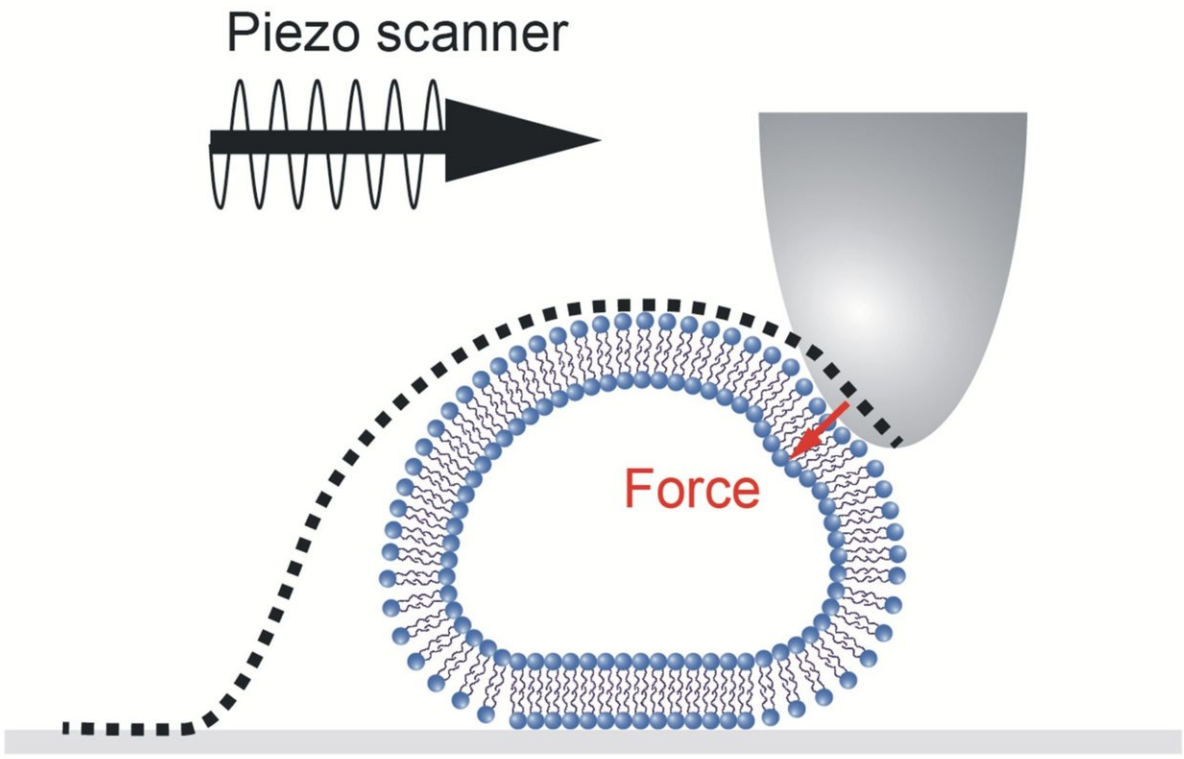
A closer look at the communication packages of cells

November 26 2018



Vesicle and AFM tip. Credit: Rijksuniversiteit Groningen

Cells communicate by sending little fat balls to one another. Wouter Roos, professor of Molecular Biophysics at the Rijksuniversiteit

Groningen, together with colleagues from Amsterdam and Utrecht, is the first to describe the mechanical properties of such fat balls, called exosomes. By studying exosomes of patients with a blood disorder, the researchers obtained unexpected results.

"Exosomes from their blood cells have very different properties than those from healthy individuals," Roos concludes. "That offers new possibilities in diagnosis and nanomedicine." The results were published in the scientific journal *Nature Communications* on 23 November.

That little balls made of fat and proteins move in and out of cells has been known for a long time. Cells compose those balls using a small part of the cell membrane, the outer wall of the cell. For a long time, it was thought that these exosomes mainly cleaned up waste from the cell. But for about 15 years, researchers have known that these exosomes are important for the communication between cells.

"So far, we have only studied them in groups to discover their properties. But thanks to a special microscope, we could now study and describe one single exosome," says Roos.

Playing with a needle

Roos started the research a few years ago in Amsterdam together with professor in physics of life processes Gijs Wuite and finished it after his arrival in Groningen. "We first looked at the red blood cell exosomes with a touch microscope," says Roos. "This AFM feels over the surface with a needle to discern what the surface looks like."

This is a bit like how a blind person feels braille letters. "We then tested the mechanical properties by pressing these small fat balls. This provides an idea of the firmness and flexibility of the exosome." By doing so, the researchers were the first to map the properties of exosomes from red

blood cells.

"Next, we looked at red blood cells of people with spherocytosis. Patients with this condition have red blood cells that are far too round and stiff. We expected that their vesicles would be harder, too. But to our surprise, they turned out to be softer."

That observation led to the insight that the soft parts of the cell form the vesicles. "We knew that people with spherocytosis make more vesicles, but we never thought that they would show such unexpected behaviour. That insight leads to many new questions, which might help to understand the genesis of the stiff red blood cells in spherocytosis, and may lead to new diagnostics."

There are still many mysteries left. "What exactly is inside such an exosome, for example? What information do they transfer? And how do they know to which cell they should transfer that information? Once we know this for healthy cells, we can also better understand how the communication in spherocytosis and cancer progresses. And then we can also develop techniques to better detect those exosomes and make medicines that influence their communication."

There is an important reason that Roos and others delve into the properties of exosomes. "Not only do healthy cells communicate with exosomes, but so do tumour cells. If we understand them better, we may be able to discover differences between exosomes of healthy cells and exosomes of tumour cells. We may then be able to use them in diagnostics and in the development of anti-cancer drugs," explains Roos. In the Netherlands alone, there are nine research groups working on this subject, organised in the Cancer-ID partnership.

More information: Daan Vorselen et al. The fluid membrane determines mechanics of erythrocyte extracellular vesicles and is

softened in hereditary spherocytosis, *Nature Communications* (2018). DOI: 10.1038/s41467-018-07445-x