**Online supplement**

**Supplementary Material and Methods**

**RNA extraction and real-time RT-PCR**

Primer sequences are reported in suppl. Table 1, all shown as 5'-3'.

| | | |
|---|---|---|
| **Ets-1 GenBank NM_001143820.1** | **Forward primer** | ACCCAGCCTATCCAGAATCC |
| | **Reverse primer** | ATGAAGCTGGGCTCTGAGAA |
| **Tissue Factor GenBank NM_001993.4** | **Forward primer** | TGATGTGGATAAAGGAGAAAACTACTGT |
| | **Reverse primer** | CTACCGGGCTGTCTGTACTCTTC |

*Table S1 :* ***Primer sequences for real-time PCR.***

**Reporter constructs and Luciferase assay**

Human genomic DNA was amplified by PCR using a common reverse primer complementary to the DNA sequence 178 base pairs downstream of the translation start site in TF gene *F3* (Suppl. Table 2) and forward primers located -678, -495 or -242 bp upstream of the translation start site (Suppl. Table 2), all shown as 5'-3'.

| | | |
|---|---|---|
| *F3* | **Forward primer [-678]** | TGATCAGGTACCGAGCCAACTGACCCTCAGAC |
| | **Forward primer [-495]** | TGATCAGGTACCACGTTTACTTCGCTGCAGGT |
| | **Forward primer [-242]** | TGATCAGGTACCGACCCGGGCAACTAGACC |
| | **Reverse primer** | CAGGCAGAGCTCGCAGGGGTCTCCATGTCTAC |

*Table S2 :* ***Primer sequences for promoter luciferase reporter assays.***

**Nuclear extracts and Electrophoretic Mobility Shift Assay (EMSA)**

For EMSA, we used an Ets-1 [5'-TGGGCAAAGCATCCGGGAAATGCC-3'] probe (-475 to -498 from translation start).

**Chromatin immunoprecipitation assay (ChIP)**

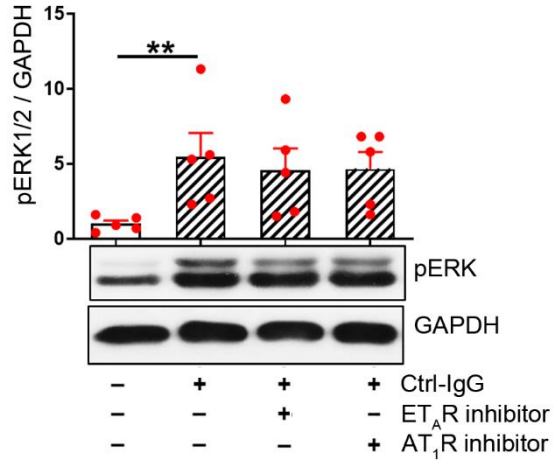
Primer sequences listed in suppl. Table 3 were used, all shown as 5'-3'.

| | | | |
|---|---|---|---|
| Specific Tissue Factor primers | Positive | **Forward primer** | AGAGGCAAACTGCCAGATGT |
| | | **Reverse primer** | TGTCTACCAGTTGGCGGAGG |
| | Negative | **Forward primer** | GAATCACATCCCAGGTGGAG |
| | | **Reverse primer** | GAAGCAGAAAGTTGCCCTTG |

