

# Cancer cells can 'infect' normal neighbours

Tiny RNAs shed by tumours can transform healthy cells into cancerous ones.

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23 October 2014

When a cancer cell throws out its trash, it can turn healthy neighbours into fellow tumour cells, researchers have found.

Many cells, including cancerous ones, shed thousands of tiny membrane-bound vesicles called exosomes that contain proteins, DNA and RNA. The process is thought to be a waste-management system, but it may also facilitate cell-to-cell communication: some of these vesicles can then merge with other cells and dump their payload inside.

In a study published online on 23 October in *Cancer Cell*<sup>1</sup>, researchers show that when human breast-cancer exosomes can cause tumours when mixed with normal cells then injected into mice. The results could pave the way to finding markers to monitor the progression of cancer, and possibly even point to targets for therapies.

"It's amazing — these vesicles were considered garbage cans," says Khalid Al-Nedawi, a cancer researcher at McMaster University in Hamilton, Canada. "This paper really brings us closer to harnessing the potential of these tiny vesicles."

## Dangerous payload

Previous studies had shown that cancer cells crank out more exosomes than normal cells<sup>2</sup>. Cancer researcher Raghu Kalluri of the MD Anderson Cancer Center in Houston, Texas, and his colleagues therefore decided to look into how the two types of exosome might differ. They isolated exosomes from cells grown in culture and found that, unlike normal exosomes, those from cancer cells contained the building blocks required to produce the short fragments of RNA called microRNA that can shut off the expression of target genes.

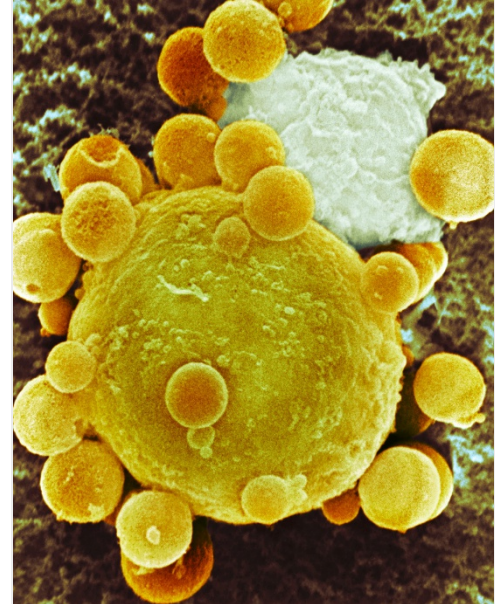
Exposure to the cancer exosomes altered gene expression in the normal cells. Those cells then caused tumours when injected into mice. Exosomes from normal cells did not yield tumours, however, and tumour growth was reduced in cells exposed to cancer exosomes in which the microRNA-producing molecular machinery had been disabled.

The team also collected exosomes from the blood of 8 healthy individuals and 11 people with breast cancer. Five of the 11 exosome samples from the patients induced tumour growth when mixed with normal cells and injected into mice; none of the exosome samples from healthy people did so.

It is unclear how far exosomes can travel in the body, says Kalluri, but the fact that the team could isolate them from blood suggests that they could be quite mobile. And even if their effect is only local, they could still make nearby cancer cells more aggressive, or transform healthy cells into cancerous ones, he says.

But trying to slow cancer by blocking exosomes is a difficult proposition, says Al-Nedawi. It is unclear how that would affect normal cells, he notes, and some exosomes from healthy cells have been shown to contain proteins that prevent cancer<sup>3</sup>.

A more imminent application might be to use exosomes as a way to detect and monitor cancer, he adds. Kalluri notes that exosomes are more abundant and easier to isolate than tumour cells floating in the blood, which have also been used to track disease. "There are millions of exosomes being made by each cell," he says. "That's very powerful."



*Dr Andrejs Liepins/Science Photo Library*

A cancer cell (yellow) sheds membrane vesicles.

Nature | doi:10.1038/nature.2014.16212

## References

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1. Melo, S. A. *et al.* *Cancer Cell* <http://dx.doi.org/10.1016/j.ccell.2014.09.005> (2014).
  2. Logozzi, M. *et al.* *PLoS ONE* **4**, e5219 (2009).
  3. Putz, U. *et al.* *Science Signaling* **5**, ra70 (2012). <http://dx.doi.org/10.1126/scisignal.2003084>