

Supplementary Fig S1. (A) Increase in fibroblast number density elicited by 5 day treatment with 10% FBS compared to 0% FBS. (B) Increase in *COL1A1* mRNA expression in control fibroblasts elicited by 3 day treatment with 2.5 ng/ml TGF- $\beta$ 1. (C-G) Lack of effect of DMSO vehicle on the viability (C), fibroblast number density (D) and percentage of cycling fibroblasts (E) in control fibroblasts treated with 10% FBS for 5 days. (F-G) Lack of effect of DMSO vehicle on the expression of *COL1A1* (F) and  $\alpha$ -SMA (G) of control fibroblasts treated with 2.5 ng/ml TGF- $\beta$ 1 for 3 days. \* $P \le 0.05$ , \*\*  $P \le 0.01$  and \*\*\*  $P \le 0.005$  were determined by Student's *t*-test (n=3-5).





Supplementary Fig S2. Lack of effect of DMSO vehicle on ADC-TAFs and SCC-TAFs in terms of viability (A), fibroblast number density (B), percentage of cycling fibroblasts (C) and expression of *COL1A1* (D) or a-SMA (E). TAFs were cultured as in Supplementary Fig. S1. \* $P \le 0.05$ , \*\*  $P \le 0.01$  and \*\*\*  $P \le 0.005$  were determined by Student's *t*-test (n=3-6).



Supplementary Fig S3. Representative Western blot of the activation marker  $\alpha$ -SMA and  $\beta$ -actin (used as loading control) of ADC-TAFs and SCC-TAFs cultured in the absence or presence of 2.5 ng/ml TGF- $\beta$ 1

ADC



Supplementary Fig S4. Additional illustrative images of Ki-67 and α-SMA stromal stainings in histologic sections from ADC and SCC patients obtained with a 40× objective. Images were obtained from different patients than those used in Fig. 4



Supplementary Fig S5. (A) Lack of effect of 2 µm nintedanib added concomitantly with 2.5 ng/ml TGF- $\beta$ 1 for 3 days on the number density of ADC-TAFs and SCC-TAFs. (B-C) Increase in carcinoma cell density (B) or invasion (C) induced by the conditioned medium of ADC-TAFs (H1437, H522) or SCC-TAFs (SK-MES-1, H520) activated with treated 2.5 ng/ml TGF- $\beta$ 1 for 3 days in the presence or absence of 2 µm nintedanib. \**P* ≤ 0.05, \*\* *P* ≤ 0.01 and \*\*\* *P* ≤ 0.005 were determined by Student's *t*-test (n=4-5).



Supplementary Fig S6. Illustrative phase contrast images of control fibroblasts or TAFs stimulated with either 10% FBS for 5 days or 2.5 ng/ml TGF- $\beta$ 1 for 3 days in the presence of increasing nintedanib concentrations. Images were obtained with a 10× objective. Vacuolar structured were readily observed at 5  $\mu$ M nintedanib in all conditions. Vacuolar structures at 2  $\mu$ M appeared to be more readily observed in fibroblasts cultured with TGF- $\beta$ 1 than with 10% FBS, and were overall less abundant than at 5  $\mu$ M nintedanib. No vacuolar structures were observed at lower nintedanib concentrations ( $\leq 1 \mu$ M).

Control fibroblasts

TAFs