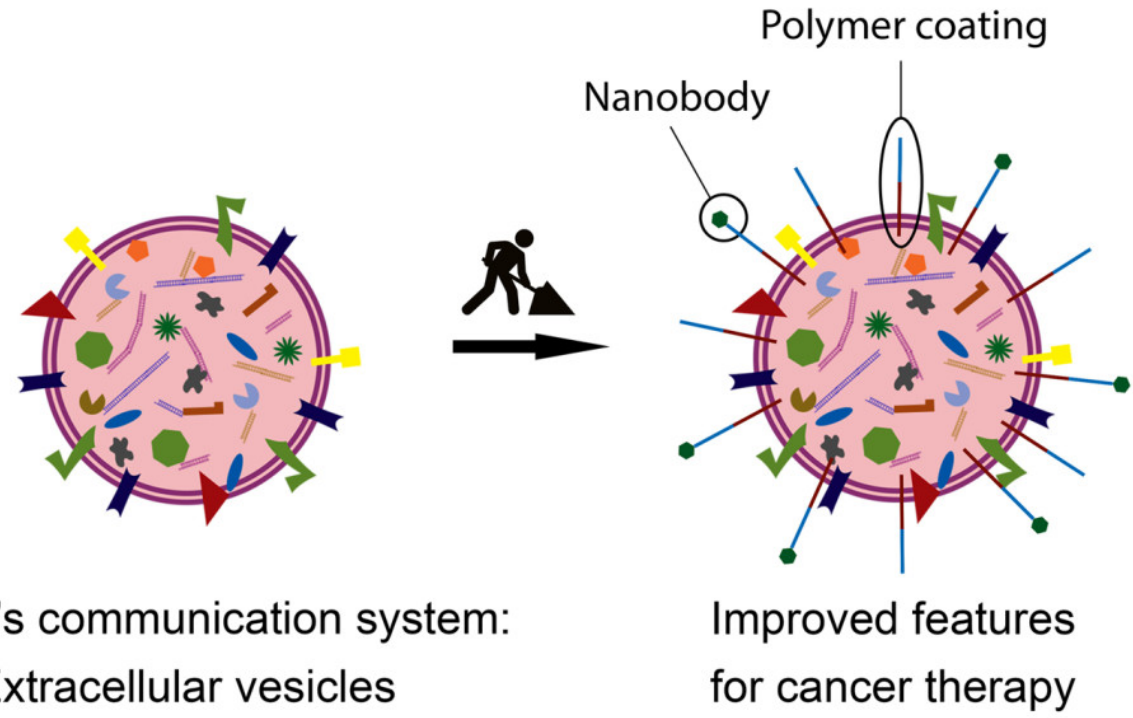
Improving nature’s own communication system to fight cancer

Our bodies are composed of trillions of different cells, which communicate with each other in order to keep us healthy. There are several ways in which messages can be sent back and forth between cells. One of these is known as ‘extracellular vesicles’ (EVs). These are tiny spherical structures (ten thousand times smaller than the thickness of a finger nail), in which cells can load pieces of information. EVs protect this information during their travel through the bloodstream, and properly deliver it to the intended cells. This highly sophisticated communication network could possibly be used to our advantage to treat a variety of diseases. For example, if EVs could be ‘reprogrammed’ to carry drugs to diseased (e.g. cancer) cells instead of healthy cells, this could greatly improve the therapeutic effects of these drugs, and reduce their side effects. As a first step in such a ‘reprogramming’ process, we studied whether we could improve natural EVs to make them preferentially interact with cancer cells instead of other cells.



One of nature's own communication systems, designed to transfer messages from one cell to another, is known as 'extracellular vesicles'. With some adjustments, this system could possibly be used for the treatment of cancer. In our study, we investigated a novel method to 'reprogram' extracellular vesicles to improve their therapeutic value.

To achieve this, we developed a novel method to coat the surface of EVs with a layer of water-soluble polymers (‘PEG’), and show that, due to this layer, EVs could not properly interact with cells anymore. However, when we coupled the outer layer of the polymers to ‘nanobody’ proteins, which strongly bind specifically to cancer cells, the interaction of EVs with cancer cells was greatly improved. Hence, we restricted the interaction of natural EVs with healthy cells, while improving their binding to cancer cells. In a follow-up experiment, we administered these modified EVs to mice and measured the time that the EVs could circulate in the bloodstream. We observed that normal EVs (without polymer coating) were quickly removed from the bloodstream, presumably by cells of the immune system that protect our body against disease-causing micro-organisms. However, when the polymer coating was applied, the recognition of the EVs by these cells was largely prevented, causing them to circulate much longer in the body. This is important, because the blood vessels surrounding tumor cells are known to be slightly leaky, allowing EVs to exit the blood stream and enter into the tumor. The longer EVs stay in the blood stream, the higher the chance that they will eventually pass through these gaps and accumulate in the tumor. After successful entry into the tumor site, the nanobodies attached to the polymers come into play. These could assure that EVs actually enter into the tumor cells, which is required to deliver the therapeutic message carried by the EVs.
In conclusion, in this study we describe a novel method to coat EVs with polymers and nanobodies, which could greatly improve their accumulation in tumor tissue and reduce their interaction with other (healthy) cells. Our work thereby contributes to the ongoing development of safe and effective anti-cancer treatment.

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Publication

PEGylated and targeted extracellular vesicles display enhanced cell specificity and circulation time.
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