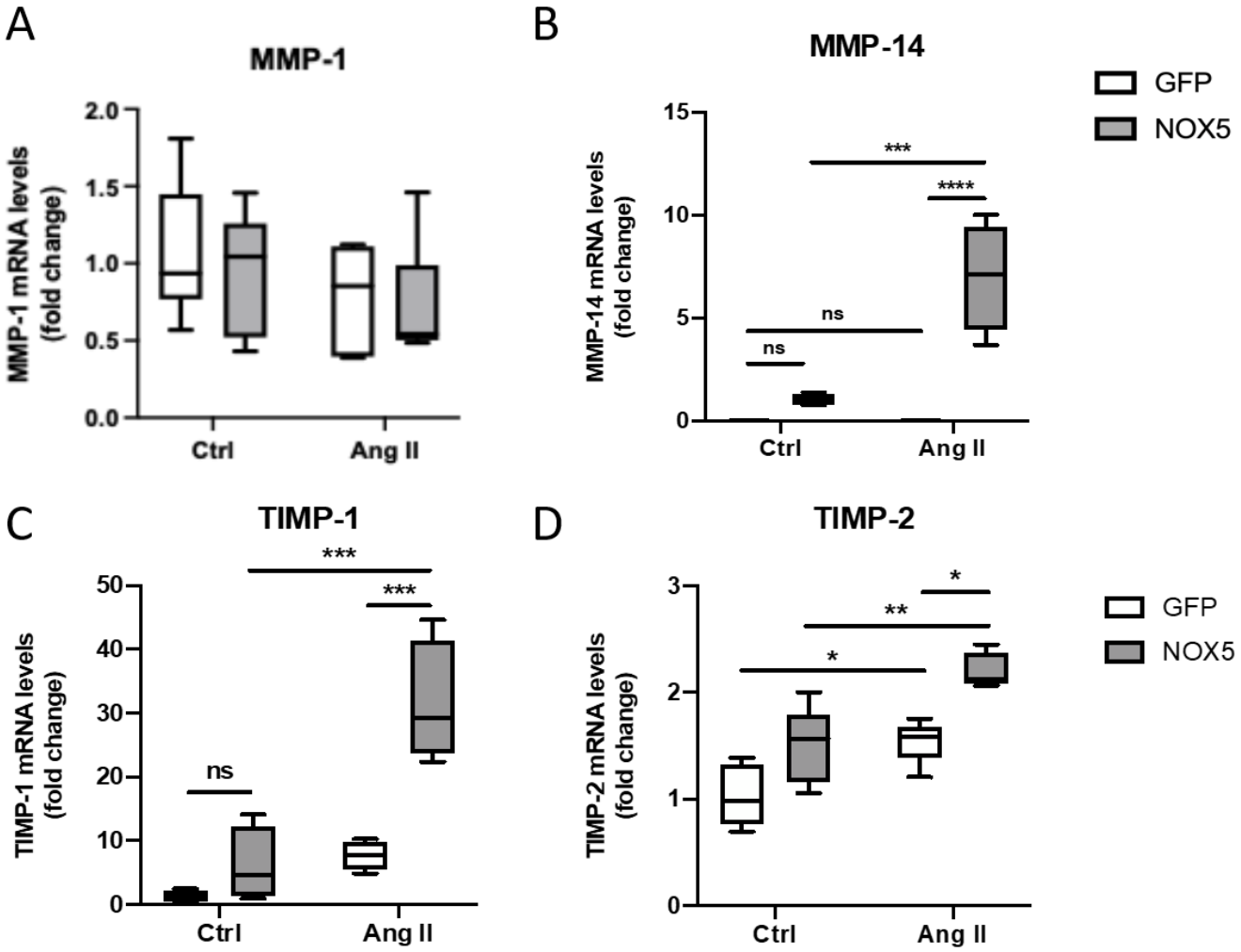


Figure S1. Ang II-mediated NOX5-β stimulation upregulates genes associated with extracellular matrix remodelling. (A) MMP-1 mRNA levels after 24 h of infection and 16 h of Ang II stimulation (n=6). (B) MMP-14 mRNA levels after 24 h of infection and 16 h of Ang II stimulation (n=6). (C) TIMP-1 mRNA levels after 24 h of infection and 16 h of Ang II stimulation (n=6). (D) TIMP-2 mRNA levels after 24 h of infection and 16 h of Ang II stimulation (n=6). GFP: teloHAEC infected with GFP-encoding adenovirus. NOX5: teloHAEC infected with NOX5-encoding adenovirus. Ctrl: non-stimulated cells. Ang II: cells stimulated with Ang II 0.1 μM. ns: not significant differences, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001. Data are presented as median and IQR.

