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LETTER TO THE EDITOR

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Memory may be enhanced from exercise-induced myokine production of cathepsin B

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Dear Editor,

Lysosomal cysteine protease cathepsin B (CTSB) is expressed throughout the body, with high levels associated with cancer, ischemia, cell death, and neurological disorders. However, the role of CTSB in normal physiology has been less investigated.

Emerging experimental work provides evidence that acute and chronic exercises can enhance memory function [1], with recent work suggesting that exercise-induced CTSB may be a novel myokine contributing to enhanced memory function. For example, *in vivo*, exercise has been shown to elevate CTSB plasma levels and hippocampal CTSB gene expression, which suggests that exercise may have both direct and indirect CTSB effects on memory function [2]. Elevated exercise-induced CTSB enhanced neurogenesis and spatial memory, which was prevented in CTSB knockout mice [2]. Thus, it appears that CTSB is an important mediator through which exercise may influence neurogenesis and memory function. Furthermore, CTSB may also play an important role in subserving neurotransmission in the dentate gyrus [2], a critical brain structure involved in memory function. Other potential mechanisms through which exercise-induced CTSB may influence memory include alterations in BDNF (brain-derived neurotrophic factor) expression and clearance of neural debris [2].

These exciting findings place CTSB as a potential novel biomarker mediating the effects of exercise on memory. However, additional research is urgently needed in this novel line of inquiry. To my knowledge, only five studies have evaluated the effects of exercise on CTSB [2–6], with few evaluating CTSB as a potential mediator in the exercise–memory interaction. Further highlighting the urgent need for additional research in this area, the limited studies on this topic have produced mixed findings. For example, Smuder et al. [5] reported reduced CTSB gene expression in cardiac muscle of mice following 5 days of treadmill running; Salminen [6] reported minimal changes in CTSB after 8 hours of exhaustive exercise in mice; Gourgouvelis et al. [4] reported that 8 weeks of exercise among young adults had no effects on CTSB; and lastly, Wyczalkowska-Tomasik et al. [3] showed that, among rats, acute exercise differentially altered CTSB based on training status (increased CTSB levels after exercise in trained rats, with decreased levels in untrained rats).

Memory function is, unquestionably, critical for many areas of life. Thus, optimizing memory is of great interest. Loprinzi et al. [1] suggest that exercise may help contribute to enhanced optimization of memory, yet the mechanisms of this effect are not fully understood. A novel mechanism that may, in part, account for this exercise–memory interaction is alterations in CTSB. Mechanistic research on this topic is warranted, and specifically, should evaluate the role of CTSB on the relationship between exercise and memory. Such work should evaluate

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potential moderators of this effect, such as training status, exercise intensity, and memory type.

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