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Angiotensin II and leukocyte trafficking: New insights for an old vascular mediator

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Angiotensin-II (Ang-II) is implicated in atherogenesis. We demonstrated that 4h exposure to Ang-II *in vivo* caused arteriolar leukocyte adhesion in the mesenteric microcirculation of the rat through the interaction with its AT₁ receptor¹. While mononuclear cells were the main leukocytes attached to the arteriolar endothelium, neutrophils were predominantly cells interacting with the venular endothelium. Since, the same cell adhesion molecules (CAMs) were expressed on both the arteriolar and venular endothelia in response to Ang-II¹, other mechanisms seemed to be responsible for the differential cellular distribution. Indeed, arteriolar mononuclear leukocyte recruitment by Ang-II was found to be largely mediated by tumor necrosis factor- α (TNF α)² and, fractalkine (CX₃CL1) expression was detected in both cremasteric arterioles and post-capillary venules 24h after Ang-II intrascrotal injection³. Arteriolar leukocyte adhesion was the unique parameter significantly reduced (83%) in animals lacking CX₃CL1 receptor (CX₃CR1). When human arterial and venous umbilical endothelial cells (HUAEC and HUVEC) were stimulated with 1 μ M Ang-II increased CX₃CL1 expression was detected, yet neutralization of CX₃CL1 activity only significantly inhibited Ang-II-induced mononuclear cell-HUAEC interactions. The use of siRNA revealed the involvement of TNF α in Ang-II-induced CX₃CL1 up-regulation and mononuclear cell arrest. Nox5 knock down with siRNA or pharmacological inhibition of ERK1/2, p38 MAPK and NF κ B also abolished these responses. These results suggest that targeting CX₃CL1-CX₃CR1 axis may constitute a new therapeutic strategy in the treatment of Ang-II-associated cardiovascular disorders.

- Alvarez et al., Blood 104:402-8 (2004)
- Mateo et al., Blood 110:1895-902 (2007)
- Rius et al. Arterioscler Thromb Vasc Biol 33:96-104 (2013)

Biography

Maria-Jesus Sanz completed his Ph.D. at the age of 26 years at the University of Valencia. She did Postdoctoral studies at the NHLI, Imperial College, London, UK and at the University of Calgary, Canada. She is Full Professor at the Faculty of Medicine (University of Valencia) and Head of the Inflammation group at the Health Institute INCLIVA (University Clinic Hospital of Valencia). She has published more than 80 papers in reputed journals (Circulation, Circ. Res., Blood, J. Immunol., Arterioscler Thromb Vasc Biol., Thorax, Cardiovascular Res., Br. J. Pharmacol., etc) and has been serving as an editorial board member of different journals.

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