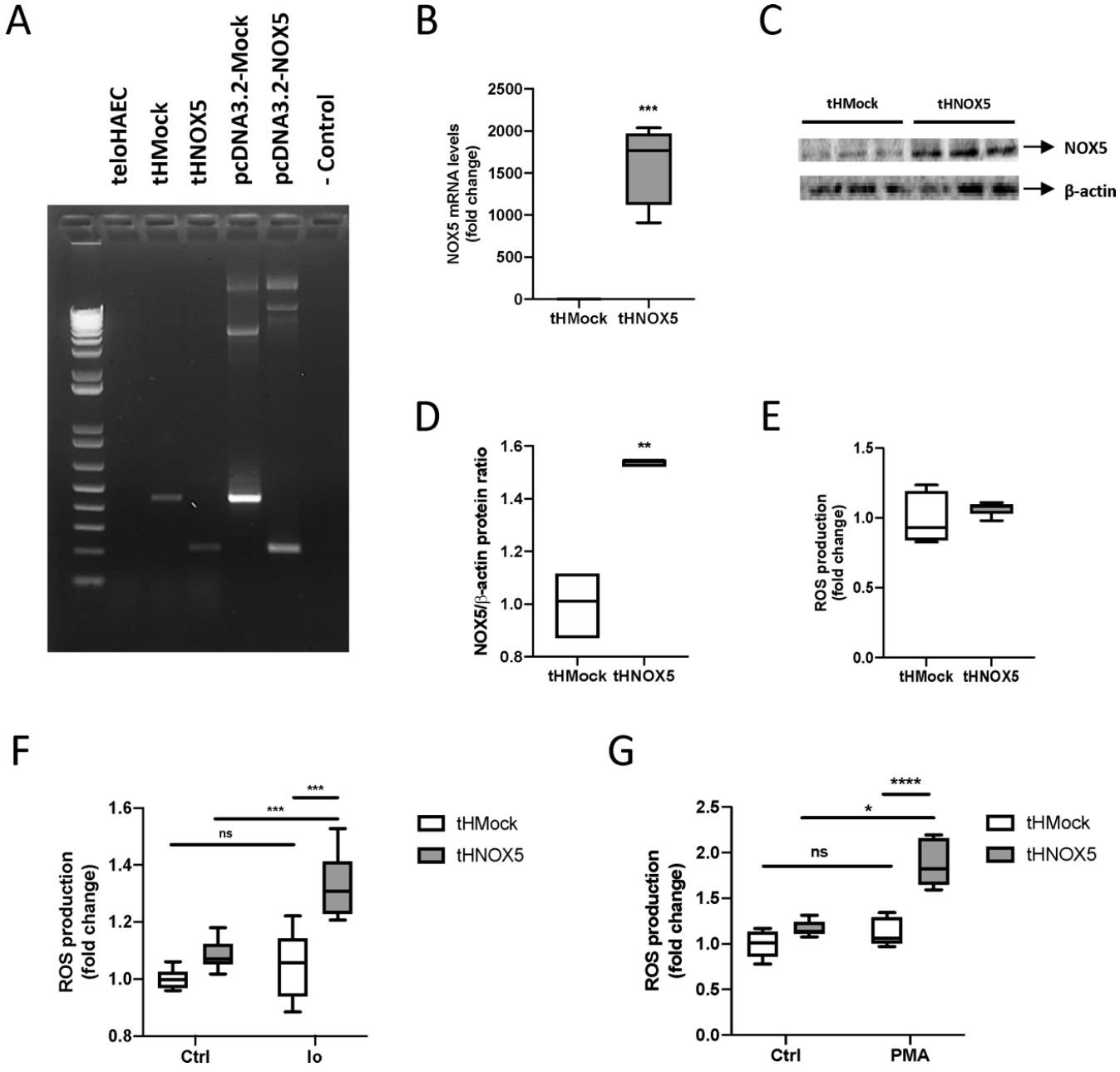


Figure S2. The stable teloHAEC cell line expressing NOX5 (tHNOX5) serves as model of chronic NOX5 overexpression. (A) Agarose gel image of the genotyping PCR. Specific primers P1, P2 and P3 were used to detect Mock and NOX5 plasmid sequences in the gDNA of teloHAEC cell lines. Lane 1: molecular weight marker. Lane 2: teloHAEC gDNA amplification. Lane 3: tHMock gDNA PCR amplification. Lane 4: tHNOX5 gDNA PCR amplification. Lane 5: pcDNA3.2-Mock plasmid PCR amplification. Lane 6: pcDNA3.2-NOX5 plasmid PCR amplification. Lane 7: PCR negative control. (B) NOX5 mRNA levels of tHMock and tHNOX5 cell lines (n=6). (C) NOX5 and β-actin immunoblots of tHMock and tHNOX5 cells (n=3). (D) NOX5 protein levels quantification of tHMock and tHNOX5 cells (n=3). (E-G): ROS leves produced by tHMock and tHNOX5 cell lines at baseline (E; n=6) and after Io (F; n=6) or PMA (G; n=6) stimulation. tHMock: stable cell line transfected with pcDNA3.2-Mock. tHNOX5: stable cell line transfected with pcDNA3.2-NOX5. ns: not significative differences, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001. Data are presented as median and IQR. Io: 100 nM ionomycine; PMA: 100 nM phorbol 12-myristate 13-acetate.

