Role of Neutrophil Extracellular Traps in Abdominal Aortic Aneurysm Disease Development and Progression.

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ABSTRACT

Background: Abdominal aortic aneurysm (AAA) is a common disease involving chronic inflammation and pathophysiological characteristics. Depletion of medial smooth muscle cells (SMC) is the main reason leading to segmental expansion. Neutrophils are the first line of defense of immune system in response to infection, with releasing cellular content in the form of networks include DNA and proteins, which are termed of neutrophil extracellular traps (NETs). Recent studies demonstrated the presence of NETs in human atherosclerotic lesions, as well as AAA tissues. Necrosis has long been thought to be unregulated, however, increasing evidence asserts that it is designed by well-orchestrated signaling pathway, then it is renamed “Necroptosis”. In my research, NETs treatment contribute to SMCs death through apoptosis pathway, in the meanwhile, NETs treatment also leads to the upregulation of several genes including Receptor interacting protein kinase 1,3 (RIPK1, 3), mixed lineage kinase-like domain protein (MLKL) and Platelet-derived growth factor (PDGF). RIPK1, RIPK3 and its substrate MLKL are recognized as key steps and molecular hallmarks of necroptosis.

Aims of the study: Clarify the specific pathophysiological characteristics of AAA, investigate the influence of NETs on SMCs destiny in AAA and the underlying mechanisms, provide new treating therapy for AAA.

Results and Conclusions: Both Necroptosis and apoptosis are involved in SMCs destiny. NETs are present in AAA disease and exacerbate AAA progression and development.

Future plan: Prove the co-localization of SMCs, NETs and necroptosis/apoptosis markers through immunohistochemistry and immunofluorescence. Does inhibition of RIPK2 or MLKL affect AAA development in RIPK1+ and RIPK3− mice? (in experimental genetic murine models of RIPK1 and RIPK3 deficiency)

DISCLOSURES

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In the control group, stable increase of SMCs number is observed, in the NETs treatment group, decrease of total SMCs number is followed with slightly increase.

plate3 - Custom Region Mean vs Time
Green Objective Count (1/500X) over 3 days

In the control group, caspase signal remains stable, in the NETs treatment group, obvious increase of caspase signal is observed.

More caspase green signal is observed in NETs treatment group. NETs induces SMCs death through Apoptosis pathway.

NETs treatment leads to the change of several genes in human aortic SMCs.