'Molecular Velcro' enables tissues to sense and react to mechanical force

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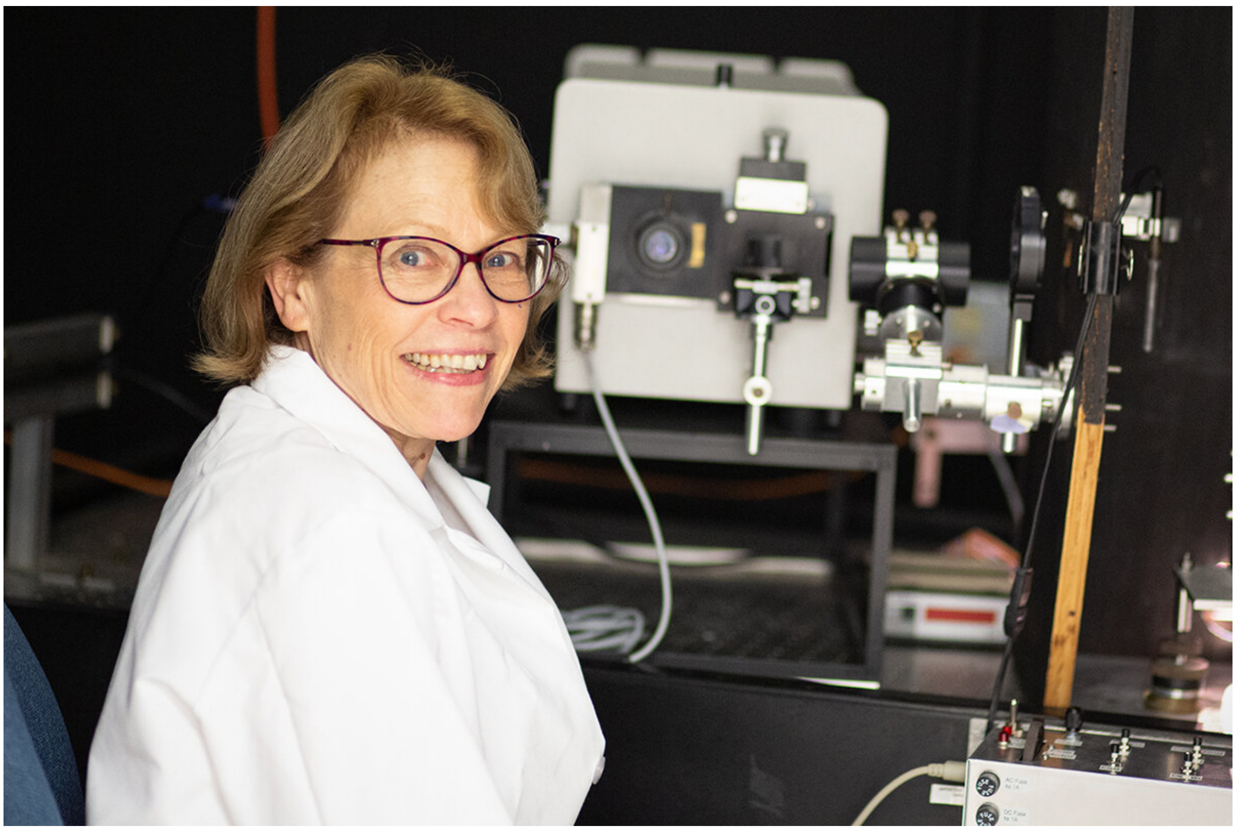

University of Illinois professor Deborah Leckband led a study that revealed how Velcro-like cellular proteins called cadherins sense tissue mechanics to regulate cell communication and biological tissue growth. Credit: Claire Benjamin

The Velcro-like cellular proteins that hold cells and tissues together also perform critical functions when they experience increased tension. A new University of Illinois Urbana-Champaign study observed that when tugged upon in a controlled manner, these proteins—called cadherins—communicate with growth factors to influence in vitro tumor growth in human carcinoma cells.

The study, led by chemical and biomolecular engineering professor Deborah Leckband, found that cadherins that bond with growth factor receptors can sense mechanical force and respond by altering cell communication and growth.

The findings are published in the *Proceedings of the National Academy of Sciences*.

When bound to cadherin molecules in normal tissue, growth factor receptors cannot communicate with growth factor proteins—the substance they need to promote tissue growth. However, the study shows that changes in tensional stress on cadherin bonds disrupt the cadherin-growth factor interaction to switch on growth signals in tissues.

To demonstrate how tension influences tissue growth, the researchers set up an experiment to observe how in vitro human carcinoma cells convert mechanical information into biochemical signals, Leckband said.

The team used a self-built "cell stretcher" in which the carcinoma cells are grown in a thin layer on the surface of a flexible medium. When the cells are stretched, the researchers observed changes that could increase tissue growth and tumorigenesis.

"This study confirms that cadherins use force to switch on biochemical growth signaling," Leckband said. "By confirming these force-induced disruptions, we may be able to find a way to mutate cadherin molecules in order to prevent certain types of tissue growth, such as metastatic transformation and tumorigenesis."

The team has observed the cadherin-growth factor receptor complex in human epithelial tissue and plans to expand this concept by working with in vitro human breast tissue.

Illinois graduate students Brendan Sullivan and Vinh Vu; undergraduate student Adrian Kapustka; and researchers from Johns Hopkins University contributed to this study.

Leckband also is a professor of chemistry and of bioengineering, and is affiliated with the Beckman Institute for Advanced Science and Technology, the Carl R. Woese Institute for Genomic Biology and the Nick Holonyak Micro and Nanotechnology Laboratory.

More information: Brendan Sullivan et al, Mechanical disruption of E-cadherin complexes with epidermal growth factor receptor actuates growth factor–dependent signaling, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2100679119

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