*Table S3:* ***Primer sequences for CHIP.***

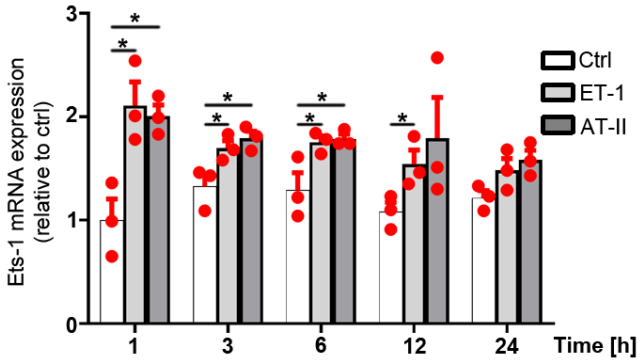
## Supplementary figures

### Suppl. Figure S1



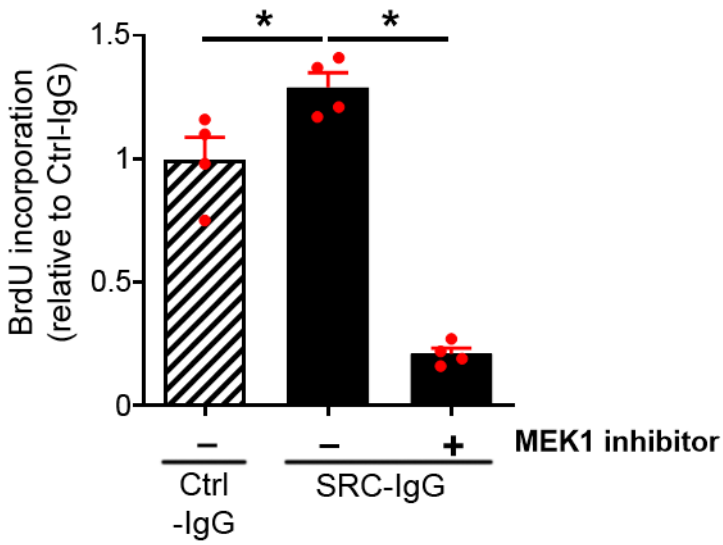

***Legend Figure S1. ERK1/2 activation (phosphorylation) after stimulation with IgG isolated from healthy individuals (Ctrl-IgG).*** *HMEC-1 were stimulated 15 minutes with Ctrl-IgG and specificity was assessed via one-hour pre-incubation $AT_1R$ or $ET_AR$ inhibitors (Valsartan and Sitaxsentan, respectively). Data derived from five experiments.*

### Suppl. Figure S2



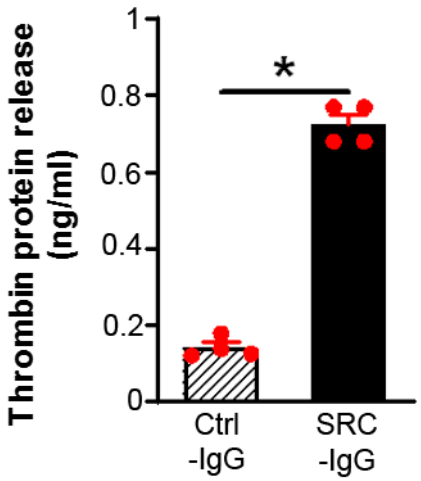

***Legend Figure S2. Transcriptional regulation of Ets-1 after stimulation with Endothelin-1 (ET-1) or Angiotensin II (AT-II).*** *Non-stimulated cells were used as control. HMEC-1 were stimulated for increasing time. Data derived from three experiments.*

**Suppl. Figure S3**




***Legend Figure S3. Endothelial cell proliferation triggered by SRC-IgG via ERK1/2 – Ets-1 signalling.*** *Ctrl-IgG-stimulated cells were used as control. HMEC-1 were stimulated 24 hours and specificity was assessed via two-hour pre-incubation MEK1 inhibitor. Data derived from four experiments.*

**Suppl. Figure S4**




***Legend Figure S4. Thrombin protein release after stimulation with Ctrl- or SRC-IgG.*** *HMEC-1 were stimulated 24 hours. Data derived from four experiments.*

| | Patient no. | 1 | 2 | 3 | 4 | median (min-max)<br>frequency (%) |
|---|---|---|---|---|---|---|
| **Patient characteristics** | **age [years]** | 47 | 52 | 47 | 68 | 49.5 (47-68) |
| | **sex** | f | f | f | f | 4/4 (100%) female |
| | **disease duration [month]** | 91 | 91 | 70 | 5 | 80.5 (5-91) |
| | **diffuse/limited SSc** | limited | diffuse | diffuse | diffuse | 3/4 (75%) diffuse |
| | **antibodies** | - | Scl-70 | Scl-70 | Scl-70 | 3/4 (75%) Scl-70 pos. |
| | **mean $AT_1R$-IgG level [U/mL]** | 16.94 | 23.77 | 29.89 | 15.45 | 20.36 (15.45-29.89) |
| | **mean $ET_AR$-IgG level [U/mL]** | 17.00 | 28.15 | 32.14 | 15.96 | 22.58 (15.96-32.14) |
| **Clinical presentation** | **hypertensive (≥140/85 mmHg)** | + | - | + | - | 2/4 (50%) |
| | **systolic [mmHg]** | >300 | 90 | 220 | 120 | 170 (90->300) |
| | **diastolic [mmHg]** | 140 | 60 | 100 | 85 | 92.5 (60-140) |
| | **initial kidney function/creatinine [mg/dL]** | 3.64 | 4.68 | anuria, HD | 4.00 | 1/4 (25%) HD; 4.00 (3.64-4.68) |
| **Histology** | **preglomerular TMA** | + | + | - | - | 2/4 (50%) |
| | **glomerular TMA** | + | + | - | - | 2/4 (50%) |
| | **fibrinoid necrosis** | + | + | - | - | 2/4 (50%) |
| | **myxoid intimal deposition** | + | + | + | - | 3/4 (75%) |
| | **concentric intimal sclerosis** | + | + | + | + | 4/4 (100%) |
| | **IF/TA** | 20% | 20% | <5% | 15% | 3/4 (75%) |

*Table S4:* ***Demographical characteristics.***

f - female; Scl-70 – anti-topoisomerase I; TMA - thrombotic microangiopathy; IF/TA - interstitial fibrosis/tubular atrophy