The Ottawa Hospital | L'Hôpital d'Ottawa

Research project summary

# Enhancing ovarian cancer immunogenicity by increasing antitumoral responses using engineered oncolytic vaccines

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Cancer immunotherapy is a revolutionary approach based on methods that stimulate the immune responses in our body to kill the cancer cells. Immune cells called cytotoxic T lymphocytes (CTLs) specifically recognize cancer cells to eliminate them. However, when a tumor is established, cancer cells use several mechanisms that dampen the immune system. Growing tumors establish an immunosuppressive microenvironment that renders CTLs dysfunctional. Tumors also escape from immune recognition by their ability to decrease the expression of proteins in their cell surface called major histocompatibility complex I (MHC-I). In this project, we propose to combine different approaches in cancer immunotherapy to efficiently target and eliminate tumor cells. First, oncolytic virus (OV) are able to specifically replicate and kill tumor cells directly but also by stimulating CTL responses. Second, OV can be modified to make them express proteins that will empower immune cells sitting in the tumor niche. Using OV modified to express the proteins IL-15 and IL-21, tumor cells will produce a more supportive environment for CTLs to execute their killing capacities and generate a long-lasting protection against tumor cells. Third, MHC-I proteins can be increased on tumor cells by delivering NLRC5, a master protein that promotes the expression of MHC-I and other related proteins to increase tumor cell visibility towards CTLs. We have developed an infected cell vaccine (ICV) platform using tumor cells infected with the OV Maraba MG1 modified to express IL-15 and IL-21. The ICV-IL15+IL21 expressing NLRC5 will be used as a vaccine to stimulate the activation of antitumoral CTLs. Focusing on ovarian cancer, a cancer that is in dire need of more effective treatments, the combination of these three approaches should result in a treatment that generates robust CTL responses and stimulates the formation of memory that will confer long-lasting protection against relapse.

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