New microscopy analysis allows discovery of central adhesion complex

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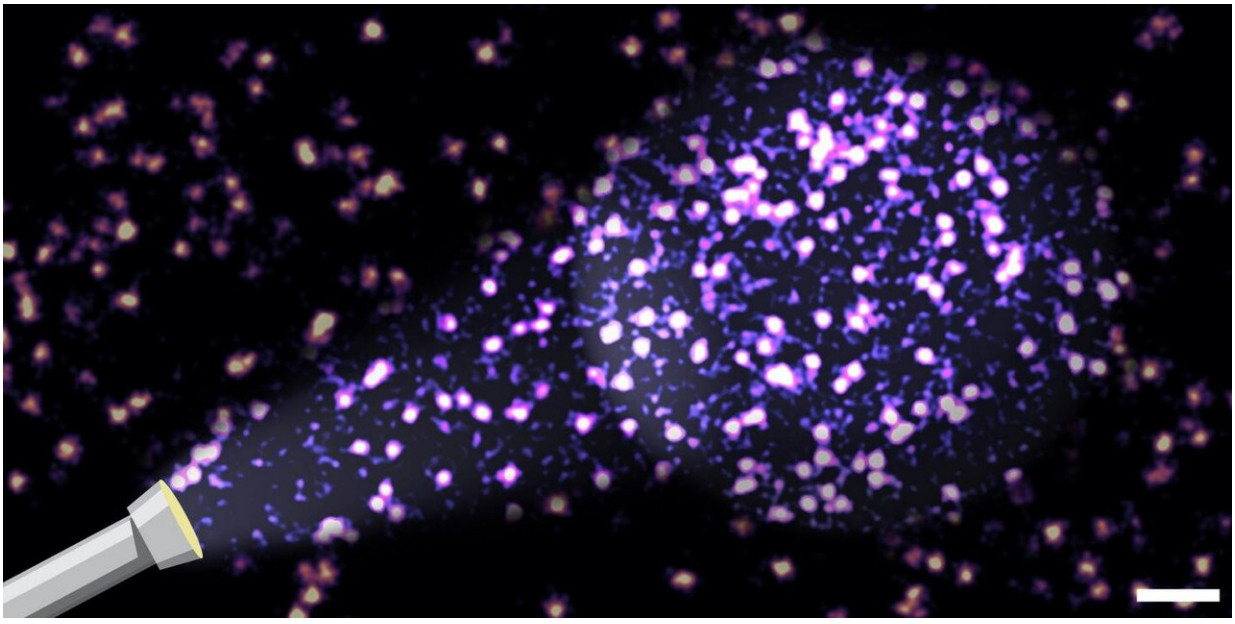

Localization clouds of individual adhesion proteins in cells. Many proteins remained undetectable when using conventional analytical methods. By using the new analytical method actual molecular parameters can be determined. Scale bar: 100 nm. Credit: Lisa Fischer and Carsten Grashoff

Cells of organisms are organized in subcellular compartments that consist of many individual molecules. How these single proteins are organized on the molecular level remains unclear, because suitable analytical methods are still missing. Researchers at the University of

Münster together with colleagues from the Max Planck Institute of Biochemistry (Munich, Germany) have established a new technique that enables quantifying molecular densities and nanoscale organizations of individual proteins inside cells. The first application of this approach reveals a complex of three adhesion proteins that appears to be crucial for the ability of cells to adhere to the surrounding tissue. The research results have been published in the journal *Nature Communications*.

Background and methodology

The attachment of cells is mediated by multi-molecular adhesion complexes that are built by hundreds of different proteins. The development of super-resolution microscopy, which was honored with the Nobel Prize in 2014, allowed the identification of basic structural elements within such complexes. However, it remained unclear how individual proteins assemble and co-organize to form functional units. The laboratories of Prof. Dr. Carsten Grashoff at the Institute of Molecular Cell Biology (University of Münster) and Prof. Dr. Ralf Jungmann at the Max Planck Institute of Biochemistry (Munich) now developed a novel approach that allows the visualization and quantification of such molecular processes even in highly crowded subcellular structures.

"A substantial limitation even of the best super-resolution microscopy techniques is that many molecules remain undetected. It is therefore nearly impossible to make quantitative statements about processes of molecular complex formation in cells," explains Lisa Fischer, Ph.D. student in the Grashoff group and first author of the study. This difficulty could now be circumvented with a combination of experimental controls and theoretical considerations.

"By applying our new analytical method, we were able to provide evidence for the existence of a long suspected ternary adhesion complex.

We knew already before that each of these three molecules is very important for cell adhesion," explains Fischer. "However, it was not clear whether all three proteins come together to form a functional unit." As the method is broadly applicable, the researchers believe that many other cellular processes will be studied with the new analysis procedure.

More information: Lisa S. Fischer et al, Quantitative single-protein imaging reveals molecular complex formation of integrin, talin, and kindlin during cell adhesion, *Nature Communications* (2021). DOI: 10.1038/s41467-021-21142-2

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