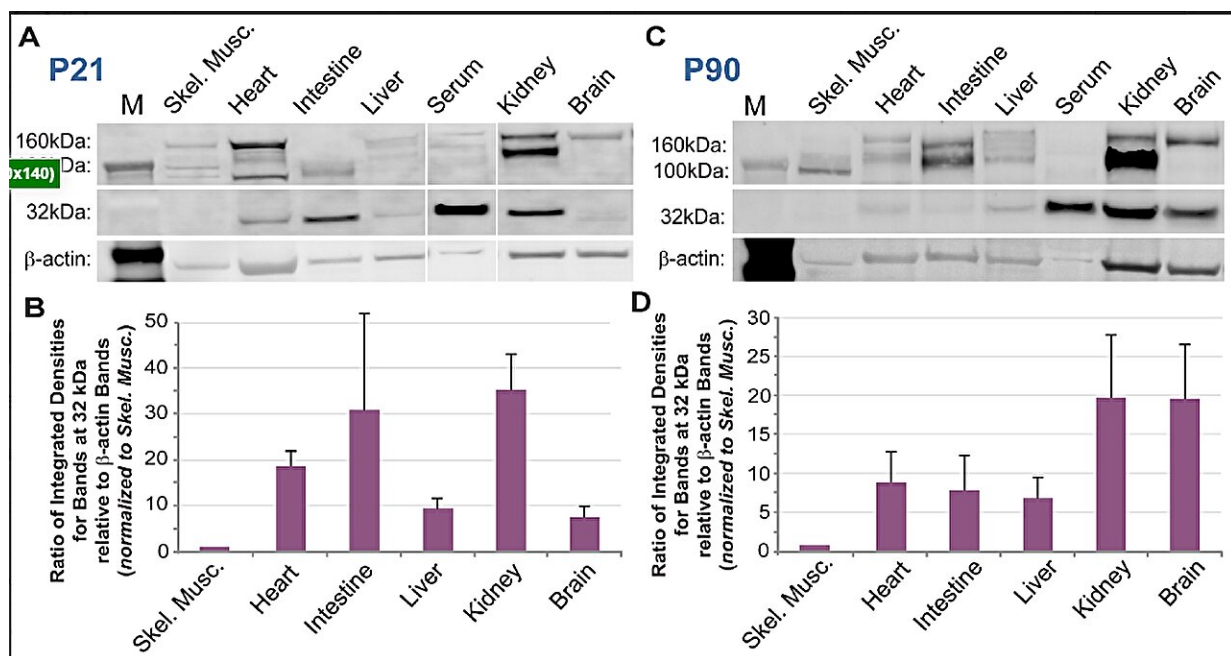


# Fundamental understanding of a molecule's normal function could inform treatments for a variety of brain disorders

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A truncated isoform of PDGFR $\beta$  was detected alongside full-length receptors across a range of murine tissues at different ages. (A) Representative images of a Western blot for proteins from select murine tissues at postnatal day 21 (P21) (from  $n = 3$  biological replicates, both sexes) detected by immunolabeling for PDGFR $\beta$  and  $\beta$ -actin—lane 1: molecular size marker (M), lane 2: skeletal muscle (Skel. Musc.), lane 3: heart, lane 4: intestine, lane 5: liver, lane 6: blood serum, lane 7: kidney, lane 8: brain. (B) Graph of the ratio of integrated densities for bands at the 32 kDa size range relative to  $\beta$ -actin bands for each tissue indicated, all of which were normalized to the skeletal muscle samples. Bars are averages with standard deviations. (C) Representative images of a Western blot for

proteins from select murine tissues at postnatal day 90 (P90) (from  $n = 3$  biological replicate, both sexes) detected by immunolabeling for PDGFR $\beta$  and  $\beta$ -actin—lane 1: molecular size marker (M), lane 2: skeletal muscle (Skel. Musc.), lane 3: heart, lane 4: intestine, lane 5: liver, lane 6: blood serum, lane 7: kidney, lane 8: brain. (D) Graph of the ratio of integrated densities for bands at the 32 kDa size range relative to  $\beta$ -actin bands for each tissue indicated, all of which were normalized to the skeletal muscle samples. Bars are averages with standard deviations. Credit: *Biomolecules* (2023). DOI: 10.3390/biom13040711

