

My broad research interests include understanding the underlying metabolic changes in skeletal muscle that trigger muscle atrophy in aging and age-related diseases. I was trained in studying aging biology under the guidance of Dr. Holly Van Remmen, Dr. Arlan Richardson, Dr. Sue Bodine, and Dr. Benjamin Miller during my postdoctoral studies where I studied underlying mechanisms that contribute to sarcopenia. My prior work has shown that lipid mediators known as oxylipins are key contributors of age-related muscle atrophy. I am currently funded by the American Federation for Aging Research (AFAR) to study if biologically active lipid mediators impair recovery of disuse-atrophy in aged rats.

Current Research

Older humans fail to recover skeletal muscle mass and function after disuse atrophy, which contrasts with young and adult humans. These failed periods of recovery accelerate sarcopenia, and the associated increases in morbidity and mortality. We do not understand why older adults fail to recover muscle mass and function following disuse atrophy.

Oxylipins (mono-oxygenated and lipid hydroperoxides) are bioactive lipids derived from polyunsaturated fatty acids. Oxylipins generated by 12/15-Lipoxygenase (12/15-Lox) can impair muscle by promoting inflammation and oxidative stress. Our data show that oxylipins generated by 12/15-Lox are greater in muscle from aged rats when compared to muscle from adult rats. The generation of lipid hydroperoxides via 12/15-Lox can trigger lipid peroxidation, which is a chain reaction of oxidation of unsaturated fatty acids. Our preliminary study also showed that 4-HNE, a marker of lipid peroxidation, is greater in aged muscle after disuse atrophy when compared to aged weight bearing muscle. We have shown that phospholipid hydroperoxide glutathione peroxidase (GPx4) is an antioxidant enzyme that can protect against lipid peroxidation and mitigate sarcopenia in aged mice. We show that when compared to aged weight bearing muscle, GPx4 protein content is lower in muscle after disuse atrophy as well as after 14 days of recovery.

Our hypothesis is that oxylipins generated by 12/15-Lox impair the recovery of muscle mass and function after disuse atrophy in aged rats. We are using pharmacological approaches designed to block 12/15-Lox or reduce lipid hydroperoxides in aged rats to test this central hypothesis.

Future Research

Many cancers are associated with cachexia, a severe loss of muscle mass and function that often involves loss of fat mass. Cachexia affects 50% of patients with cancer and is associated with a poor cancer survival prognosis. Reports have demonstrated that mitigating cancer-induced muscle atrophy slows tumor growth, which suggests that treating cachexia improves cancer outcomes. Cancer predominantly occurs in aged individuals. Despite this fact, the majority of current research studying cancer and cancer-related outcomes such as cachexia is performed in young pre-clinical models. Therapeutic interventions that work in young pre-clinical models for cancer and cancer-cachexia may not work in aged models, leading to the failure to translate therapies for cancer and cancer cachexia.

We have shown that biologically active lipid mediators generated from 12/15-Lox are drivers of both age and cancer-related muscle atrophy and dysfunction. We hypothesize that targeting lipid mediators generated from 12/15-Lox will mitigate cancer cachexia in aged pre-clinical models.