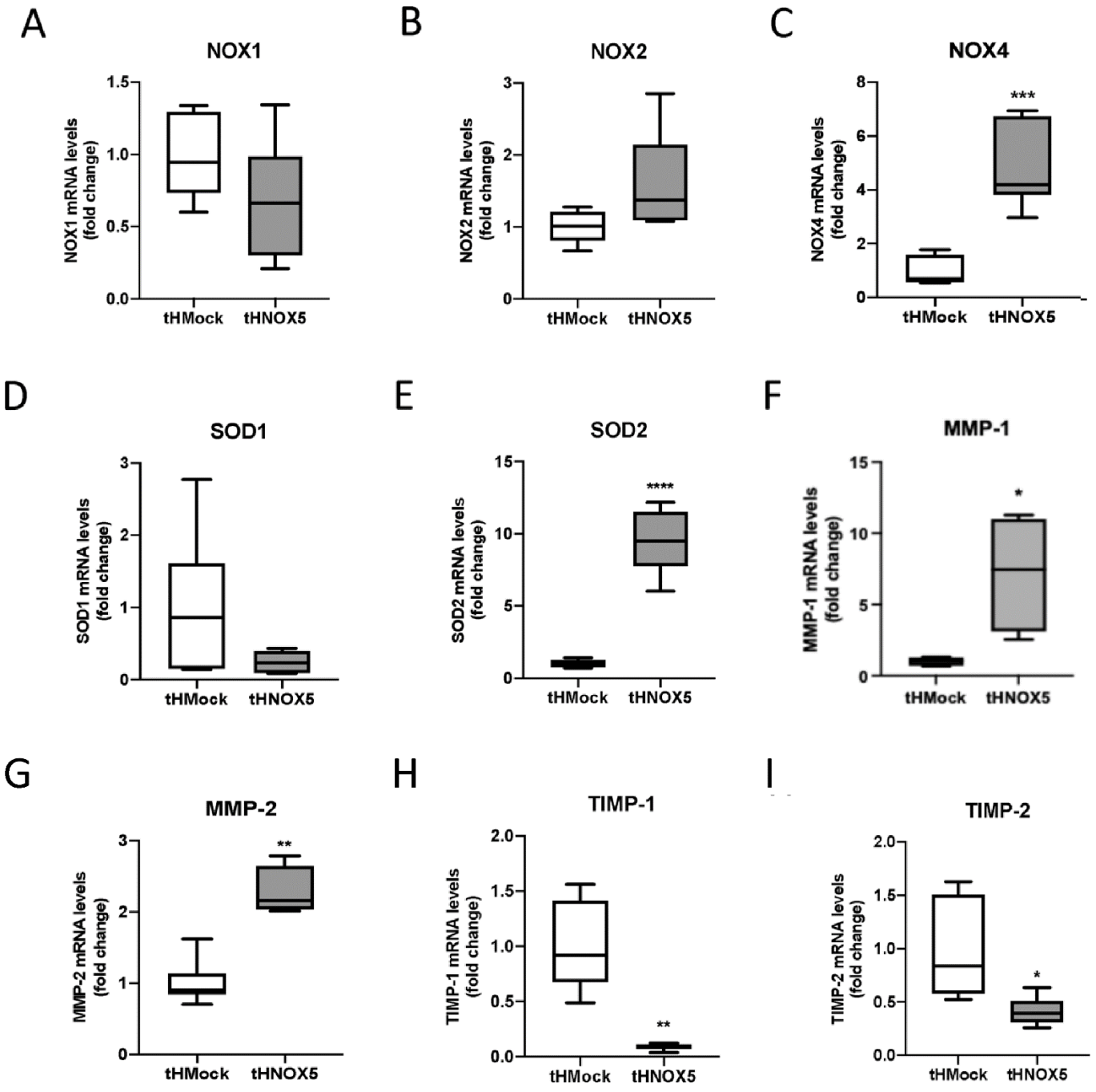


Figure S3. NOX5 chronic overexpression affects other redox and MMP-related genes. In tHMock and tHNOX5 cell lines mRNA levels of NOX1 (A), NOX2 (B), NOX4 (C), SOD1 (D), SOD2 (E), MMP-1 (F), MMP-2 (G), TIMP-1 (H) and TIMP-2 (I) were analyzed by real time qPCR (n=6). tHMock: stable cell line transfected with pcDNA3.2-Mock. tHNOX5: stable cell line transfected with pcDNA3.2-NOX5. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001. Data are presented as median and IQR.

