

## Supplementary Materials:

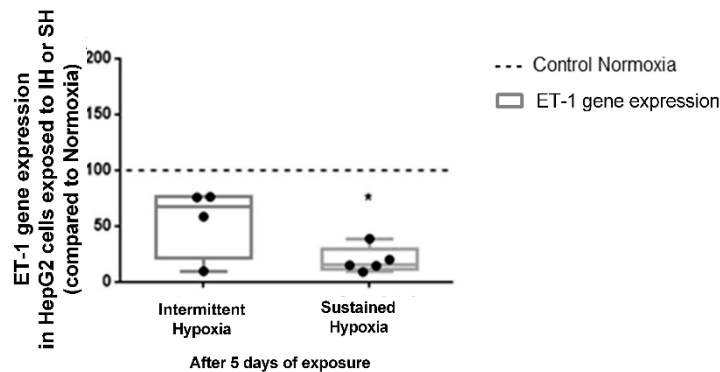
- Supplementary data

### QPCR Primers

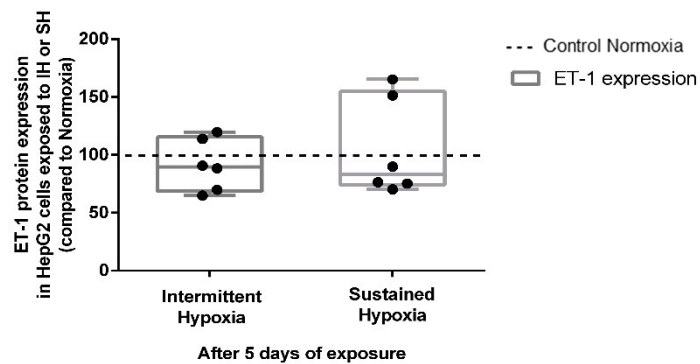
Gene expression was normalized to HPRT1 and RPLP0 rRNA content as internal controls and expressed as fold change compared with control. The primers sequences associated with the 3 genes tested are summarized were as follows: with the following qPCR program: 1 cycle: 15min, 95°C, 40 cycles: 15sec-94°C, 30sec-60°C, 30sec-72°C, 1 cycle: 1min-95°C, 30sec-60°C, 30sec-95°C.

Gene expression was quantified using the comparative threshold cycle (Ct) method<sup>14</sup> with a normalization against HPRT1 (F- TCTTTGCTGACCTGCTGGATTACAT, R- CCAGGGAAAGCAAAGTTTGCATT) and RPLP0 (F- CCCTGCACTCTCGCTTCTGGA, R- AGGGCAGCAGCCGCAAATG). HIF-1 $\alpha$  (Hif1a F- CGGCGACATGGTTTACATTCTG, R- CTTTCTCACTGGGCCATTCTGT), endothelin-1 (Edn1, F- CGTACCGTATGGACTGGGAG, R- GAGCGCACTGACATCTAACTG), VEGF-A (Vegfa F- CTTCAAGCCATCCTGTGTGC, R- TTGCTCTATCTTTCTTTGGTCTGC).

- Supplementary Figures



(a)

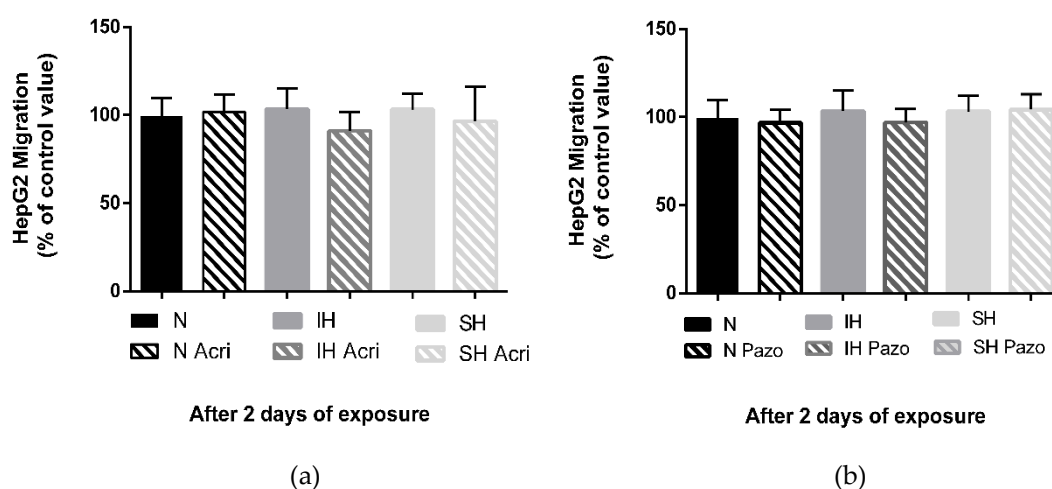


(b)

