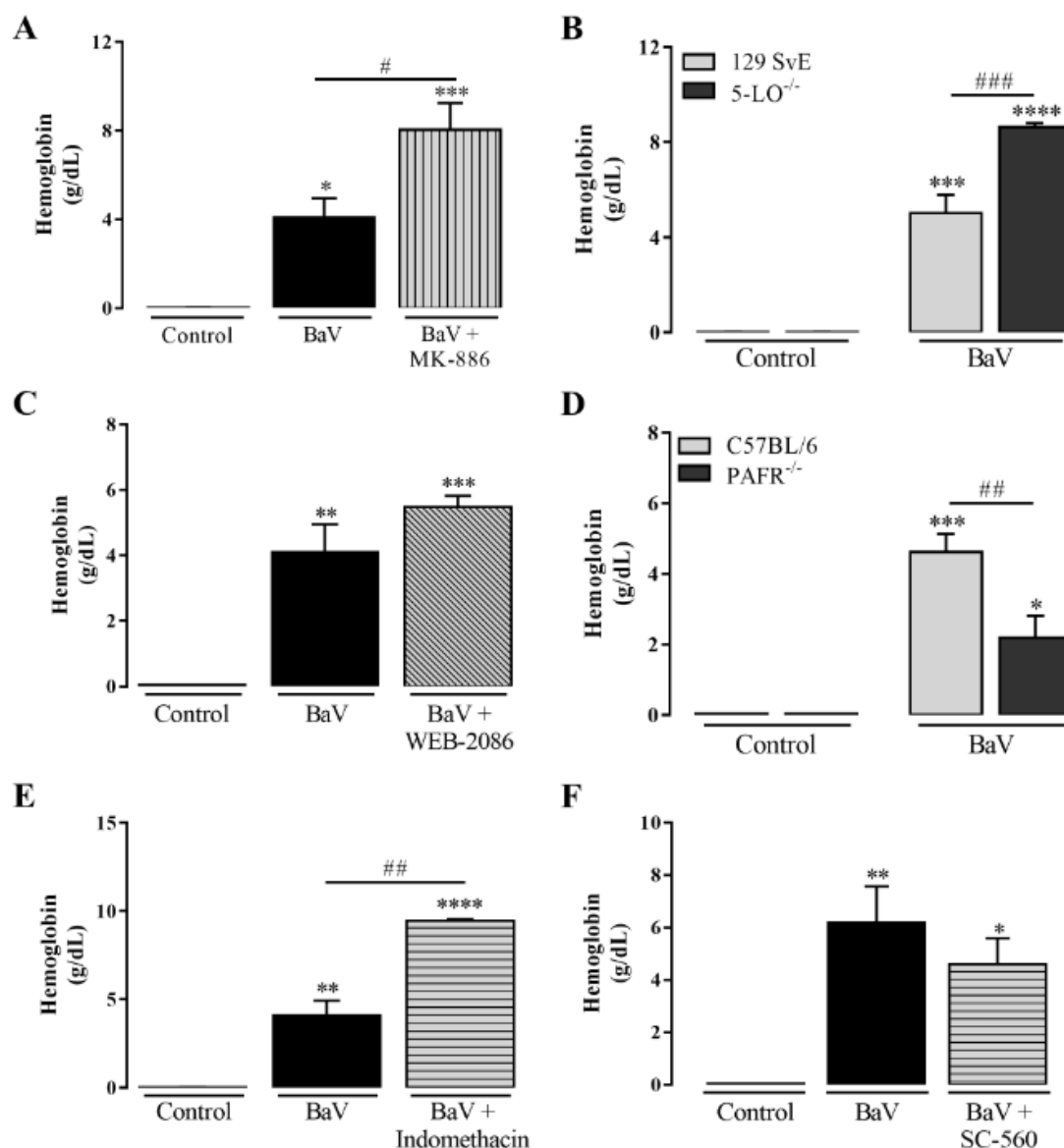
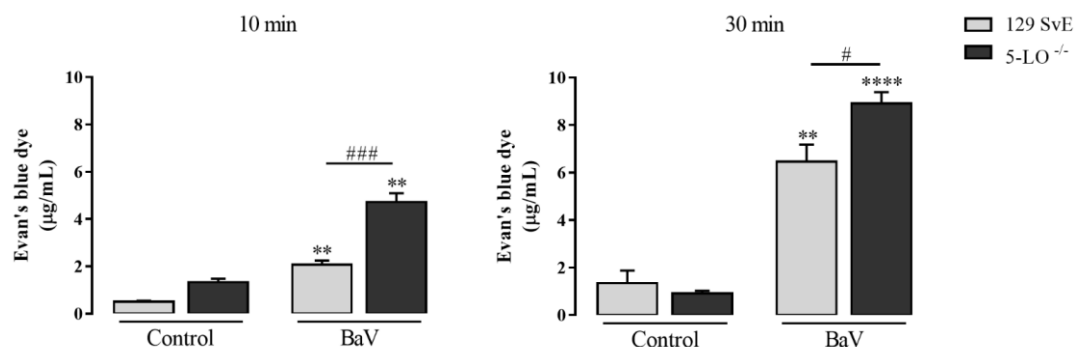


