Extracellular Vesical Profile: Potential Biomarkers for Abdominal Aortic Aneurysms (AAA)

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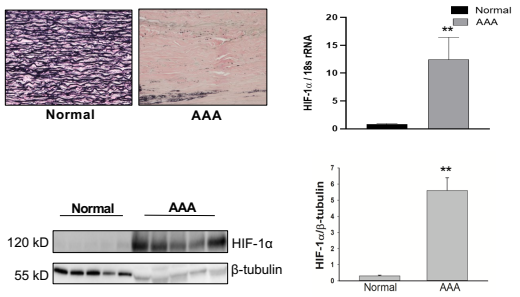
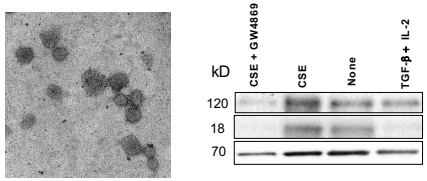
Abstract

Background: Abdominal aortic aneurysms (AAA) are a common and life-threatening condition affecting 1 in 20 elderly Americans. Cigarette smoking is a major risk factor of AAA. Aneurysm rupture is usually fatal, and currently the 15th leading cause of mortality in the USA. Thus far, AAA is the one of the few cardiovascular diseases for which there is no medical therapy to prevent or inhibit growth. Surgical repair is the only treatment option. Most patients with AAA identified by imaging (CT scan or ultrasound) are below the threshold diameter for repair and patients undergo serial imaging surveillance until the diameter is at or near the threshold for repair (diameter > 5.5 cm in men, 5.0 in women). Surveillance imaging is unsettling to patients and costly and exposing patients to increased radiation in the form of CT scans. Therefore, for both identification and risk stratification of patients with aneurysms, circulating biomarkers would be invaluable.
Objectives: To identify circulating biomarkers and thus, to identify factors that contribute to aneurysm formation.
Methods: Isolation of EVs were performed using ultracentrifugation method. Briefly, human plasma samples and cell culture media were centrifuged and ultra-centrifuged. The EVs were pelleted, verified, and characterized by transmission electron microscopy (TEM). EV protein content were extracted and analyzed by Western blot analysis.
Results: The expression of hypoxia-inducible factor 1alpha (HIF-1α) in EVs were increased in AAA patients and T cells with cigarette smoke extract exposure.
Conclusion: A specific EV profile related to AAA could be identified, and eventually be used for early diagnosis and monitoring disease progress.

Increased expression of HIF-1α is associated with AAA in human.

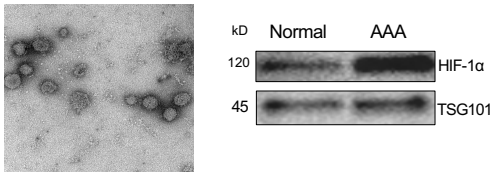


HIF-1α and IL-17 are presented in EVs isolated from CD4⁺ T cell culture media



CSE: cigarette smoke extract; GW4869: an EV inhibitor

HIF-1α is present in EVs isolated from human plasma



Conclusion and future direction

- HIF-1α is upregulated in human AAA.
- HIF-1α are present in EVs isolated from human plasma and has a trend toward higher in AAA patients.
- Cigarette smoke extract (CSE) induced HIF-1α levels in EVs isolated from CD4⁺ T cell culture media. EV release can be inhibited by GW4869, an exosome inhibitor.
- Further determining inflammatory cytokines in EVs will be performed by cytokine array.
- Further metabolome profiling of EVs from patients will be studied.

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