Supplementary Figure S1. In vitro effects of IH and SH on ET-1 gene expression and protein expression

(a). SH but not IH is associated with a significant decrease of ET-1 gene expression in HepG2 cells after 5 days of exposure ( $p<0.05$ ). The levels of ET-1 gene expression was measured by RT-QPCR;  $n= 3$  independent experiments/group. \* $p<0.05$ , Mann-Whitney test.

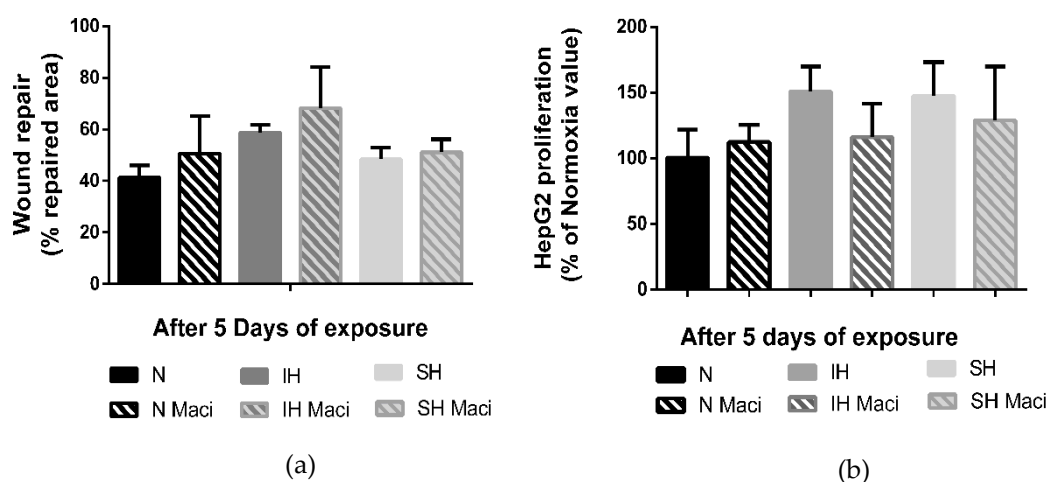
(b). Neither Intermittent Hypoxia nor Sustained Hypoxia modify ET-1 protein secretion by HepG2 cells after 5 days of exposure. The levels of Et-1 protein secreted was measured by Elisa on super natant;  $n= 3$  independent experiments/group, Mann-Whitney test.



Supplementary Figure S2.

(a). Migration, expressed as a % of control values, of viable HepG2 cells after 2 days of Normoxia, Intermittent Hypoxia or Sustained Hypoxia and treated or not by acriflavine (acri);  $n=3$  independent experiment/group (9 wells/group: 2 transwells/experiments). Mann-Whitney test.  $p$  NS, Mann-Whitney test.

(b). Migration, expressed as a % of control values, of viable HepG2 cells after 2 days of Normoxia, Intermittent Hypoxia or Sustained Hypoxia and treated or not by pazopanib (pazo);  $n=3$  independent experiment/group (9 wells/group: 2 transwells/experiments). Mann-Whitney test.  $p$  NS, Mann-Whitney test.



Supplementary Figure S3

(a). Wound healing repair, expressed as a % of repaired area, of HepG2 t least 3 wells/experiment after 5 days of Normoxia, Intermittent Hypoxia or Sustained Hypoxia and treated or not by macitentan (maci). p NS, Mann-Whitney test.

(b) Proliferation, expressed as a % of Normoxia, of viable HepG2 cells quantified by MTT staining after 5 days of Normoxia, Intermittent Hypoxia or Sustained Hypoxia and treated or not by macitentan (maci); n=3 independent experiment/group (6 wells/group: 2 transwells/experiments). p NS, Mann-Whitney test.