**CXCR6/CXCL16 AXIS IS INVOLVED IN MONONUCLEAR CELL ADHESION INDUCED BY ANGIOTENSIN II, POTENTIAL IMPLICATION IN ABDOMINAL AORTIC ANEURYSM (AAA) FORMATION?**

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*Background and Objectives*: Abdominal aortic aneurysm (AAA) is a degenerative disease of the aorta that mainly affects elderly population over the age of 65. Nowadays the pathways involved in its onset and progression remain unknown and angiotensin-II (Ang-II) has been widely implicated. Therefore, the potential link between CXCR6/CXCL16 axis in AAA was investigated.

*Methods and Results*. Apolipoprotein E-deficient mice (apoE-/-) were subjected or not to a high-fat diet and infused with Ang-II (500 ng/kg/min) for 28 days. Some of the animals were daily treated with losartan at 10 or 30 mg/kg/day. Flow cytometry and immunofluorescence were used to determine CXCL16 expression on human umbilical vein or artery endothelial cells (HUVEC and HUAEC, respectively). Parallel-plate flow chamber assay was employed to evaluate leukocyte adhesion to Ang-II (1 microM)-stimulated human endothelium. Mice subjected to a high-fat diet and infused with Ang-II showed higher incidence of AAA, increased macrophage, CD3+ lymphocyte and CXCR6+ cell infiltration and enhanced neovascularization than unchallenged animals. These effects were accompanied by increased MCP-1/CCL2, CXCL16, CXCR6 and VEGF mRNA expression within the lesion. These events were reduced when losartan was administered at 30 but not at 10 mg/kg/day. When HUVEC and HUAEC were stimulated with 1 microM Ang-II (24h), a significant increase in CXCL16 expression was detected by flow cytometry and immunofluorescence. However, neutralization of CXCL16 activity only significantly inhibited Ang-II-induced mononuclear leukocyte-HUAEC interaction by 49% without affecting their interaction with HUVEC. Ang-II-induced CXCL16 expression was found to be dependent on Nox5 expression and subsequent RhoA/p38-MAPK/NFkB activation. *Conclusion*: These results suggest that the CXCR6/CXCL16 axis could constitute a new therapeutic strategy in the treatment of cardiovascular diseases associated with activation of the renin-angiotensin system (RAS).