# Supplementary Materials: *Bitis arietans* Snake Venom Induces an Inflammatory Response Which is Partially Dependent on Lipid Mediators

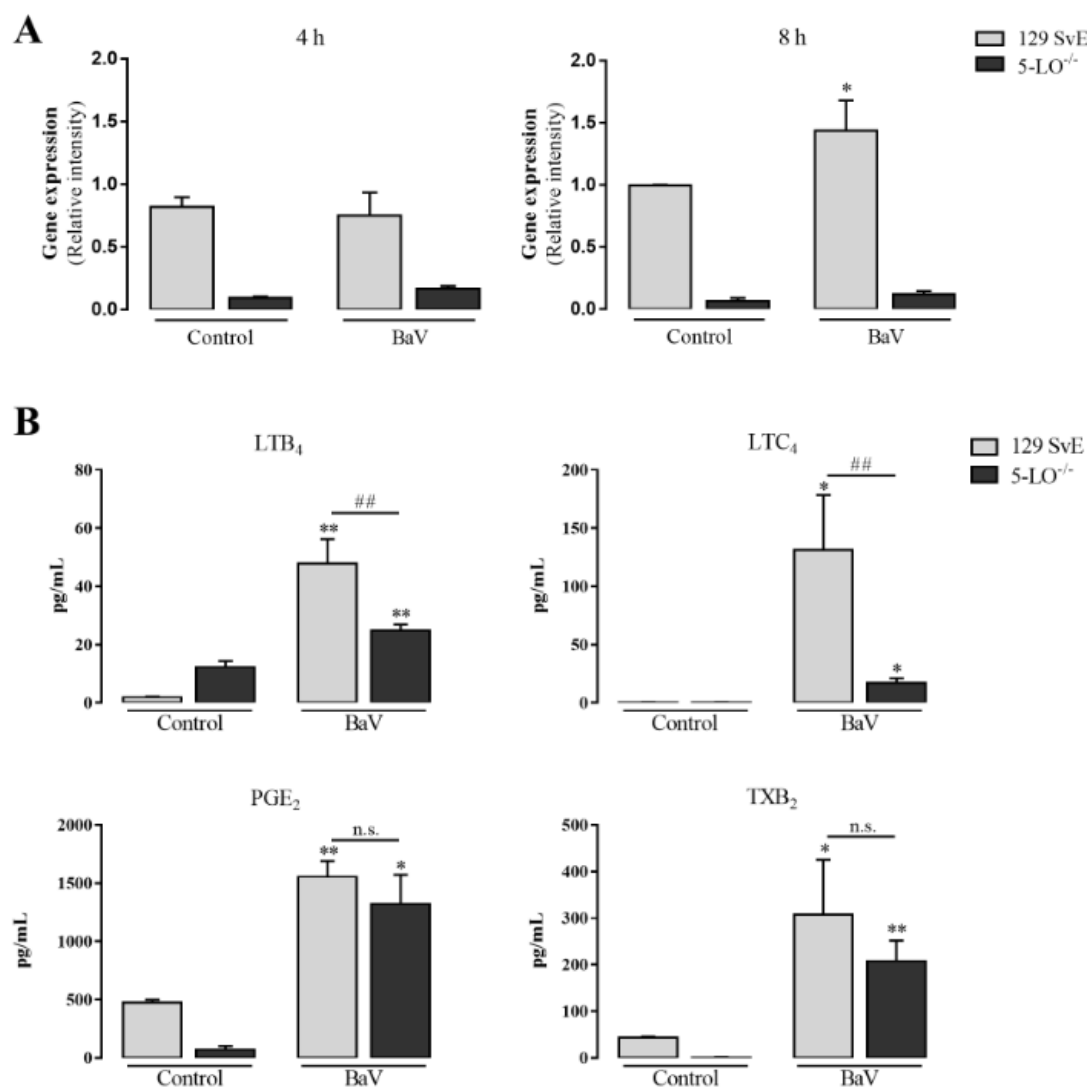
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**Figure S1.** Local hemorrhage induced by BaV. Hemorrhage was evaluated in C57BL/6 mice pre-treated with anti-inflammatory drugs and in 5-LO<sup>-/-</sup> and PAFR<sup>-/-</sup> genetically deficient mice. After 4 h of i.p. BaV inoculation (0.5 mg/kg), peritoneal exudate was harvested to evaluate the hemorrhage by hemoglobin quantification. The participation of leukotrienes was evaluated in: (A) mice pre-treated with MK-886 or (B) in mice genetically deficient of 5-LO (5-LO<sup>-/-</sup>). The participation of PAFR was evaluated in: (C) mice pre-treated with WEB-2086 or (D) in mice genetically deficient of PAFR (PAFR<sup>-/-</sup>). The participation of prostanoids was evaluated in mice pre-treated with: (E) Indomethacin; and (F) SC-560. (\*) Differences between BaV and control; (#) differences between mice pre-treated or not with anti-inflammatory drugs and 5-LO<sup>-/-</sup> and PAFR<sup>-/-</sup> mice compared to 129 SvE and C57BL/6 mice, respectively. Results were expressed as mean ± SD (4–5 mice) of three reproducible assays. (\* or #)  $p < 0.05$ , (\*\* or ##)  $p < 0.01$ , (\*\*\*)  $p < 0.001$  and (\*\*\*\*)  $p < 0.0001$ .

