Supplemental Figure Legends

Supplemental Figure 1. *ECM induced endothlein-1 expression*. In (A), stellate cells were isolated as in Methods and grown in medium containing 20% serum for 5 days, trypsinized, and plated on multi-well plates pre-coated with type I collagen, fibronectin, type IV collagen or laminin respectively in serum-free medium for 24 hours. Preproendothelin-1 mRNA (A) or immunoreactive endothelin-1 (B) were detected as in Methods ($n = 4$, $^*p < 0.05$ compared to control). Abbreviations: Col I = type I collagen, Fn = fibronectin, Lm = laminin, Col IV = type IV collagen.

Supplemental Figure 2. *Fibronectin does not induce ECE expression.* In (A) and (B), activated stellate cells as in Figure 1 were exposed to 10 μg/mL fibronectin for 24 hours. ECE mRNA and protein were detected as in Methods. In (C), activated stellate cells were exposed to 10 μg/mL fibronectin for 24 hours with or without phosphoramidon (100 μM), and endothelin-1 was detected in conditioned culture supernatant as in Methods ($n = 3$, $^*p < 0.05$ compared to control; # compared to fibronectin). Abbreviations: Ctr = control; Fn = fibronectin.

Supplemental Figure 3. *Fibronectin induced endothelin-1 synthesis through integrin α5β1.* In (A), stellate cells as in Figure 1 were exposed to 10 μg/mL fibronectin for 24 hours with or without neutralizing antibody α5, β1 or α5β1 (all 1:500 dilution). Cells

were harvested and preproendothelin-1 mRNA was measured as in Methods. In (B), RGD (150 μg/mL) was tested as in (A) (n = 3, *p < 0.05 compared to control; #p < 0.05 compared to fibronectin alone).

Supplemental Figure 4. *Type I collagen induced endothelin-1 synthesis.* Stellate cells as in Figure 1 were exposed to 10 μg/mL type I collagen added to the cell culture medium as in Methods for 24 hours with or without neutralizing antibody α5, β1, α5β1 (1:500), or RGD. Preproendothelin-1 mRNA (A) and immunoreactive endothelin-1 peptide (B) were detected as in Methods (n = 3, *p < 0.05 compared to control; #p< 0.05 compared to type 1 collagen alone). Abbreviations: Ctr = control; Col I = type I collagen.

Supplemental Figure 5. *Fibronectin does not induce TGFβ expression.* Stellate cells as in Figure 1 were exposed to 10 μg/mL fibronectin for 24 hours and TGFβ1 mRNA was detected as in Methods.

Supplemental Figure 6. *Recombinant ET-1 induces ERK activity.* Activated stellate cells as in Figure 1 were exposed to endothelin-1 (50 nM) for the indicted times and whole-cell lysates were subjected to immunoblotting to detect ERK, phospho-ERK as in Methods. A representative immunoblot is shown.

Supplemental Figure 7. *Src inhibitor-1 blocked fibronectin induced ERK*

phosphorylation. Stellate cells as in Figure 1 were exposed to 10 μg/mL fibronectin for 15 minutes with or without pretreatment with Src inhibitor-1 (SI) for 1 hour, cell lysates were subjected to immunoblotting to detect phosphorylated proteins as indicated or beta actin. The image is representative of 3 others.

Supplemental Figure 8. *FAK does not mediate fibronectin dependent synthesis of endothelin-1 in activated stellate cells*. In (A), activated stellate cells were exposed to fibronectin as in Figure 3 and subjected to immuoblotting to detect phospho-FAK with the indicted antibodies. In (B), activated stellate cells were infected with the adenoviruses shown (MOI = 5) in medium containing 20% serum for 24 hours. Cells were washed and serum free conditions were introduced for a further 24 hours, stimulated with 10 μg/mL fibronectin for 15 minutes, and cell lysates were subjected to immunoblotting to detect total ERK and phospho-ERK. An empty virus (EV, MOI = 5) containing the same viral backbone at the other 2 viruses was used as a control. In (C) and (D), cells as above were stimulated with 10 μg/mL fibronectin for 24 hours, lysates were prepared and preproendothelin-1 mRNA and immunoreactive endothelin-1, respectively, were detected as in Methods ($n = 3$, $^*p < 0.05$ compared to control). Abbreviations: EV = empty virus, AdFAK = adenovirus wild type FAK, AdFRNK = adenovirus FAK kinase domain negative.

Supplemental Figure 9. *The effect of liver injury on fibronectin induced kinase activity.*

Stellate cells were isolated from normal or CCl_4 injured rat livers and were grown in 20% serum containing medium for 2 days. Cells were starved for 24 hours and then stimulated with 10 μg/mL fibronectin for 15 minutes. Cell lysates were subjected to immunoblotting to detect the phosphorylated proteins indicated. In the graphs shown below the representative immunoblots, phosphorylated signals were quantitated, normalized, and expressed graphically ($n = 3$, $^{*}p < 0.05$ compared to normal stellate cells without fibronectin, or no fibronectin on the right; $^{\#}p < 0.05$ compared to normal stellate cells without fibronectin; § $p < 0.05$ compared to injured stellate cells without fibronectin).