

Supplementary table 1: Decellularization protocol

| Type of scaffold | Step | Solution | Frequency of oscillation (Hertz) | Time (minutes) | Repetitions |
|---------------------------|------|------------------------------|----------------------------------|----------------|-------------|
| Healthy scaffold | 1 | Deionized water | 20 | 2 | 12-18 |
| | 2 | Phosphate buffered saline 1X | 20 | 2 | 1-2 |
| Cirrhotic scaffold | 1 | Deionized water | 30 | 5 | 7 |
| | 2 | Reagent mixture | 30 | 5 | 2 |
| | 3 | Deionized water | 30 | 5 | 4 |
| | 4 | Reagent mixture | 30 | 5 | 2 |
| | 5 | Deionized water | 30 | 5 | 4 |
| | 6 | Reagent mixture | 30 | 5 | 2 |
| | 7 | Deionized water | 30 | 5 | 4 |
| | 8 | Reagent mixture | 30 | 5 | 2 |
| | 9 | Deionized water | 30 | 5 | 4 |
| | 10 | Reagent mixture | 30 | 5 | 2 |
| | 11 | Deionized water | 30 | 5 | 4 |
| | 12 | Reagent mixture | 30 | 5 | 2 |
| | 13 | Deionized water | 30 | 5 | 4 |
| | 14 | Reagent mixture | 30 | 5 | 2 |
| | 15 | Phosphate buffered saline 1X | 30 | 5 | 5 |

Supplementary table 2: Primary antibodies for immunohistochemistry staining

| Antibody | Species | Company | Catalogue number | Dilution |
|--|----------------|----------------|-------------------------|-----------------|
| Platelet derived growth factor receptor-beta (PDGFR- β) | Rabbit | Abcam | Ab32570 | 1: 75 |
| Epithelial Cell Adhesion Molecule (EPCAM) | Rabbit | Abcam | Ab71916 | 1:50 |
| Ki-67 | Rabbit | Abcam | Ab21700 | Pre-diluted |

Supplementary table 3: Applied Biosystems Taqman Gene Expression Assay.

| Gene Name | Gene Abbreviation | Taqman Gene Assay No. |
|---|--------------------------|------------------------------|
| Albumin | ALB | Hs00609411_m1 |
| Alpha-fetoprotein | AFP | Hs01040598_m1 |
| Collagen Type 1, alpha 1 chain | Col1A1 | Hs00164004_m1 |
| Collagen Type 3, alpha 1 chain | Col3A1 | Hs00943809_m1 |
| Cytochrome P450 3A4 | CYP3A4 | Hs00604506_m1 |
| Fibronectin-1 | FN-1 | Hs01549976_m1 |
| Glyceraldehyde-3-phosphate dehydrogenase | GAPDH | Hs02758991_m1 |
| Hepatocyte nuclear factor 4 alpha | HNF4a | Hs00230853_m1 |
| Interleukin-6 | IL-6 | Hs00985639_m1 |
| Lysyl oxidase | LOX | Hs00942480_m1 |
| Platelet-derived growth factor receptor beta | PDGFR- β | Hs01019589_m1 |
| Transforming growth factor, beta 1 | TGF β 1 | Hs00998133_m1 |
| Uridine 5'-diphospho glucuronosyltransferase family 1 member A1 | UGT1A1 | Hs02511055_m1 |

