



## Letter to the Editor

## NLRP1 inhibiting pathway to be explored in anti-atherosclerosis treatment approach

Silvia Bleda<sup>\*</sup>, Joaquin De Haro

Angiology and Vascular Surgery Department, Hospital Universitario de Getafe, Madrid, Spain

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## To Dr. Li,

Inflammation plays a crucial role in atherosclerosis. Apolipoprotein-A-IV has anti-inflammatory and likely anti-atherosclerotic effects [1]. Inflammasomes activation contributes to the vascular inflammatory response driving to atherosclerosis development and progression [2]. Peng J et al. have posed as hypothesis that apolipoprotein-A-IV may reduce inflammation acting on NLRP3/IL-1-pathway. However, this need to be further clarified.

The association between inflammation-atherosclerosis has widened way for new therapeutic approaches. The CANTOS trial has demonstrated that canakinumab reduces the risk of cardiovascular events in patients with residual inflammatory risk [3]. In contrast, in CIRT trial methotrexate has not been proved to decrease IL-1- $\beta$ , IL-6 or C-reactive-protein either cardiovascular events [4]. Due to CIRT's patients presented C-reactive-protein within the normal range, it is feasible that inflammation inhibition may only slow down atherosclerosis in a persistent pro-inflammatory response. We have previously reported that methotrexate inhibits the development of atherosclerotic

lesions. So maybe, the ability of methotrexate to reduce inflammation depends on previous inflammatory state. A novel oral NLRP3-inhibitor has already demonstrated to reduce atherosclerotic lesions [5].

These therapeutic targets represent an advance for treatment of cardiovascular diseases. However, the investigation upon the inhibition of the NLRP1 inflammasome also merits consideration. Previous researches have elucidated the role of NLRP1 in the endothelial dysfunction [2]. Therefore, assuming it as a potential successfully anti-atherosclerotic therapeutic approach and that we might be in front of a novel therapeutic approach for atherosclerosis it should be considered the study of several new drug effects on NLRP1 as a worthy research-path to be carried out.

## Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

## References

- [1] D. Recalde, M.A. Ostos, E. Badell, A.L. Garcia-Otin, J. Pidoux, G. Castro, et al., Human apolipoprotein A-IV reduces secretion of proinflammatory cytokines and atherosclerotic effects of a chronic infection mimicked by lipopolysaccharide, *Arterioscler. Thromb. Vasc. Biol.* 24 (2004) 756–761.
- [2] S. Bleda, J. de Haro, C. Varela, L. Esparza, A. Ferruelo, F. Acin, NLRP1 inflammasome, and not NLRP3, is the key in the shift to proinflammatory state on endothelial cells in peripheral arterial disease, *Int. J. Cardiol.* 172 (2014) 282–284.
- [3] P.M. Ridker, B.M. Everett, T. Thuren, J.G. MacFadyen, W.H. Chang, C. Ballantyne, et al., CANTOS Trial Group, Antiinflammatory therapy with canakinumab for atherosclerotic disease, *N. Engl. J. Med.* 377 (2017) 1119–1131.
- [4] P.M. Ridker, B.M. Everett, A. Pradhan, J.G. MacFadyen, D.H. Solomon, E. Zaharris, et al., CIRT Investigators, Low-dose methotrexate for the prevention of atherosclerotic events, *N. Engl. J. Med.* (Nov 10, 2018). <https://doi.org/10.1056/NEJMoa1809798>.
- [5] S. Carbone, A.G. Mauro, A. Prestamburgo, M.S. Halquist, P. Narayan, N. Potere, et al., An orally available NLRP3 inflammasome inhibitor prevents western diet-induced cardiac dysfunction in mice, *J. Cardiovasc. Pharmacol.* 72 (2018) 303–307.

<sup>\*</sup> Corresponding author at: Angiology and Vascular Surgery Department, Hospital Universitario Getafe, Ctra Toledo Km 12,500, 28905 Madrid, Spain.

E-mail address: [silbleik@yahoo.es](mailto:silbleik@yahoo.es) (S. Bleda).