

# New pathway for DNA transfer discovered in tumor microenvironment

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University of Notre Dame researchers have discovered another way tumor cells transfer genetic material to other cells in their microenvironment, causing cancer to spread.

In their latest study, published in *Cell Reports*, Crislyn D'Souza-Schorey, the Morris Pollard Professor in the Department of Biological Sciences, and collaborators discovered that DNA "cargo" is transported in small informational sacs called extracellular microvesicles. Their study is a continuation of work her lab has undertaken to further understand the sharing of information between cells.

"We've shown that DNA present in these microvesicles is related to metastasis, so now we have a great platform to assess for genetic aberrations," said D'Souza-Schorey, who is also affiliated with the Berthiaume Institute for Precision Health, the Boler-Parseghian Center for Rare and Neglected Diseases and the Harper Cancer Research Institute.

Cancer cells, unlike [normal cells](#), are often filled with cytosolic DNA, which is DNA found in the jelly-like fluid outside of the cell's nucleus. This DNA can be derived from multiple sources, but recent evidence suggests that chromosomal instability is a primary source of cytosolic DNA in tumor cells.

The research team used a cell model from a male cancer patient to show how Y-chromosomal DNA—present in the cytosol due to [chromosomal instability](#)—is carried by extracellular vesicles and transferred to a female mammary epithelial cell line.

"These female cells do not have Y-chromosomal DNA present without exposure to the male microvesicles," said James Clancy, research assistant professor of biological sciences, who is the first author on the paper. "This is an accessible way to show people that the DNA was transferred, making it easier to prove this form of communication."

The researchers demonstrated that cytosolic DNA is moved to microvesicles alongside an enzyme, cGAS, which was discovered in part

because of its role during the immune response to bacterial and viral infections. Scientists have increasingly recognized that cGAS may play a part in tumor progression, and this new study delineated a way the DNA is modified to aid that progression.

Work [published by D'Souza-Schorey's lab in 2019](#) in *Nature Cell Biology* described how microRNA within tumor [cells](#) is moved to microvesicles just beginning to form at the cell periphery. Once shed, these vesicles are taken up by non-[tumor cells](#) in the microenvironment. Microvesicles can also be found circulating through the body in fluids like blood and urine, and can be used as biomarkers that point to the presence of cancer.

While microRNA can affect [protein expression](#) more quickly than DNA, the researchers were interested in the DNA content as it is the actual part of a person's genome, including any tumor-associated mutations, Clancy said. It was also more difficult to prove that DNA has moved from one cell to another.

The lab's continued foundational research in this area may lead to early detection of different types of tumors.

In addition to D'Souza-Schorey and Clancy, others who worked on the study include Colin Sheehan, class of '19, and Alex C. Boomgarden, a fourth-year doctoral student at Notre Dame and recipient of a Berthiaume Institute for Precision Health predoctoral fellowship. Sheehan is now pursuing his doctoral degree at the University of Chicago. The study was supported in part by the National Cancer Institute and the Boler Family Foundation.

**More information:** James W. Clancy et al, Recruitment of DNA to tumor-derived microvesicles, *Cell Reports* (2022). [DOI: 10.1016/j.celrep.2022.110443](#)

Provided by University of Notre Dame

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