Abstract: **P4144**

**Pericyte-specific deletion of ninjurin1 induces abnormal vasa vasorum formation and persistent inflammation and enhances intimal hyperplasia of injured vasculature.**

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Introduction - Atherosclerosis is fundamental pathological condition inducing severe ischemic diseases such as ischemic heart disease and stroke. New concept has been proposed that adventitial abnormalities including enhanced malformation of adventitial microvessel, vasa vasorum are associated with development and vulnerability of atherosclerotic plaque. However, the role of vasa vasorum malformation in vascular remodelling has not been fully clarified. We recently reported that Ninjurin1 (Ninj1) is critical adhesion molecule to associate pericytes (PCs) with endothelial (EC) tubes to form stabilized mature neovessels. The purpose of this study is to examine if formation of adventitial microvessels affects the vascular remodelling of injured vessels using PCs-specific Ninj1 deletion mouse model.

Methods & Results - Deletion of Ninj1 gene in NG2-positive PCs was induced by tamoxifen(Tam)-treated NG2-CreER/Ninj1loxp mice (Ninj1KO, n=9). Tam-treated-NG2-CreER (n=4) or Tam-nontreated NG2-CreER/Ninj1loxp (n=5) mice were used as Control (Ct1 and Ct2 respectively). Femoral arteries were injured by insertion of coiled wire. After 4 weeks of surgery, blood vessels were stained by venous injection of FITC-lectin. Isolated femoral arteries were fixed with paraformaldehyde and decolorized with CUBIC reagent. Wire-mediated vessel injury induced intimal hyperplasia, as assessed by intima/media (I/M) ratio and accordingly grew microvessels in adventitia. Intimal hyperplasia in Ninj1KO were significantly enhanced compared to Controls. Although there was no significant difference in total length of adventitial microvessels among three groups, extravasation of FITC-lectin from adventitial microvessels were significantly enhanced in Ninj1KO. The number of infiltrated macrophages in adventitia were increased in Ninj1KO.

Conclusion - Deletion of Ninj1 in PCs contributes to formation of immature microvessels in adventitia of injured vasculature and to adventitial microbleeding, and subsequently enhances intimal hyperplasia. Ninj1 is an attractive target to normalize microvessels for anti-atherosclerotic therapy.