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Muscle wasting severity linked to type, size and location of tumor in mice

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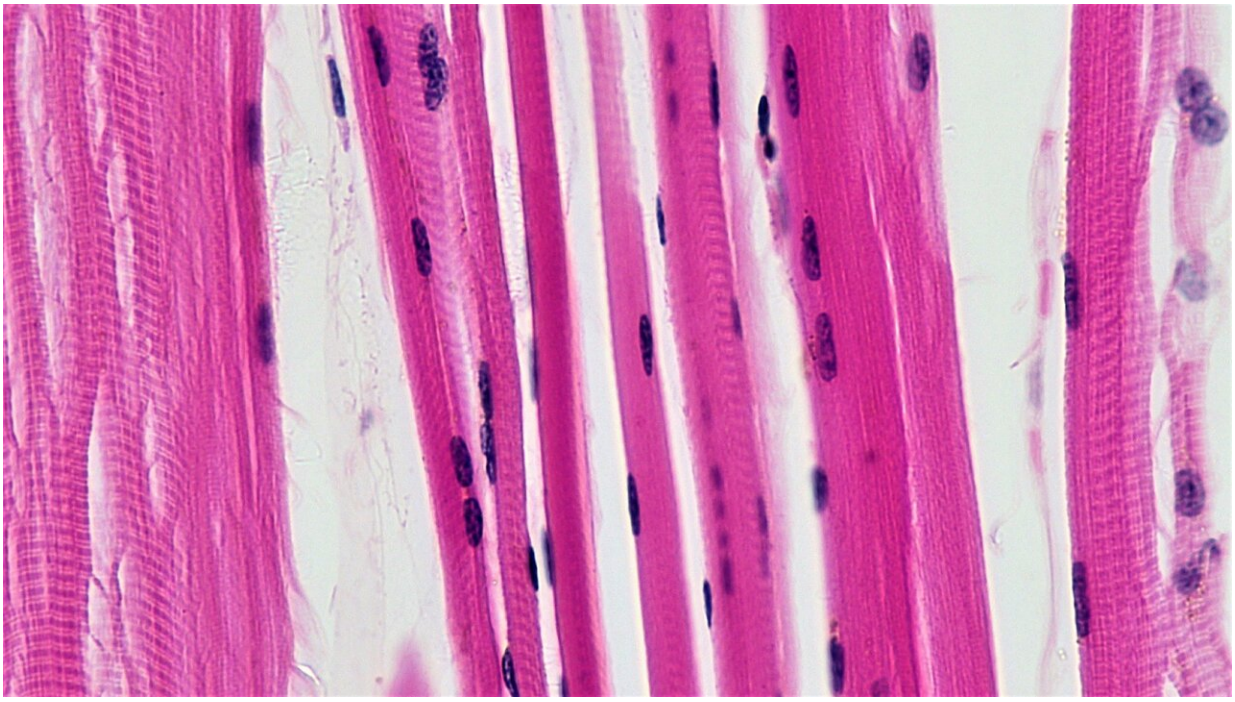

Skeletal muscle fibers. Credit: Berkshire Community College Bioscience Image Library / Public domain

About 80% of people with cancer suffer from significant muscle wasting, or loss of muscle tissue, and 30% of these patients die from this condition. New research in mice finds that the severity of muscle wasting is related to the type, size and location of the tumor.

"Muscle wasting, and not the tumor itself, is often the killer," said Gustavo Nader, associate professor of kinesiology, Penn State. "That's why it is important to study what is happening at the cellular level in skeletal muscle that may be contributing to the wasting problem."

Nader's previous research in ovarian cancer revealed that muscle wasting is related to reduced production of ribosomes—or particles in the cell that make proteins. Yet, he said, relatively little is known about the mechanisms driving down muscle protein synthesis and wasting in cancer patients.

In new research published in two papers appearing in the same issue of the *Journal of Applied Physiology*, the team investigated the mechanisms involved in muscle wasting in lung cancer and colorectal cancer in mice. The researchers found that the type, size and location of the tumor influenced the severity of muscle wasting through divergent mechanisms.

In the lung cancer study, the team examined the effects of two different types of lung cancer-derived tumors—LP07 and Lewis lung carcinoma (LLC). Tumor growth resulted in significant muscle weakness in mice with the LP07 tumor type, which was also associated with a reduction in ribosome production, while muscle wasting in the LLC tumor type caused muscle wasting but did not produce weakness or lowered ribosomal levels.

In the colorectal cancer study, the team examined two types of colorectal tumors—HCT116 and C26—and studied them using two models to define the role of tumor burden on muscle wasting. Tumor burden is the number of cancer cells, the size of a tumor, the amount of cancer in the body or the disease severity associated with the tumor. The findings indicate that the location of the tumor is an important factor in determining the severity of muscle wasting but this also depends on the

type of tumor.

"There are no effective treatments for muscle wasting in cancer patients," said Nader. "We are beginning to understand how different tumors cause muscle wasting, which is crucial because cancer treatments are less effective in patients with low muscle mass."

The Penn State team collaborated with David Waning from Hershey Medical Center, Esther Barreiro from the Universitat Pompeu Fabra in Barcelona, and Andrea Bonetto from Indiana University. Research in the Nader lab is supported by The National Institutes of Health.

More information: Daniel J. Belcher et al, LP07 and LLC preclinical models of lung cancer induce divergent anabolic deficits and expression of pro-inflammatory effectors of muscle wasting, *Journal of Applied Physiology* (2022). DOI: 10.1152/japplphysiol.00246.2022

Hyo-Gun Kim et al, Metastatic or xenograft colorectal cancer models induce divergent anabolic deficits and expression of pro-inflammatory effectors of muscle wasting in a tumor-type-dependent manner, *Journal of Applied Physiology* (2022). DOI: 10.1152/japplphysiol.00247.2022

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