John Chappell, a cardiovascular scientist in the Center for Vascular and Heart Research at the Fralin Biomedical Research Institute at VTC, didn't quite believe what he was seeing.

"This can't be right. Let's run it again."

But more tests yielded the same result. The lab had discovered that a molecule commonly linked to [neurodegenerative diseases](#) was actually present in healthy brain tissue.

"This was a bit of a surprise because current literature identifies this particular molecule as a biomarker of disease—and for Alzheimer's in particular," said Chappell.

In a paper published in the journal *Biomolecules*, scientists said a [protein receptor](#) that exists in the smallest blood vessels of our body, called the microvasculature, could play a crucial role in its regulation.

The microvasculature provides our tissues with the oxygen and nutrients required for basic functioning. In the brain, these [small blood vessels](#) supply neurons with the capacity to coordinate their activity, facilitating the ability to think and learn.

Chappell, who is also a faculty member with the Department of Biomedical Engineering and Mechanics in the Virginia Tech College of Engineering, and his team discovered that an isoform of platelet-derived growth factor receptor- $\beta$ —isoforms are versions of proteins that are similar but not identical—likely affects the regulation of cells that play an important role in the integrity of the blood-brain barrier that protects our brain from harmful toxins.

In this study, the Virginia Tech scientists said soluble forms of the receptor are present in the brain and that higher levels of the protein are produced with age and in response to a lack of oxygen in the brain, which may fuel the risk for stroke and other neurological disorders.

Discovering something new is exciting, said Laura Beth Payne, research assistant professor in the Chappell lab and the study's first author.

"Understanding the elements and components of the microvasculature when tissue is healthy is both valuable and significant. How is this protein regulating the function of the microvasculature?" she said. "And in what scenarios and in certain diseases is the level of that protein changing?"

Answering these questions could provide insight for new medical interventions for a host of diseases related to a dysfunctional vasculature including heart disease, brain cancer, and other neurodegenerative diseases.

Identifying the isoform's functionality could potentially produce new therapeutic targets, said Hanaa Abdelazim, a student in the Translational Biology, Medicine, and Health Graduate Program who works on the project with Chappell and Payne.

In addition to [potential therapeutic targets](#), the Chappell lab hopes to

identify correlations between an increase or decrease of the protein and determine how those findings relate to early diagnosis of disease.

"Understanding the components and processes that have roles in establishing and maintaining, healthy human tissue is an essential part for the development of scientifically rational interventions when those same processes become dysfunctional," said Michael Friedlander, Virginia Tech vice president for [health sciences](#) and technology and executive director of the Fralin Biomedical Research Institute.

"This discovery makes a novel contribution to a better understanding of the critical elements in our circulatory system that could eventually lead to improved tools for prevention, diagnosis, and treatment of various diseases."

The Chappell lab hopes that future exploration of this [protein](#) and its role in the body will lead to hopeful outcomes for patients.

"Now the excitement continues, right?" said Payne. "We get to follow this discovery and hopefully have the opportunity to apply our findings to real world scenarios and pathologies to improve lives, which is why we're here doing this."

**More information:** Laura Beth Payne et al, A Soluble Platelet-Derived Growth Factor Receptor- $\beta$  Originates via Pre-mRNA Splicing in the Healthy Brain and Is Upregulated during Hypoxia and Aging, *Biomolecules* (2023). [DOI: 10.3390/biom13040711](https://doi.org/10.3390/biom13040711)

Provided by Virginia Tech

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