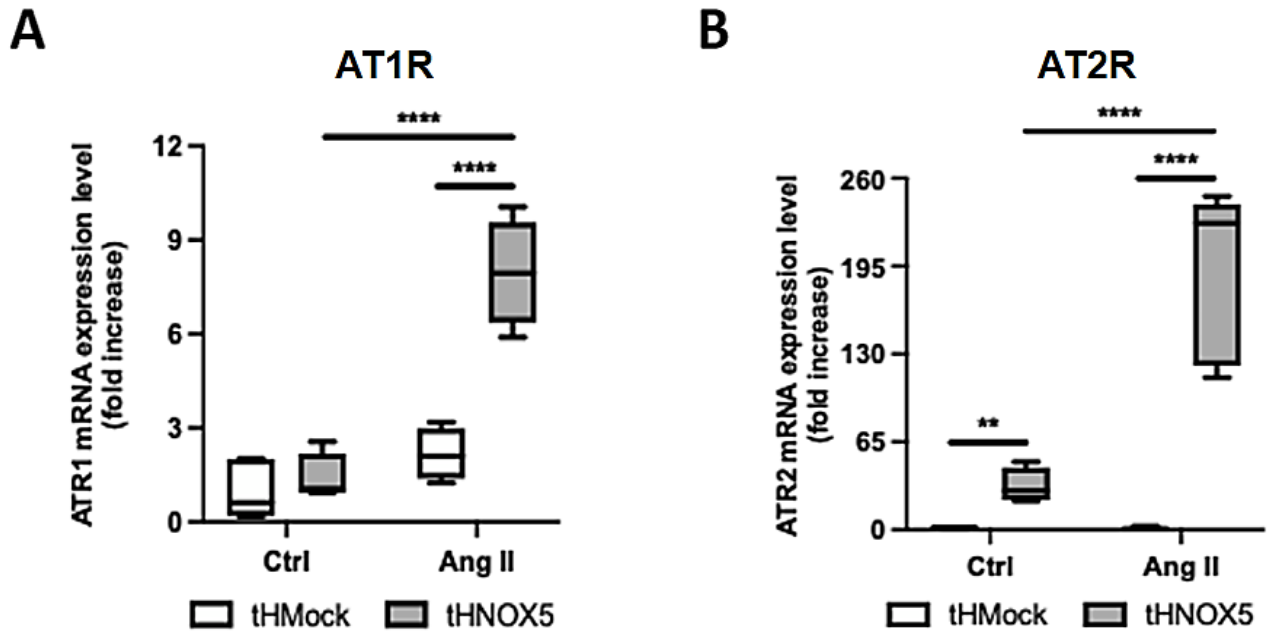


Figure S4. NOX5 chronic overexpression seems to affect Ang II receptors (AT1R and AT2R) expression, with a more intense effect on AT2R. (A) AT1R mRNA levels of tHMock and tHNOX5 cell lines after 8 h of Ang II stimulation (n=4). (B) AT2R mRNA levels of tHMock and tHNOX5 cell lines after 8 h of Ang II stimulation (n=4). tHMock: stable cell line transfected with pcDNA3.2-Mock. tHNOX5: stable cell line transfected with pcDNA3.2-NOX5. **p<0.01, ****p<0.0001. Data are presented as median and IQR.

