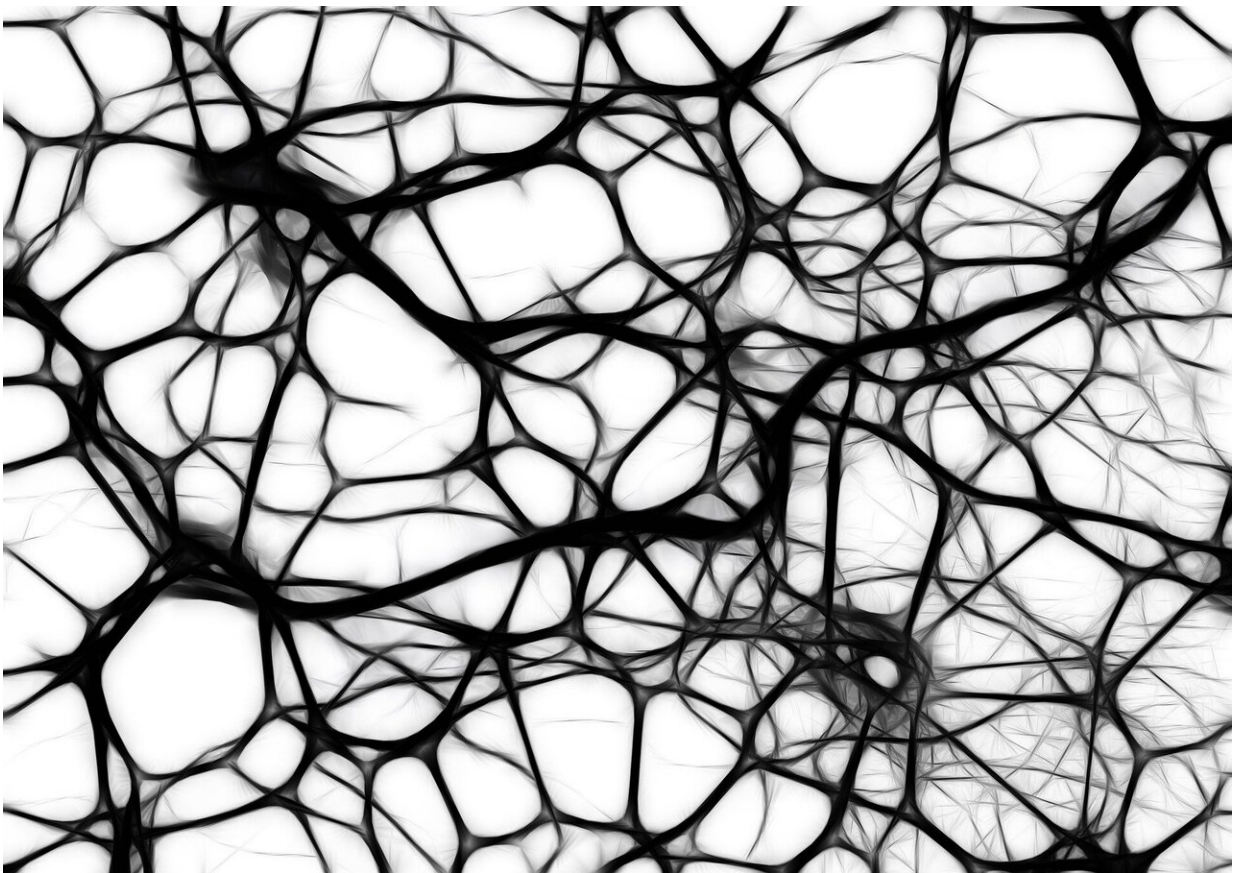


# Researchers identify secretion mechanisms for a protein necessary for maintaining healthy connective tissues

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Researchers have discovered that a defective form of the protein aortic

carboxypeptidase-like protein (ACLP) from patients with Ehlers-Danlos syndrome (EDS) is retained in cells and induces cellular stress. This finding may provide targets for pharmacologic and therapeutic interventions in treating individuals with EDS as well as wound healing disorders and fibrosis.

EDS is a prevalent genetic disease that results in weakened connective tissues. This disease results in joint hypermobility, vascular disruption, and aberrant wound healing. Mutations in the gene that encodes for ACLP have recently been identified to cause a novel variant of EDS. Furthermore, excessive amounts of ACLP cause fibrosis in multiple organs including the lung, liver, and [adipose tissue](#).

Researchers from Boston University School of Medicine (BUSM) and College of Engineering identified mechanisms that control ACLP secretion in vascular cells and fibroblasts. Detailed characterization of a mutant form of ACLP identified in an EDS patient revealed that this protein was retained in cells. They then generated [collagen fibers](#) in vitro that contained ACLP. Compared to collagen only controls, they found that fibers with ACLP exhibited increased [mechanical properties](#) consistent with a function in maintaining [connective tissue](#) integrity.

"We discovered that an EDS-causing mutation in ACLP hinders its secretion and induces cellular stress. We also identified that ACLP contributes to collagen fiber mechanics which may explain in part how ACLP contributes to connective tissue function," explains corresponding author Matthew D. Layne, Ph.D., associate professor of biochemistry at BUSM.

According to the researchers, many human pathologies are the result of improper protein processing. "Our study provides new information on the mechanisms of ACLP secretion from cells. Research in these areas add to the continued understanding of [protein](#) processing and secretion

and their connections to human connective [tissue](#) disease."

Layne and his collaborators were the first to show that ACLP contributes to the mechanical strength of collagen fibers that make up numerous connective tissues including ligaments, tendons, and cartilage.

These findings appear online in the *Journal of Biological Chemistry*.

**More information:** Neya Vishwanath et al. Mechanisms of aortic carboxypeptidase-like protein secretion and identification of an intracellularly retained variant associated with Ehlers–Danlos syndrome, *Journal of Biological Chemistry* (2020). [DOI: 10.1074/jbc.RA120.013902](#)

Provided by Boston University School of Medicine

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