ABSTRACT FOR THE GENERAL PUBLIC

Uncontrolled cell division in any tissue may lead to cancer. There can be many different reasons for such cell rebels' insubordination, including environmental toxicity, stress, or genetic predisposition. Luckily, the growth of cancer cells' is not entirely out of hand. The organism has its natural soldiers - the immune cells with a mission to recognize and nip cancer rebels in the bud. Yet, as cancer cells usually are under strict immune surveillance, the controllers are unfortunately not omnipotent.

At some point, cancer is diagnosed and, in most cases, surgically removed. However, the rebels can resurface if the immune soldiers will not scout the terrain to detect and subdue the remaining small pockets of resistance controlled by the rebels. Such action requires to overcome cancer cells' defensive strategies and to recruit immune cell soldiers into the vicinity of malignant rebellion. Thus, this proposal aims to minimize the chance of cancer relapse by a two-pronged approach that kills cancer rebels and mobilizes and boosts immune cells.

The boosting of immune cells, combined with the anti-tumor properties, holds promise. As combinatorial approaches require tedious optimization of dosage and delivery, the "two-in-one" approach is optimal. Based on our ongoing studies, we selected a small RNA molecule (microRNA) toxic to aggressive brain cancer cells. But in contrast to cancer cells, immune cells need this molecule to stand up and fight cancer cells for the patient's benefit.

RNA encapsulated within lipid vesicles efficiently turns on immune response, as we now have the chance to observe the development of the anti-COVID-19 vaccine. Capitalizing on that knowledge, we propose to use extracellular vesicles naturally secreted by cells producing our selected microRNA. Such designed cells will produce both the therapeutic agent and delivery vehicle to both cancer and immune cells.

While the time is ripe for immunotherapy approaches that have yielded a high therapeutic response chance, they still suffer from high cost and less than universal success rate. The strategy proposed here is not only low-hanging fruit as it uses a naturally existing cellular process of vesicle secretion and small RNA packing, but it also has significantly reduced the cost of preparation of the anti-cancer vaccine. Finally, if such an approach will work against tumors as aggressive as a brain tumor, it will help develop a therapy for other cancers.