log rank P value = 0.43
- HR = 1.03 (0.87-1.22)

**B**

Receiving chemotherapy (n=274)

- Survival Probability
- Log rank P value = 0.019
- HR = 0.62 (0.41-0.93)

No chemotherapy (n=3455)

- Survival Probability
- Log rank P value = 0.9
- HR = 1.01 (0.90-1.13)