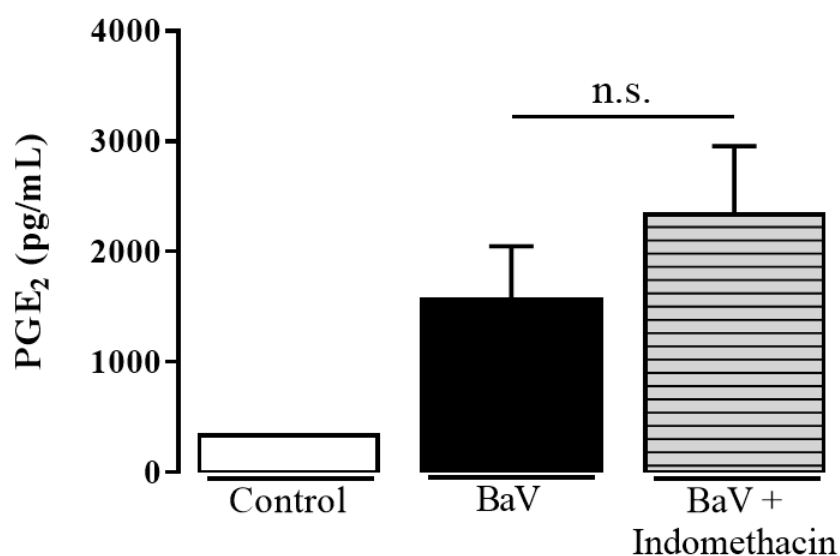


**Figure S2.** Vascular leakage in 129 SvE and 5-LO<sup>-/-</sup> mice. After 10 min and 30 min of i.p. BaV inoculation (0.5 mg/kg), peritoneal exudate was harvested to evaluate the increase in vascular permeability by Evan's Blue dye extravasation. (\*) Differences between BaV and control; (#) differences between 129 SvE and 5-LO<sup>-/-</sup> mice. Results were expressed as mean  $\pm$  SD (4–5 mice) of three reproducible assays. (#)  $p < 0.05$ , (\*\*)  $p < 0.01$ , (\*\*\*)  $p < 0.001$  and (\*\*\*\*)  $p < 0.0001$ .



**Figure S3.** Expression of 5-LO enzyme and the production of lipid mediators in 5-LO<sup>-/-</sup> and 129 SvE mice. After selected periods of i.p. BaV inoculation (0.5 mg/kg), peritoneal exudate was harvested to evaluate: (A) Gene expression of 5-LO after 4 h and 8 h; and (B) production of eicosanoids LTB<sub>4</sub>, LTC<sub>4</sub>, PGE<sub>2</sub> and TXB<sub>2</sub>, after 30 min. (\*) Differences between BaV and control; (#) differences between 129

SvE and 5-LO<sup>-/-</sup> mice. n.s.: not significant. Results were expressed as mean  $\pm$  SD (4–5 mice) of three reproducible assays. (\*)  $p < 0.05$  and (\*\*) or ##)  $p < 0.01$ .



**Figure S4.** Production of PGE<sub>2</sub> after 4 h of BaV inoculation is not attenuate by indomethacin; 1 h before i.p. BaV inoculation (0.5 mg/kg), C57BL/6 mice were s.c. treated with indomethacin (10 mg/kg). After 4 h, peritoneal exudate was harvested to evaluate the production of PGE<sub>2</sub>. n.s.: not significant. Results were expressed as mean  $\pm$  SD (4–5 mice) of three reproducible assays.