**Na+-H+EXCHANGER 1 DEFICIENCY PROTECTS ANGIOTENSIN II-INDUCED ABDOMINAL AORTIC ANEURYSM IN APOLIPOPROTEIN E-DEFICIENT MICE**

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**Background:** IgE plays important roles in abdominal aortic aneurysm (AAA). Our previous results suggest that IgE acts through Na+-H+ exchanger 1**(**Nhe1). Yet the function of Nhe1 in AAA remains unknown. Here we examined the function of Nhe1 in AAA progression in the apolipoprotein E-deficient (*Apoe−/−*) murine AAA model.

**Methods:** To test a direct participation of Nhe1 in AAA, we crossbred Nhe1-deficient (*Nhe1+/−*) mice with *Apoe−/−* mice and produced *Apoe−/−Nhe1+/−* and *Apoe−/−Nhe1+/+* littermates, followed by infusing them with angiotensin II (Ang II) at 1000 ng/kg/min or vehicle via subcutaneous osmotic pump. We used a pH-sensitive fluorescent dye pHrodo-succinimidyl ester (SE) to monitor pH changes in AAA lesions. We also performed near infrared fluorescent (NIRF) imaging on Ang II-induced *Apoe−/−Nhe1+/−* mice and *Apoe−/−Nhe1+/+* mice with pH sensitive probe LS662.

**Results:**In human AAA lesions, areas that contained clusters of macrophages and high amount of IgE were acidic; in contrast, regions that contained few macrophages and low levels of IgE were not. Nhe1-deficiency slowed AAA formation in *Apoe−/−*micewith reduced lesion macrophage-positive area, CD4+ T-cell number per lesion area, median SMC loss, collagen content, and media elastica fragmentation. Nhe1-deficiency also blocked lesion acidification in areas rich in macrophages and IgE, reduced cell apoptosis, and decreased serum level of TCTP (translationally controlled tumor protein). *Ex vivo* NIRF imaging showed significantly higher plaque target fluorescence to background ratio (TBR) in Ang II-induced *Apoe−/−Nhe1+/+* mice injected with a pH sensitive probe LS662 compared to Ang II-induced *Apoe−/−Nhe1+/−*or WT mice without AAA production.

**Conclusion**: Nhe1-deficiency limits AAA progression by regulating lesion inflammation, extracellular matrix remodeling, pH changes and cell apoptosis. NIRF imaging strategies may be utilized as a non-invasive and radiation-free imaging technique to improve real-time monitoring of AAA disease progression.