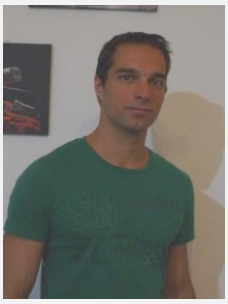
ImmunoTools *special* Award 2014



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Pathophysiology of thoracic aortic aneurysms: Cell based proteomic analyses and characterization of cell biology

Aortic aneurysms (AAs) are an increasing health problem. Based on the increased age of the population and improved diagnostic tools, the number of reported cases rises more and more. The asymptomatic progression and the fact that 90% of ruptured AAs are lethal, let aortic aneurysms become a life threatening disease.

According to their location they could be classified into abdominal aortic aneurysms (AAAs) located in the infrarenal section and thoracic aortic aneurysms (TAAs) located either at the aortic arch, the ascending or descending aorta. TAAs show a 5-years survival rate of only 64% in untreated patients.

The development of TAAs is a multifactorial process, involving pathological re-modelling of the aortic vessel wall. This results in dilatation and weakening of the vessel wall, as well as loss of vascular smooth muscle cells (v-SMCs) and degeneration of the extracellular matrix (ECM). Expression of matrix metalloproteinases (MMPs) and their inhibitors (TIMPs), which are necessary for the functionality of the ECM and are among others produced by macrophages, are altered leading to a functional disruption of the vessel wall. This could lead to destruction of elastin and collagen and in this way to loss of stability and elasticity. Reasons for the altered expression are mainly unknown. Also the impact of invading inflammatory cells like T-cells and monocytes during TAA formation is not clear until now but could be of high importance, which became an interesting topic of our research.

Because no prognostic markers or drug treatment is available, the only option is monitoring and in case of risk of rupture, surgical removal. Understanding TAA development, unravelling of underlying molecular mechanism could be the first step for potential non-surgical treatment options. To get a more precise insight, it is necessary to distinguish better and more accurately the changes go ahead.

In the course of the present project our group aims at comparing differences in protein expression of cells from aneurysmal and healthy aortas. After having received specimens from the Department of Cardiac Surgery, we investigate structural differences through various histological staining techniques. Preliminary data suggests the presence of macrophages within the aortic media, representing a hint for an impact of inflammation in TAA development. Based on these preliminary data we plan an in deep investigation of the influence of other immune cells on TAA development.

First we investigate the subtypes and the influence of inflammatory cells and their secreted cytokines on expression of cells from the aorta. From patient material we are able to isolate primary smooth muscle and fibroblast cells and detected already increased secretion IL-6 levels in supernatants of SMCs and fibroblasts from TAV patients compared to cells of healthy donors. We want to investigate this difference between the groups and also expression differences of other inflammatory cytokines like IL-2, IL-4, IL-8, TNF-α, IFN-γ which are playing a role for inflammatory cell recruiting and development. Further we want to stimulate primary SMCs with recombinant cytokines like IL-4, IL-6, IL-8, IL-10, TNF-α, IFN-γ, TGF-β, MCP-1, MIP-1α which would be secreted by such inflammatory cells and investigate expression response of our cells via RealTime-PCR and ELISA to examine the inflammatory cascade. Also differences in survival and proliferation of SMCs from healthy and aneurysm aortas will be investigated via Annexin V staining and scratch assay technique to get a better knowledge of the processes which lead to medial degeneration.

For the present study high quality antibodies and recombinant cytokines would be an important tool and with the terrific ImmunoTools reagents we could bring the contribution of inflammatory cells in aneurysm development to light.

ImmunoTools *special* AWARD for **Christian Stern** includes 25 reagents

FITC - conjugated Annexin V,

human IFN-gamma ELISA-set for 96 wells, human IL-4 ELISA-set for 96 wells, human IL-6 ELISA-set for 96 wells, human IL-8 ELISA-set for 96 wells, human TNF-alpha ELISA-set for 96 wells, (each 3 reagents),

recombinant human cytokines: rh IFNgamma, rh IL-4, rh IL-6, rh IL-8, rh IL-10, rh MCP1 / CCL2, rh MIP-1α/ CCL3, rh TGF-beta3, rh TNFα

DETAILS more AWARDS