The purine nucleoside, adenosine is a critically important molecule in the heart is both released to act as a local hormone and taken up and metabolized by heart cells. Adenosine and adenosine analogs are used clinically to treat various cardiac conditions. Since adenosine is not lipophilic, it requires specialized transport proteins, transporters, to cross celllular membranes. These transporters are known as nucleoside transporters because they transport other nucleosides (such as inosine and guanosine) and the presence and activity of nucleoside transporters can significantly modulate the levels of nucleosides such as adenosine resulting in complex cellular effects. Although adenosine and adenosine signaling have been very widely studied in mammalian cells and human tissues, nothing is known about the presence and function of nucleoside transporters in the human heart. Therefore, we undertook a project in collaboration with the cardiac team at Southlake Regional Healthcare Centre, to study the distribution of all seven nucleoside transporter isoforms in human heart tissue. We obtained very small amounts of human tissue from patients undergoing a variety of cardiac procedures. This tissue was then used in quantitative real-time PCR to determine the expression levels of nucleoside transporters. We found that individual patients have very different transporter profiles, almost like fingerprints, but that one isoform predominanted in all patients. This is the first study to examine nucleoside transporter profiles in human cardiovascular tissue and lays the foundation for a deeper understanding of the role of these transport proteins in human cardiovascular physiology.

Reference: Marvi M, Rose JB, Bang A, Moon BC, Pozeg Z, Ibrahim M, Peniston C, Coe IR. Nucleoside transporter expression profiles in human cardiac tissue show striking individual variability with overall predominance of hENT1. Eur J Pharm Sci. 2010 Dec 23;41(5):685-91.

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Increased muscle activity, through functional overload, is an important stimulus for blood vessel growth, a process termed angiogenesis. Angiogenesis in response to muscle overload is associated with increased levels of both vascular endothelial growth factor (VEGF) and matrix metalloproteinase (MMP)-2. However, the key cellular sources of VEGF and MMP-2 have not yet been established. Mast cells are immune cells that reside within the muscle tissue and are known to produce VEGF and MMP-2. In this paper we sought to examine the potential role of mast cells in muscle overload-induced angiogenesis. We observed an increase in mast cell number and activation following 7 days of muscle overload. In order to assess the importance of mast cell activation to overload-induced angiogenesis, we treated animals with cromolyn, an inhibitor of mast cell activation. While cromolyn treatment blocked the muscle overload-induced increase in mast cell activation, it did not prevent the overload-induced increase in blood vessel growth. We also observed that the overload-induced increases in VEGF and MMP-2 were not altered with cromolyn treatment. These studies reveal that while mast cell activation is sensitive to mechanical overload in skeletal muscle, this activation is not necessary for the increased levels of pro-angiogenic factors or the increase in blood vessel growth in skeletal muscle.

Reference: Doyle JL, Haas TL.The angiogenic response to skeletal muscle overload is not dependent on mast cell activation. Microcirculation. 2010 Oct;17(7):548-56.

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