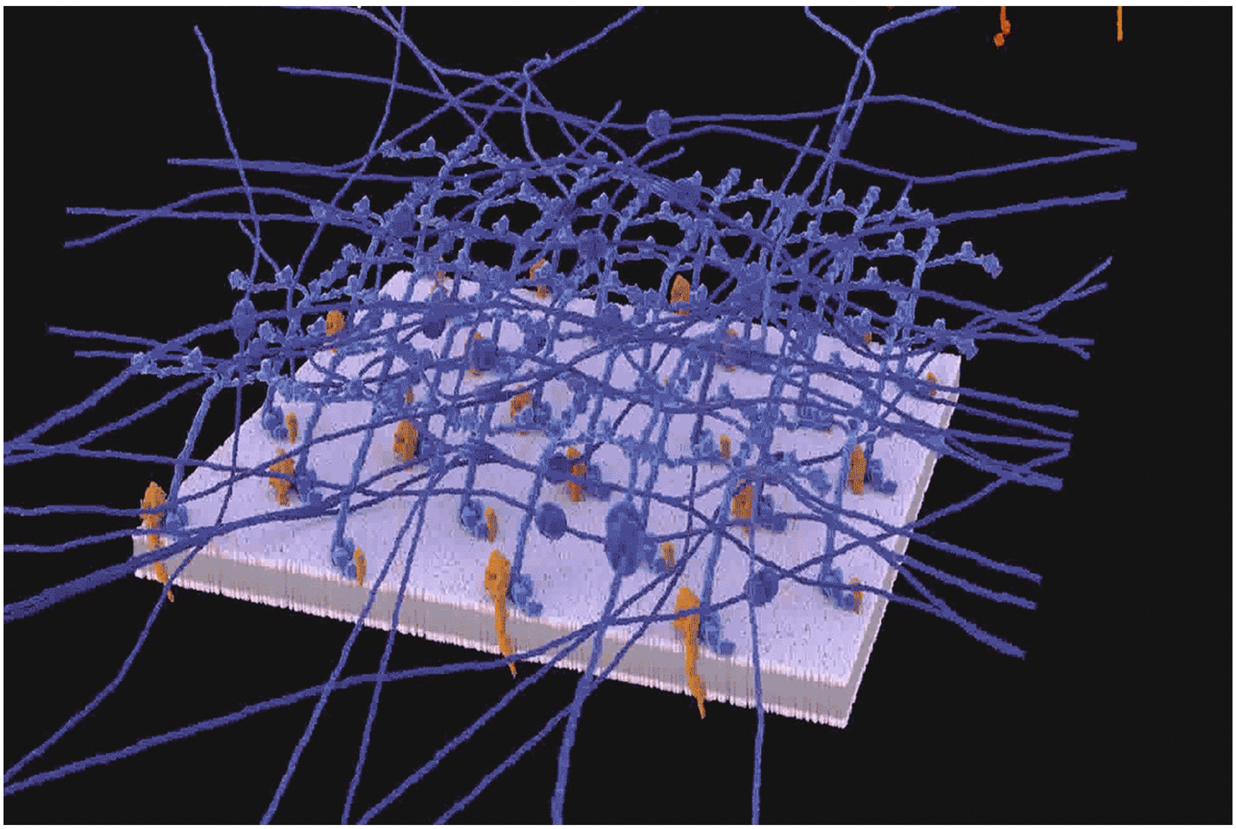
PHYS.ORG

Green glowing worms provide live-action movies of the body's internal scaffolding

July 8 2020, by Robin A. Smith, Véronique Koch



Protein molecules move within a stable scaffolding in the sheet-like mesh that surrounds and supports most animal tissues. Credit: A. Kawska

