別紙４

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主　論　文　の　要　旨

論文題目　Age-dependent Functional Remodeling in Thermosensory Neurons and Behaviors of the Nematode *Caenorhabditis elegans*. (線虫温度受容神経細胞の老化に伴う機能と行動の再構築)

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論　文　内　容　の　要　旨

Physiological states modulate sensory perception and behaviors of animals. Such perceptual and behavioral flexibility is crucial for animals to meet their internal needs under various physiological conditions. Senescent state systemically alters the physiological conditions of animals across many phyla in the animal kingdom. However, the neural basis of the sensory and behavioral remodeling in animals under senescent states remains largely elusive. To approach this question, we scrutinize age-dependent changes in the stimuli-evoked activity of the thermosensory neuron AFD and thermosensory behaviors of the nematode Caenorhabditis elegans. In young adult animals, AFD forms response plasticity corresponding to the thermal preference of their thermosensory behaviors, which are set by the experiences of food availability and the temperatures. At the neurophysiological level, we find that the primary thermosensory neuron AFD in aged C. elegans is hypersensitive to high temperatures and shows sustained sensory-evoked calcium dynamics, resulting in a wide operating range. At the behavioral level, aged animals display cryophilic behaviors but remain plastic to acute temperature changes to reset the thermal memory utilized in thermotaxis behaviors. Over the course of aging, AFD sensory endings showed progressive reduction in

structural integrity, characterized by loss of the actin-based microvilli. While morphological changes are robust neural aging markers in C. elegans, we find no apparent correlations with either thermosensory activity or behaviors in aged animals. To address the underlying molecular mechanisms of functional remodeling observed during aging, we find that loss of the GCY-8 guanylyl cyclase activity reduces both these age-dependent morphological and behavioral changes while a wide AFD operating range still exists in gcy-8 mutants. Our work identifies the hallmarks of aging in sensory activity and learning behaviors and establishes a C. elegans model to elucidate conserved mechanisms of sensory and behavioral modulation under senescent states in animals across phyla.