

Responses to Reviewer #2

Comment #1: At a first glance, this study on NSA and AAA appears coherent and carefully conducted. Unfortunately, the main issue lies with the histochemical and immunohistochemical stains, which are captured at too low magnification and do not appear to be representative. For instance, this reviewer cannot identify any specific staining for SMC in Fig.1 A. Additionally, an image of the Masson's trichrome stain, which is used to assess collagen content, is missing. A similar problem exists with Figure 6: Large parts of the adventitia are stained and apparently included in the evaluation, which is not representative. These issues are critical, as the entire evaluation depends on valid histochemical and immunohistochemical staining.

Response: This is a great point. As suggested, Figures 4-6 have been revised to include histological images at low and high magnifications. Figure legends have been revised accordingly.

Comment #2: What is the proposed mechanism of the induction of AAA by Ang II? This should be stated in the introduction.

Response: Thank you for your point. While Ang II-induced AAA in ApoE-deficient mice is widely used for AAA studies, underlying mechanisms are largely undefined. We included a short description for this model in the Introduction as *“Chronic subcutaneous infusion of angiotensin (Ang) II induces AAAs in suprarenal aorta in male hyperlipidemic apolipoprotein (ApoE)-deficient (ApoE -/-) mice in a blood pressure independent manner [30, 31]. Because AAAs induced by Ang II infusion simulates several features of clinical AAAs such as the progressive expansion of the aortic lumen due to the destruction of medial elastin and smooth muscle cells (SMCs), extracellular matrix remodeling, and the accumulation of macrophages and B and T lymphocytes[32], it has been widely used an AAA model to study the pathogenesis and pharmacological intervention of AAA disease[32]”*.

Comment #3: Page 7: ... NSA- (9/12, 83,3 %), than that in vehicle- (4/11, 36,4 %) should be the other way round (see parentheses)

Response: Thank you for pointing out this error. It has been corrected as *“AAA incidence was significantly lower in NSA- (4/11, 36.4%), than that in vehicle- (9/12, 83.3%), treated mice (Figs. 3A & 3B)”*.

Comment #4: English language needs improvement: Page 2: “with the later” = with the latter; Table 1: “Huaman” = human; Figure 2: “Superarenal” = suprarenal; Figure 3: “twenty-dight” = twenty-eight.

Response: We really apologize for these errors. All these have been corrected. Additionally, we have checked our manuscript to avoid any typo errors.