Supplementary Figure legends

**Figure S1. CXCL14-stimulation of fibroblasts induces Hmox1 and Nos1.** (A) qRT-PCR analysis of Nos1, Nos3 and Hmox1 expression in NIH-ctr fibroblasts cultured in serum-reduced medium and stimulated with 10ng/ml CXCL14 for the time points indicated. (B) Hmox1 expression in NIH-ctr and NIH-CXCL14 fibroblasts cultured in serum-reduced medium detected by qRT-PCR. Data are derived from four independent analyses and are expressed as the means ± S.E.M. *, p < 0.05, **, p < 0.01 (two-way ANOVA in (A) and Mann Whitney test in (B)).

**Figure S2. Nos1 knockdown in CXCL14-fibroblasts.** qRT PCR analyses of NIH-CXCL14 derivatives stably expressing non-targeting shRNA (shCtr) or shRNA targeting Nos1 (shN1:1, shN1:2, shN1:3). The figure shows the summary of four independent analyses as the means ± S.E.M. **, p < 0.01, (one-way ANOVA).

**Figure S3. Enhanced activation of Hif1α-signaling in CXCL14-fibroblasts.** (A) Hif1α-reporter gene (HRE) activation in NIH-ctr (□) and NIH-CXCL14 (■) cells, and (B) NIH-ctr and NIH-CXCL14-derivatives with or without stable downregulation of Nos1. CXCL14-induced activation of the HRE reporter in (A) was measured after treatment of NIH-ctr cells cultured in 1% FBS with 200ng/ml recombinant CXCL14 over night. Data in (A and B) are derived from four independent analyses and are expressed as the means ± S.E.M. *, p < 0.05, **, p < 0.01 (one-way ANOVA).
Figure S4. Nos1 is induced upon oxidative stress in NIH3T3 fibroblasts. Quantification and statistical analysis of immunoblots of Figure 3D. Data from three independent experiments are depicted as the means ± S.E.M. *, p < 0.05, (one-way ANOVA).

Figure S5. NO and glutathione protect CXCL14-fibroblasts. (A) Growth analysis of NIH-ctr and NIH-CXCL14 fibroblasts using crystal violet staining cultured for three days in serum-reduced medium in the absence or presence of either 10μM PTIO or 2μM BSO or both compounds in combination. Data are expressed as the means ± S.E.M. *, p < 0.05 (one-way ANOVA). (B) Crystal violet stained cultures of NIH-ctr/ shCtr, NIH-CXCL14/ shCtr and NIH-CXCL14/ shN1:3 cells grown for three days in serum-reduced medium alone and supplemented with 2μM BSO, respectively. Data in (A, B) are derived from three independent analyses, each performed in quadruplicates.

Figure S6. Expression of CAF marker by engineered fibroblasts. (A) mRNA expression analysis by qRT-PCR of several marker associated with CAFs in the different engineered fibroblast populations (NIH-ctr/ shCtr, NIH-CXCL14/ shCtr, NIH-CXCL14/ shN1:1 and NIH-CXCL14/ shN1:3). Data are derived from four independent analyses and are expressed as the means ± S.E.M. (B) Contractility assay of collagen-embedded NIH-ctr and NIH-CXCL14 cells incubated in low serum-containing medium. Pictures of collagen discs were taken after 72h of culture (left) and the collagen surface area was quantified using Image J (right). The figure shows the summary of three independent experiments.
Figure S7. *Nos1* is dispensable for the growth of CXCL14 fibroblasts under conditions of oxidative stress but important for their paracrine-mediated effects. (A) NIH-ctr/ shCtr, NIH-CXCL14/ shCtr and the NIH-CXCL14-derivatives with *Nos1* knockdown (shN1:1, shN1:2, shN1:3) were cultured for four days in presence or absence of 1µM DMNQ (left panel) and 100µM H₂O₂ (right panel). The figure displays the growth of fibroblasts under oxidizing conditions in relation to the growth of non-treated cells (100%). GFP-expressing prostate cancer cells (B) and breast cancer cells (C) were grown in presence or absence of 1µM DMNQ (left panel) and 100µM H₂O₂ (right panel) together with the indicated NIH-CXCL14-derivatives. The growth of cancer cells under the different treatments was determined by measuring GFP fluorescence following 9 days of co-culture with fibroblasts. The figure shows the growth of cancer cells exposed to the oxidizing reagents in relation to non-treated cultures (100%) from four independent experiments. Data derived from four independent analyses are expressed as the means ± S.E.M. *, p < 0.05, (one-way ANOVA).

Figure S8. Recruitment of blood vessels into fibroblast-stimulated prostate and breast tumors. Quantification of immunohistochemical analyses for blood vessels (anti-CD31) in prostate (A) and breast (B) tumors derived from co-injection of LNCaP and MCF7 cancer cells, respectively, and different fibroblast populations (NIH-ctr/shCtr, NIH-CXCL14/shCtr, NIH-CXCL14/shN1:1 and NIH-CXCL14/shN1:3) as depicted. A scoring system ranging from 0-5 (no staining to abundant staining) was applied to evaluate the immunohistochemistry signals in the core of the tumor. Tumor groups composed of n=5-7 animals per group were analyzed. Data in (A, B) are expressed as the means ± S.E.M. **, p < 0.01 (one-way ANOVA). Scale in (A, B) is 100µm.
**Figure S9. Lymphatic vessel recruitment into fibroblast-stimulated prostate and breast tumors.**
Quantification of immunohistochemistry analyses for lymphatic vessels (anti-LYVE-1) in prostate (A) and breast (B) tumors derived from co-injection of LNCaP and MCF7 cancer cells, respectively, and different fibroblast populations (NIH-ctr/ shCtr, NIH-CXCL14/ shCtr, NIH-CXCL14/ shN1:1 and NIH-CXCL14/ shN1:3) as depicted. A scoring system ranging from 0-5 (no staining to abundant staining) was applied to evaluate the immunohistochemistry signals in the core of the tumor. Quantifications are derived from analyses of tumor groups composed of n=5-7 animals per group. Data in (A, B) are expressed as the means ± S.E.M. **, p < 0.01 (one-way ANOVA). Scale in (A, B) is 100µm.

**Figure S10. NOS1 and CXCL14 mRNA expression correlates in human breast cancer data sets.**
Publically available gene expression data sets derived from (A) breast cancer stroma (GEO dataset; GSE12622 (22)) and (B) ductal carcinoma in situ (DCIS) of the mammary gland (GEO dataset: GSE26304 (23)) were used to investigate the relation of NOS1 and CXCL14 transcript levels. $r = 0.285, p = 0.038$ in (A) and $r = 0.470, p = 0.0076$ in (B) determined by Spearman analysis indicate a significant correlation between NOS1 and CXCL14 expression.