Title - Skeletal Muscle May Interact With Vasculature Through O-GlcNAc transferase (OGT)

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Abstract: Cellular communication occurs in a variety of ways such as the initiation of signaling cascades and regulation of gene expression. Through another such process, post-translational modification, proteins may be modified by enzymes such as O-linked N-Acetylglucosamine Transferase (OGT), which adds an N-acetylglucosamine (O-GlcNAc) moiety to a serine or threonine residue of the protein. On the other hand O-GlcNAcase (OGA) catalyzes the removal of an N-acetylglucosamine modification via hydrolytic cleavage. Through OGT and OGA working in tandem, a cycling effect of O-GlcNAc modification is created. O-GlcNAcylation is important because it can affect various functions and other modifications of proteins. Thus, it could affect phosphorylation pathways as both modifications may occur on the same amino acid residues. O-GlcNAcylation is also implicated in metabolic syndromes such as diabetes. At the center of metabolism, vasculature not only distributes nutrients and metabolites, but also actively interacts with surrounding tissue and remodels itself in response to physiologic and pathophysiologic stimuli. This sometimes occurs via chemokines secreted from muscle cells, which are known as myokines. Many myokines are involved with inflammation, meaning that they could be markers of vascular disease such as atherosclerosis. Using an OGT skeletal muscle knock-out murine model, we have set out to examine the effects of OGT on vasculature with the goal of identifying basic mechanisms underlying interactions between skeletal muscle and

vasculature. Here, we hope to examine whether OGT knock-out has an effect on myokines that are known to affect vasculature. This study may shed new light on heterocellular metabolism and present new therapeutic potential for metabolic syndromes.

Christian worldview integration: Our Christian worldview has played a critical role in the design and communication of our research, which studies the interactions between skeletal muscle and vasculature. Firstly, we acknowledge that in whatever we do, we must work whole-heartedly as if working for God, as the Bible tells us. Also, in designing our research, we were careful to follow principles that honor God. One example is that in the handling of mice or other animals, we recognize that these animals are God's creation. As a result, we intentionally treat them with the most care and respect that is possible, in light of the experiments we are doing. We also intend to use our research not for selfish purposes, but to better allow us and others to understand the wonder of God's creation. This is important, because as the intricate workings of God's creation are revealed, it can serve as a testimony to the glory of God and open people's eyes so that they may see and know him. The research we are presenting here is not only important for the scientific community, but it is relevant to the culture we all live in. Understanding the interactions between skeletal muscle and vasculature that we discuss can have huge roles in understanding the pathogenesis of countless diseases, some of which are prevalent in the United States. Once the understanding of these interactions is sufficient, it will be possible for therapies to be developed based on the understanding of the interactions. This will allow for the treatment of many diseases that are plaguing Americans today.