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Conference Abstract

# P.30 Angiotensin II Infusion Leads to Aortic Dissection in LRP8 Deficient Mice

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## ABSTRACT

**Background/Objectives:** Myeloid cells are crucial for the development of vascular inflammation. Low-density lipoprotein receptor-related protein 8 (LRP8) or Apolipoprotein E receptor 2 (ApoER2), is expressed by macrophages, endothelial cells and platelets and has been implicated in the development of cardiovascular diseases. Our aim was to evaluate the role of LRP8, in particular from immune cells, in the development of vascular inflammation.

**Methods:** $LRP8^{+/+}$ and $LRP8^{-/-}$ mice (on B6;129S background) were infused with angiotensin II (AngII, 1 mg/kg/day for 7 to 28 day) using osmotic minipumps. Blood pressure was recorded using tail cuff measurements. Vascular reactivity was assessed in isolated aortic segments. Leukocyte activation and infiltration were assessed by flow cytometry of aortic tissue and intravital videomicroscopy imaging. Histological analysis of aortic sections was conducted using sirius red staining.

**Results:** AngII infusion worsened endothelial-dependent vascular relaxation and immune cells rolling and adherence to the carotid artery in both $LRP8^{+/+}$ as well as $LRP8^{-/-}$ mice. However, only $LRP8^{-/-}$ mice demonstrated a drastically increased mortality rate in response to AngII due to aortic dissection. Bone marrow transplantation revealed that chimeras with LRP8 deficient myeloid cells phenocopied $LRP8^{-/-}$ mice.

**Conclusion:** AngII-infused LRP8 deficient mice could be a useful animal model to study aortic dissection reflecting the lethality of this disease in humans.

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