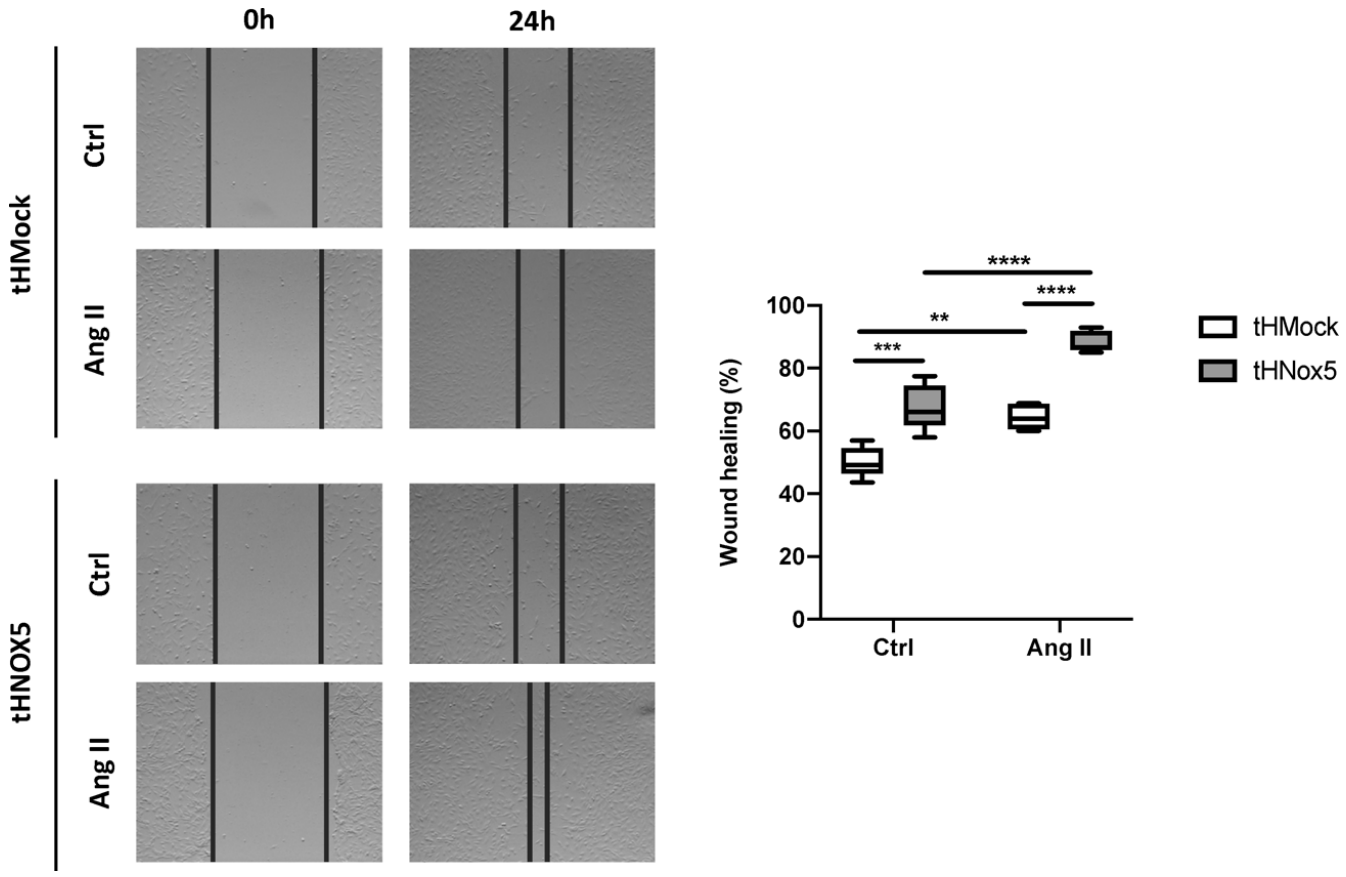


Figure S5. Ang II potentiates the promigratory phenotype of NOX5 overexpressing cells. Left panel: Representative images of tHMock and tHNOX5 cells at baseline and stimulated with 0.25μM Ang II 0 and 24 h after the scratch of wound healing assay. Right panel: Quantification of the wound healing assay of tHMock and tHNOX5 cultures at baseline and stimulated with 0.25 μM Ang II (n=6). tHMock: stable cell line transfected with pcDNA3.2-Mock. tHNOX5: stable cell line transfected with pcDNA3.2-NOX5. ns: not significant differences, **p<0.01, ***p<0.001, ****p<0.0001. Data are presented as median and IQR.

