Conference Abstract

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

Jeremy Lagrange1,2,*, Stefanie Finger1, Sabine Kossmann2,3,4, Venkata Garlapati1, Wolfram Ruf2,3, Philip Wenzel2,3

1INSERM 1116
2Center for Thrombosis and Hemostasis, University Medical Center Mainz
3Center for Cardiology–Cardiology I, University Medical Center Mainz
4The Heart Research Institute
5Department of Immunology and Microbial Science, Scripps Research

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.

REFERENCES

[1] Wenzel P, Knorr M, Kossmann S, Stratmann J, Hausing M, Schuhmacher S, et al. Lysozyme M-positive monocytes mediate angiotensin II-induced arterial hypertension and vascular dysfunction. Circulation 2011;124:1370–81.

[2] Kossmann S, Lagrange J, Jäckel S, Jurk K, Ehiken M, Schöpf T, et al. Platelet-localized FXI promotes a vascular coagulation-inflammatory circuit in arterial hypertension. Sci. Transl. Med. 2017;9.

© 2020 Association for Research into Arterial Structure and Physiology. Publishing services by Atlantis Press International B.V. This is an open access article distributed under the CC BY-NC 4.0 license (http://creativecommons.org/licenses/by-nc/4.0/).

*Corresponding author. Email: jeremy.lagrange@inserm.fr