Improving antibody-based immunotherapy

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Monoclonal antibodies are employed in the treatment of cancer and it has been established as one of the most successful therapies for hematologic malignancies in the past two decades. In addition, monoclonal antibodies are also promising biological drugs for autoimmune diseases. The therapeutic antibodies are employed to target specific antigens on the tumor, and this event lead to the stimulation of immune cells to kill the cancer cells. Fc receptors (FcRs) on macrophages sense the Fc parts of the tumor-bound antibodies which will activate the macrophages to phagocytose and eradicate the tumor cells. Despite the major evolution of antibody-based cancer therapy, the success rate still needs to be improved. To achieve this, a novel approach will be used to explore a personalized based treatment. The individual diversity of FcR expression on immune cells will be taken into consideration when designing the antibody treatment. Thus, there are differences in the affinity among IgG subclasses (IgG1, IgG2, IgG3 and IgG4) for FcRs. If certain FcRs are specifically expressed in an individual, selection of antibody isotypes that exclusively bind those FcR expressed will be used. Also, if the patient has a low level of FcR expression it can be enhanced by immune stimulating agents (e.g. IFN-ɣ) prior the antibody treatment. Furthermore, a combination of isotypes will be explored to maximize the interaction between the antibodies on the surface of the tumor cells with the FcRs present on the immune cells, facilitating the tumor cell killing. Overall, the main goal of this project work is to improve the efficacy of antibody-mediated killing of cancer cells by exploring combinations of immune effector cells with therapeutic antibodies and tumor target cells in vitro.