Supplementary table 4: Primary and secondary antibody for western blot analysis

| Type | Antibody | Species | Company | Dilution |
|---------------------------|---------------------|---------|--------------------------|----------|
| Primary antibody | Alpha-tubulin | Rabbit | Cell Signaling | 1:1,000 |
| | Cleaved PARP-1 | Rabbit | Abcam | 1:2,500 |
| | E-cadherin | Rabbit | Cell Signaling | 1:1,000 |
| | EPCAM | Rabbit | Abcam | 1:1,000 |
| | GAPDH | Mouse | Santa Cruz Biotechnology | 1:200 |
| | PDGFR- β | Rabbit | Abcam | 1:5,000 |
| | P-STAT3 | Rabbit | Cell Signaling | 1:1,000 |
| | SHP-1 | Rabbit | Abcam | 1:1,000 |
| | STAT3 | Rabbit | Cell Signaling | 1:1,000 |
| | Vimentin | Mouse | Abcam | 1:1,000 |
| | Histone | Rabbit | Cell Signaling | 1:1,000 |
| Secondary antibody | Anti-rabbit IgG HRP | Goat | Santa Cruz Biotechnology | 1:10,000 |
| | Anti-mouse IgG HRP | Goat | Santa Cruz Biotechnology | 1:10,000 |

Supplementary table 5: The densitometry readings/intensity ratio of studied western blot

| Figure 2A | Order | Net PDGF-B/GAPDH | Net EPCAM/GAPDH |
|--------------------------------|-------|------------------|------------------|
| LX2 | 1 | 1.530471479 | 0.276075 |
| | 2 | 0.935325263 | 0.234582 |
| | 3 | 0.691017018 | - |
| HEPG2 | 1 | 0.086857978 | 0.652503 |
| | 2 | 0.080116802 | 0.713105 |
| | 3 | 0.064155385 | - |
| SimCC | 1 | 0.434645048 | 0.766328 |
| | 2 | 0.172312701 | 0.785488 |
| | 3 | 0.26151477 | - |
| SeqCC | 1 | 0.868664775 | 0.574125 |
| | 2 | 0.979548709 | 0.371595 |
| | 3 | 0.688862919 | - |
| | | | |
| Healthy scaffold (Figure 4D) | Order | Net PDGF-B/GAPDH | Net PSTAT3/GAPDH |
| Control | 1 | 0.546 | 0.448534 |
| | 2 | 0.569774 | 0.325819 |
| | 3 | 0.545869 | 0.506053 |
| TGF-β1 | 1 | 0.722312 | 0.570713 |
| | 2 | 0.628336 | 0.587459 |

| | | | |
|---------------------------------------|--------------|-------------------------------------|-----------------------------|
| | 3 | 0.514984 | 0.387194 |
| Sorafenib | 1 | 0.174727 | 0.15549 |
| | 2 | 0.064897 | 0.156268 |
| | 3 | 0.078708 | 0.22321 |
| TGF- β 1 + Sorafenib | 1 | 0.197797 | 0.294274 |
| | 2 | 0.130617 | 0.350418 |
| | 3 | 0.119314 | 0.155967 |
| Cirrhotic scaffold (Figure 4D) | Order | Net PDGF-B/GAPDH | Net PSTAT3/GAPDH |
| Control | 1 | 1.575095 | 0.306686 |
| | 2 | 1.429771 | 0.349057 |
| | 3 | 1.329299 | 0.405718 |
| TGF- β 1 | 1 | 1.328629 | 0.410499 |
| | 2 | 1.23693 | 0.471446 |
| | 3 | 0.957926 | 0.456607 |
| Sorafenib | 1 | 0.335779 | 0.264145 |
| | 2 | 0.302115 | 0.200761 |
| | 3 | 0.300607 | 0.218723 |
| TGF- β 1 + Sorafenib | 1 | 0.439778 | 0.256304 |
| | 2 | 0.831272 | 0.206496 |
| | 3 | 0.693803 | 0.319257 |
| | | | |
| Figure 5B | Order | Net cleave PARP-1/Histone H3 | Net PSTAT3/HistoneH3 |
| Control | 1 | 1.163119 | 0.869111 |
| | 2 | 0.888266 | 0.992323 |
| | 3 | 0.525068 | 0.57134 |
| 10 μ M | 1 | 1.631586 | 0.103875 |
| | 2 | 1.963694 | 0.113145 |
| | 3 | 1.52087 | 0.058874 |
| 20 μ M | 1 | 6.683193 | 0.02194 |
| | 2 | 5.79775 | 0.01694 |
| | 3 | 2.998871 | 0.01144 |

