Slowing down muscle loss in heart failure patients

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Patients in advanced states of myocardial insufficiency generally lose their muscle mass and muscle strength. Indeed, that fact has, until now, negatively impacted the clinical course of the disease and has resulted in poor prognoses for patients. Such pathological muscle loss impacts the skeletal muscles in particular. The responsible molecular signaling pathways have not yet been fully understood. One cause of this degenerative process lies in the system that regulates the blood pressure and salt/water supply in the body—the so-called renin-angiotensin-aldosterone system (RAAS). This is strongly activated in the context of the disease process and associated with cardiac cachexia, leading to an increase in the formation of the effector peptide angiotensin II. Angiotensin II directly affects the muscle and increases protein degradation there, resulting in a loss of muscular mass and strength.

To date, patients suffering from heart failure have been treated with medications that inhibit the renin-angiotensin-aldosterone system. While this treatment option slows muscle loss for a certain period, conventional medications lose their efficacy after just a few years. Seeking new treatment methods, scientists collaborating with Dr. Jens Fielitz, cardiologist at the Charité and group leader at the Experimental and Clinical Research Center (ECRC) have been examining the precise signal pathway that prompts protein degradation in muscle. In particular, angiotensin II increases the production of a specific protein in muscle called muscle RING-finger 1 (MuRF1), which plays a key role in muscle loss.

"We have been able to identify and characterize the function of a new transcription factor that regulates this process. Our experiments have also revealed the specific mechanisms that either activate or inhibit the production of MuRF1 protein, that is to say that either reduce or increase muscle loss," says Privatdozent Dr. Jens Fielitz.

He adds, "Our findings can now provide insights into important unanswered questions in that they delineate a new signal pathway that is important in the emergence of cardiac cachexia." By suppressing this signal it may be possible to inhibit the muscle loss caused by angiotensin II and therefore offers high potential in terms of therapeutic options.

More information: Song, Sibylle Schmidt, Rhonda Bassel-Duby, Eric N. Olson, Jens Fielitz. "Angiotensin II Induces Skeletal Muscle Atrophy by Activating TFEB-Mediated MuRF1 Expression." *Circulation Research*, June. 2015. DOI: 10.1161/CIRCRESAHA.114.305393

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