Neurological gene *jus* is associated with aging-related muscle loss in the fly model of sarcopenia.

Soobin An, Kaveh Kiani, Melody Jabbari, Christina Talley, and Anton Bryantsev

Department of Molecular and Cellular Biology, Kennesaw State University, Kennesaw, GA

Sarcopenia is a health condition in the elderly that is associated with degradation of muscle size, mass, and function. It can cause physical disability and, in extreme cases, death. The genetic aspect of sarcopenia is still not well understood. To shed light on sarcopenia mechanisms, we investigated muscle loss in aging fruit flies, *Drosophila melanogaster*. Our hypothesis was that aging-dependent muscle degradation can be affected by suboptimal functioning of the central nervous system (CNS). We used RNA interference and tissue-specific genetic drivers to induce a selective knockdown (KD) of the *julius seizure* gene (*jus*), which is associated with neurological phenotypes. Flies with CNS-specific *jus* KD (*elav>jus* KD) demonstrated seizures and paralysis after a brief mechanical stimulation (shaking). We have compared aged *elav>jus* KD flies, (with (+) and without (-) chronic shaking treatment), with genetically matched controls (*elav*>+, + /- shaking), as well as muscle-specific *jus* KD (*Mef2>jus* KD) flies. The muscle loss was evaluated by quantifying missing muscle fibers in the jump muscle. We found that all groups had some levels of spontaneous fiber loss with age. However, *elav>jus* KD flies (+/- shaking) had strikingly more lost fibers than control (*elav*>+, +/- shaking) or *Mef2>jus* KD flies. Surprisingly, chronic stimulation of seizures and paralysis by shaking was not a contributing factor to the exacerbated muscle loss in *elav>jus* KD flies. We conclude that even subtle, not apparently noticeable, abnormalities in the functioning of the CNS can stimulate aging-related muscle loss. Our results suggest that genetic causes of sarcopenia are likely to be associated with the genes associated with the CNS functioning.