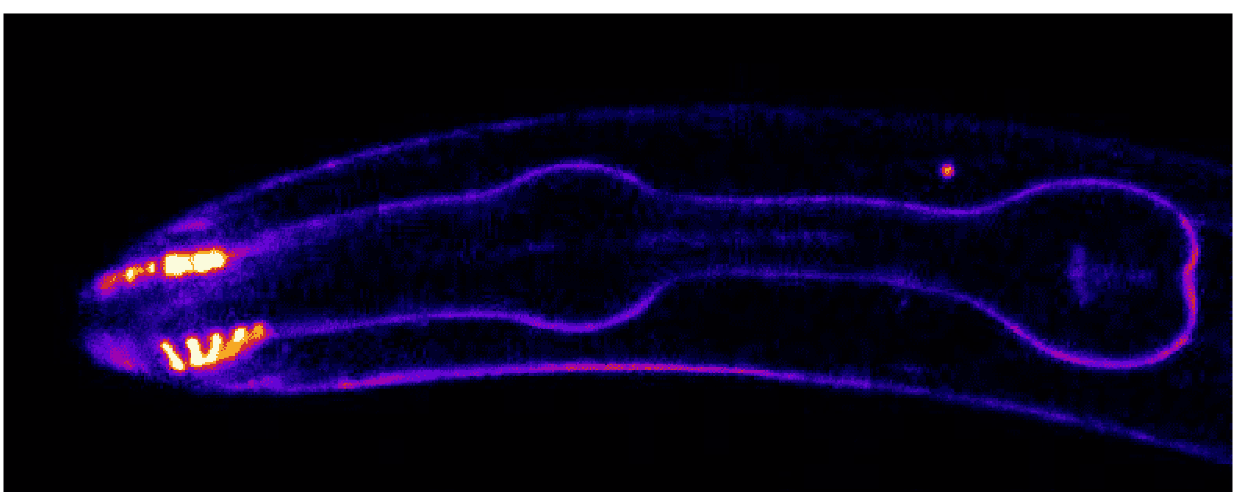
Duke University researchers have made the first time-lapse movies of the sheet-like latticework that surrounds and supports most animal tissues.

A thin layer of extracellular matrix known as the basement membrane lines many surfaces of the body such as the skin, blood vessels and urinary tract; and it surrounds muscles, fat, and peripheral nerves. While basement membranes play key roles in development, tissue function, and human disease, visualizing them in living organisms has been difficult to do, until now.

By genetically modifying C. elegans worms to create basement membrane proteins that glow under fluorescent light, the researchers say it's possible to see for the first time how basement membranes are assembled during development, and how they change and regenerate throughout life. The work may help to pinpoint what might be going wrong in human diseases ranging from kidney disease to invasive cancer.

"We wouldn't be here without basement membranes," said Duke biology professor David Sherwood, who led the research.

Basement membranes have been around for more than 600 million years, since the first multicellular animals evolved from their single-celled ancestors.



Duke University researchers used gene-editing techniques to tag and light up proteins in the basement membranes of living worms and watch them in action using time-lapse microscopy. Credit: Dan Keeley, UNC Chapel Hill

They're the Scotch tape that helps attach cells together to form tissues, maintaining healthy skin. They're the molecular sieves that filter blood in the kidneys, protect blood vessels and muscles from stretching and compression, and harbor growth factors that tell cells where to go, what to become, and when to divide.

But because most basement membranes lie deep within the body, beyond the reach of light microscopes, visualizing them in living tissues is hard to do in humans.

So Sherwood's team looked at them in millimeter-long transparent worms, using a gene-editing technique called CRISPR to label 29 basement membrane proteins with green glowing tags to see when and where each protein is found using time-lapse microscopy.

Getting a glimpse of these proteins in action inside a live animal offers a much more complete picture than previous experiments that looked at dissected and fixed tissues, which only provide a snapshot of proteins frozen in time, said postdoctoral fellow Eric Hastie.

"As a result, they have generally been thought of as 'boring' static structures," Hastie said.

In some movies, the researchers tracked fluorescent proteins moving within the basement membrane lining the worm's throat. In others, they watched the rapid remodeling of the basement membrane surrounding the worm's gonad as it grew more than 90-fold in size.

Surprisingly, the movies show that most basement membrane proteins don't stay put after they're deposited. While some core components are static, the scientists were surprised to see that many proteins moved within this stable scaffolding.

"Our findings suggest basement membranes quickly change their properties to support mechanically active tissues and they may act as highways that allow growth factors to rapidly travel," Sherwood said.

"We've just started getting to play with this tool kit," Hastie said. But the team says their work offers a new way to study the basement membrane defects underlying tissue degeneration during aging, and diseases ranging from diabetes to muscular dystrophy.

More information: Daniel P. Keeley et al. Comprehensive Endogenous Tagging of Basement Membrane Components Reveals Dynamic Movement within the Matrix Scaffolding, *Developmental Cell* (2020). DOI: 10.1016/j.devcel.2020.05.022

Provided by Duke University