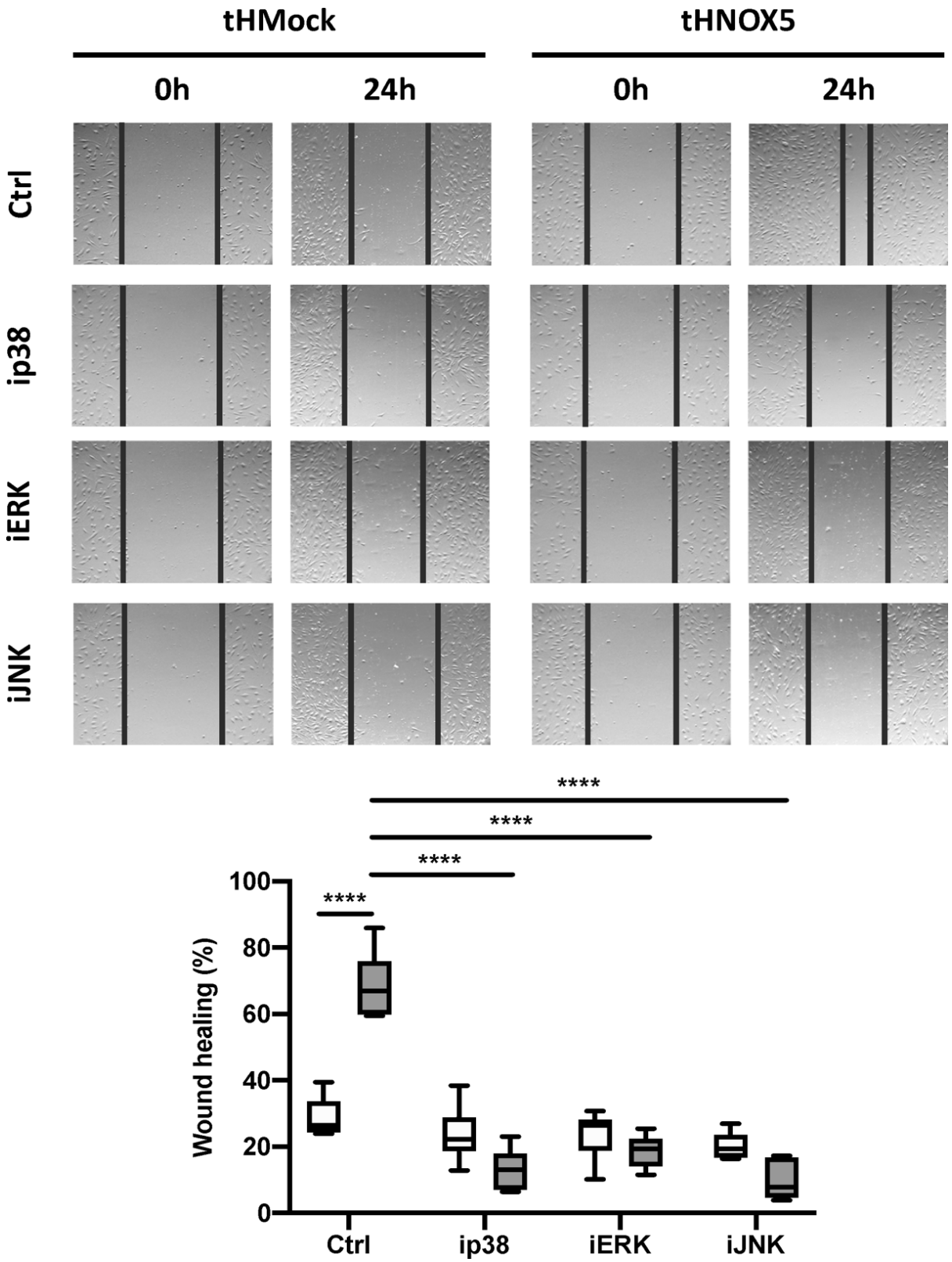


Figure S6. p38 MAPK, MEK/ERK and JNK pathways are involved NOX5-dependent endothelial cell migration. Upper panel: Representative images of tHMock and tHNOX5 cells in the absence (Ctrl) or presence of 5 μM 219138-24-6 (p28 MAPK inhibitor, ip38), PD98059 (MEK/ERK inhibitor, iERK) or JNK-IN-8 (JNK inhibitor, iJNK) 0 and 24 h after the scratch of wound healing assay (n=6). Bottom panel: Quantification of the wound healing assay. tHMock: stable cell line transfected with pcDNA3.2-Mock. tHNOX5: stable cell line transfected with pcDNA3.2-NOX5. ****$p<0.0001$. Data are presented as median and IQR.