| Healthy scaffold (Figure 6A) | Order | Net PSTAT3/Histone H3 | Net SHP-1/Histone H3 | Net E-cadherin/Histone H3 | Net Vimentin/Histone H3 |
|------------------------------|-------|-----------------------|----------------------|---------------------------|-------------------------|
| Control | 1 | 0.774449 | 1.91216 | 1.711508 | 1.385469 |
| | 2 | 0.637865 | 1.832319 | 1.961001 | 1.266615 |
| | 3 | 0.511088 | 2.242285 | 3.020526 | 1.324894 |
| TGF- β 1 | 1 | 0.265599 | 1.336909 | 0.711498 | 1.70726 |
| | 2 | 0.264304 | 1.536941 | 0.795431 | 1.649943 |

| | | | | | |
|--|--------------|------------------------------|-----------------------------|----------------------------------|--------------------------------|
| | 3 | 0.617372 | 1.140336 | 0.634874 | 1.877293 |
| Regorafenib | 1 | 0.00852 | 0.194104 | 1.579572 | 0.016445 |
| | 2 | 0.043181 | 0.349874 | 2.485745 | 0.012599 |
| | 3 | 0.00024 | 0.16396 | 1.507882 | 0.015329 |
| TGF-β1 + Regorafenib | 1 | 0.02289 | 0.293735 | 2.177803 | 0.034472 |
| | 2 | 0.010019 | 0.247217 | 1.987521 | 0.023993 |
| | 3 | 0.00112 | 0.223675 | 1.772502 | 0.024936 |
| Cirrhotic Scaffold (Figure 6B) | Order | Net PSTAT3/Histone H3 | Net SHP-1/Histone H3 | Net E-cadherin/Histone H3 | Net Vimentin/Histone H3 |
| Control | 1 | 0.13178 | 1.224588 | 2.630614 | 1.99736 |
| | 2 | 0.334 | 0.657593 | 1.440182 | 2.013163 |
| | 3 | 0.234048 | 0.893641 | 2.317789 | 1.201311 |
| TGF-β1 | 1 | 0.416526 | 0.545129 | 0.519528 | 0.0123 |
| | 2 | 0.201932 | 0.483679 | 0.531781 | 0.02169 |
| | 3 | 0.290255 | 0.424768 | 0.527973 | 0.00978 |
| Regorafenib | 1 | 0.00769 | 0.356404 | 0.958175 | 0.0123 |
| | 2 | 0.001189 | 0.38885 | 0.784613 | 0.02169 |
| | 3 | 0.00348 | 0.29649 | 1.543068 | 0.00978 |
| TGF-β1 + Regorafenib | 1 | 0.010488 | 0.464304 | 1.495245 | 0.01247 |
| | 2 | 0.010082 | 0.534939 | 1.055324 | 0.01145 |
| | 3 | 0.00193 | 0.461609 | 1.230926 | 0.00451 |

| Figure 7 | Order | Net PSTAT3/Histone H3 | Net SHP-1/ Histone H3 |
|---------------------------------------|--------------|------------------------------|------------------------------|
| Control healthy scaffold | 1 | 1.592528 | 0.294782 |
| | 2 | 1.501621 | 0.288089 |
| | 3 | 1.812561 | 0.266128 |
| Regorafenib healthy scaffold | 1 | 0.015527 | -0.0094 |
| | 2 | 0.013088 | 0.053523 |
| | 3 | 0.018406 | 0.005491 |
| Control cirrhotic scaffold | 1 | 2.199337 | 0.110006 |
| | 2 | 3.712782 | 0.02515 |
| | 3 | 3.326216 | 0.016434 |
| Regorafenib cirrhotic scaffold | 1 | 0.023959 | -0.03678 |
| | 2 | -0.0178 | -0.01881 |
| | 3 | 0.012295 | 0.235535 |

Supplementary figure H&E staining of co-cultures repopulating the healthy and cirrhotic 3D scaffolds exposed to Regorafenib and TGF- β 1

