Genetic Disruption of Interleukin-1α Signaling Potentiates Experimental Aortic Aneurysm Formation

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Objectives: Abdominal aortic aneurysms (AAAs) are common, but the inflammatory pathways responsible for their development are incompletely described. While the genetic deletion of interleukin-1β (IL-1β) and the interleukin-1 receptor (IL1R) inhibit experimental aortic aneurysm formation, the influence of interleukin-1α (IL-1α), another IL1R ligand, is unknown. We sought to evaluate the role of IL-1α in an experimental murine AAA model and hypothesized that genetic deletion of IL-1α would inhibit aneurysm development similar to that seen with IL-1β and IL1R.

Methods and Results: Male and female mice, either wildtype (WT, control; n=13) or with genetic deletion of IL-1α (IL-1α knockout [KO]; n=23), all on a C57/BL6 background, underwent infrarenal peri-adventitial application of porcine pancreatic elastase followed by micrometric aorta evaluation and harvest at post-operative day 14. The primary outcome of percent aortic dilation at harvest was defined as the percent increase in aortic diameter comparing the unaffected suprarenal control aorta to maximal aneurysm diameter. Mann-Whitney U tests were performed to compare percent dilation of WT to IL-1α KO in both male and female groups. IL-1α KO mice demonstrated significantly greater percent dilation after two week topical elastase surgical AAA model in both sexes (males: 121.7±34.7 KO vs 99.0±12.8 WT mean percent dilation, p=0.023; females: 75.6±12.7 KO vs 55.8±5.5 WT mean percent dilation, p=0.012).

Conclusions: Contrary to our hypothesis, genetic deletion of IL-1α potentiates experimental aortic aneurysm formation. Considering that neutralization of IL-1β attenuates experimental AAA formation, our results demonstrate that IL-1α has the opposite effect on the same receptor in the setting of experimental aneurysm formation.

Figure. Abdominal aorta percent dilation by IL-1α genotype in male and female mice