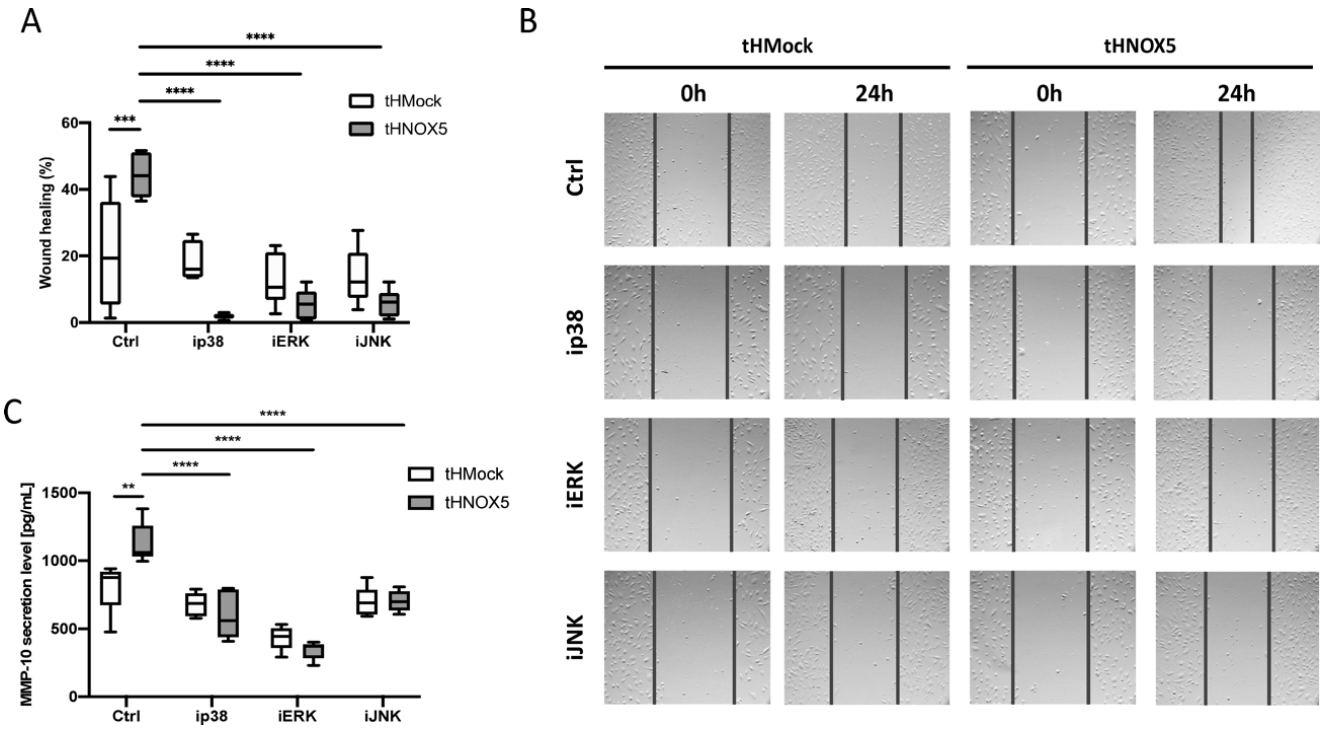


Figure S7. p38 MAPK, ERK and JNK pathways are involved in the MMP-10 secretion and endothelial cell migration triggered by Ang II-mediated NOX5 activation. (A) Quantification of the wound healing assay of tHMock and tHNOX5 control cells in the absence or presence of 5 μM 219138-24-6 (p28 MAPK inhibitor, ip38), PD98059 (MEK/ERK inhibitor, iERK) or JNK-IN-8 (JNK inhibitor, iJNK) 0 and 24 h after the scratch of wound healing assay and Ang II stimulation (n=6). (B) Representative images of the wound healing assay. (C) Accumulated MMP-10 protein in cell supernatant from tHMock and tHNOX5 cells treated as indicated in A and stimulated with Ang II for 48 h (n=6). tHMock: stable cell line transfected with pcDNA3.2-Mock. tHNOX5: stable cell line transfected with pcDNA3.2-NOX5. **p<0.01, ***p<0.001, ****p<0.0001. Data are presented as median and IQR.

pcDNA3.2-NOX5β expression plasmid (7,642 nucleotides)

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