ImmunoTools *special* Award 2014

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Small heat shock proteins and vascular dynamics

The vascular system provides vital support for sustenance, maintenance and defence of an organism. Several extrinsic and intrinsic factors govern the dynamics of blood flow within the blood vessel. Understanding the conventional and non-conventional modes of vascular dynamics thus becomes imperative not only to gain insights into the mechanisms of function, but also address approaches to control vascular diseases.

The endothelium is a thin layer of cells that lines the entire circulatory system. Endothelial cells and Smooth muscle cells are the major cell types that constantly interface blood in the vessels and are subjected to variety of physiological and non-physiological stresses that result onset of several diseases such as hypertension, hypotension and atherosclerosis. At the cellular level, the vascular tone is regulated by dynamic reorganization of cytoskeletal proteins, especially actin filaments. Dynamic regulation of actin reorganization is essential for several cellular functions such as invasion, motility, endocytosis, intracellular transport, muscle contraction etc.

Small heat shock proteins (sHsps) belong to class of low molecular weight (20-40 kDa) that are expressed in cells that in addition to their function of molecular chaperones assisting protein folding, prevent formation of toxic aggregates and amyloids of proteins. About 10 different sHsps are expressed in mammalian cells of which HspB1, B5 and B8 are stress inducible. Work from our laboratory and that of others have shown that both HspB1 and B5 bind to actin and regulate their dynamics. While HspB5 binds to stress fibres and prevent their de-polymerization HspB1 binds to monomeric actin and prevents its polymerization. Thus the dynamic interplay of these small heat shock proteins in vascular endothelium plays an important role in regulating the vascular tone.

The expression of HspB1 and HspB5 and their interaction with actin are regulated by several mechanisms that are in-turn governed by a cascade of interacting signalling pathways. We would like to explore how molecules like Endothelin, Angiotensin, VEGF, IFN-γ, and TNF-α and interleukins such as IL6, IL1 influence expression, localization or interaction of HspB1 and HspB5 with actin filaments.

Our preliminary results indicated angiotensin enhances the expression of HspB5 in vascular endothelium of rats. We are interested in exploring whether the enhanced expression of these HspB1 and B5 will lead to lymphocyte infiltration, as had been demonstrated in neurodegenerative disorders in EAE model in rats. In addition, we plan to explore whether lymphocyte infiltration would influence the interaction of sHsps with actin and hence alter the arterial smooth muscle contraction / relaxation.

Initially our study will focus on cell culture models. We will treat the cells with cytokines / growth factors and Angiotensin and study their influences on the expression / localization of Hsp B1 and B5 in vascular smooth muscle cells and vascular endothelial cells. We will explore the effects of over expression or silencing these molecules on various cellular functions such as division / migration / motility of both the cell types. The cytokine profiles under these experimental conditions will be explored by ELISA based methods. We will also explore assessing the contractile functions of smooth muscles by various direct and in direct pointers.

Thus the antibodies/ growth factors/cytokines/ ELISA reagents from ImmunoTools will be extremely helpful in conducting this research and developing leads for regulation of vascular diseases such as hypertension and atherosclerosis by alternate approaches.

ImmunoTools *special* AWARD for **K. Sridhar Rao** includes 25 reagents

FITC - conjugated anti-human CD4,

PE - conjugated anti-human CD8, IFN-gamma, IL-6, IL-8, TNF-alpha,

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

recombinant human cytokines: rh-EGF, rh-FGF2, rh-IFN gamma, rh-IGF-1, rh-PDGFBB, rh-VEGF-165, rh-TNF-alpha,

recombinant rat cytokines: rr-IFN-gamma rr-TNF-alpha, rr-VEGF

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