Abstract for the general public

In the human body, potential cancer cells arise every day. The majority of these dangerous cells are quickly destroyed by the body's immune defense. Only when a cancer cell is able to escape and overcome the immune response it can start to grow. In order to grow into a large tumor, also new blood vessels are required to supply nutrients and oxygen. Thus, cancer cells have to communicate intensively with other body cells to inhibit immune destruction and to organize adequate supply. The intercellular communication can be achieved through secreted factors like hormones, or by small vesicles that are released into the surrounding of the cell. A special class of these vesicles, called exosomes, was shown to support the survival of cancer cells in many different ways. Exosomes help to shut down anti-cancer immune responses and to induce the growth of new blood vessels. Moreover, exosomes are employed to export substances that are harmful for the cancer cell, such as cytotoxic drugs used for chemotherapy. In some cancer patients, escaping the anti-cancer immune response might become completely dependent on the activity of exosomes. In such patients, blockage of exosome production could induce an anti-cancer immune response strong enough to eliminate the cancer cells. It was shown in a mouse model, that injected prostate cancer cells were unable to grow into tumors when the exosome production was blocked. Moreover, the injection of cancer cells lacking exosomes functioned like a vaccination: the mice became resistant to consecutive challenges with cancer cell injections even when in the later injections cells were used that produced exosomes!

Based on these observations one could envision an anti-cancer immunotherapy that simply consists in the temporary blockage of exosome production to give the immune system the chance to re-activate the anti-cancer response. Several drugs that inhibit exosome production are known. Before such a treatment can enter clinical trials, several questions rise up: which side effects could be expected from such a therapy? Would exosome deficiency increase the sensitivity of cancer cells towards cytotoxic drugs and if yes, to which class of drugs? If the treatment cannot be restricted to cancer cells, exosome production would also be inhibited in non-cancerous cells. Would also these cells show increased sensitivity to drug treatment? Would the immune stimulation also work with other kinds of cancer?

Here is where the project comes in. Several of these questions can be approached experimentally in cell cultures. By using gene manipulations, melanoma cell lines will be created that lack the production of exosomes. The growth characteristics, drug sensitivity, immunogenicity, mobility (the pre-requisite for metastases) and differentiation capacity of these cell lines will be investigated.

The perspective of a potentially curative cancer therapy that is based on the blockage of exosome production for a limited time is extremely exciting. Even if this kind of therapy would work only for a small percentage of all cancer patients, the benefit for them would be overwhelming. Such a perspective justifies all efforts that support rapid realization of such a therapy and the current project is designed to contribute to the implementation of this promising approach.