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INFLAMMATION

NETs are involved in AAA

Neutrophil extracellular traps (NETs) induced by IL-1β promote abdominal aortic aneurysm (AAA) formation in mice. "Our findings fit to a model in which IL-1β triggers ceramide synthesis in aortic infiltrated neutrophils and induces NETosis, which further leads to AAA formation," says study investigator Akshaya Meher. "NETosis is beneficial for entrapment and clearance of pathogens, but induction of NETosis in sterile inflammation is deleterious for many chronic diseases," he explains.

Meher and colleagues detected NETs in murine and human AAA lesions through colocalized staining of two NET markers (citrullinated histone H3 and DNA) and neutrophil markers. NETs also colocalized with IL-1β staining. Blocking of IL-1β binding to its receptor using the IL-1 receptor antagonist (IL-1RA) inhibited NETosis in human isolated neutrophils. The researchers further showed that ceramides are involved in IL1-β-induced NETosis *in vitro*: IL-1β treatment induced synthesis of C16-ceramide, and treatment with either IL-1RA or an inhibitor of ceramide synthesis attenuated IL1-β-induced NETosis in human neutrophils. *In vivo*, neutrophils released NETs in the early phase of AAA growth in a mouse model of AAA induced by elastase perfusion. In this model, IL-1β expression in neutrophils was required for AAA formation: *Il1b*-knockout mice were protected from AAA formation, whereas adoptive transfer of wild-type neutrophils induced aortic degradation and promoted AAA formation.

Finally, Meher and colleagues showed that treatment with the NETosis inhibitor Cl-amidine, which suppresses NETosis through inhibition of protein-arginine deiminase type 4 that mediates citrullination of histones, attenuated AAA formation in mice. "Our current interest is to determine if Cl-amidine can suppress established AAA in mice, which would lead to development of a treatment strategy for AAA," says Meher.

Irene Fernández-Ruiz

ORIGINAL ARTICLE Meher, A. K. *et al.* Novel role of IL (interleukin)-1β in neutrophil extracellular trap formation and abdominal aortic aneurysms. *Arterioscler. Thromb. Vasc. Biol.* https://doi.org/10.1161/ATVBAHA.117.309897 (2018)
FURTHER READING Raffort, J. *et al.* Monocytes and macrophages in abdominal aortic aneurysm. *Nat. Rev. Cardiol.* **14**, 457–471 (2017)