DELIVERY OF MONOCLONAL ANTIBODIES FROM MICROENCAPSULATED CELLS

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Monospecific immunoglobulins (monoclonal antibodies, MAb) of therapeutic interest have received significant attention since their development by Milstein and Kohler in 1975. The exquisite specificity of MAb, or the ability to bind exclusively to its target makes it a very promising tool in medical diagnosis and therapy. A large number of MAbs have been licensed and are used in the clinic today, particularly as anticancer agents. Nonetheless, the very high cost associated to the production and purification of MAbs is a significant challenge to their successful commercialization, since a treatment can cost upwards of $100,000 per patient. Since MAb purification is the greatest technical and economic challenge this proposal aims at exploring a novel strategy for the sustained and constant delivery of MAbs. The microcapsules are produced with electrostatic bead generation of the hydrogel alginate, which after gelation are cross-linked with cationic poly-L-lysine to produce stable microcapsules that are 200-400 micrometers in diameter. In addition to the polymer, the choice of judicious cells suitable for encapsulation is critical for the success of the proposed strategy. The microcapsules are permeable to IgG and nutrients, but not to immune cells. As a result of the immune isolation the enclosed allogeneic cells are not rejected, making tissue matching unnecessary for the treatment. This proposal is aimed at investigating the potential of encapsulated myoblasts and MSC cells to produce –and secrete- clinically relevant levels of monoclonal antibodies (MAbs) aimed at preventing tumor growth such as epidermal growth factor receptor (EGFR) as well as MAb against CD-20, to deplete tumorigenic B lymphocytes. Both MAbs have been proved efficacious in patients with carcinoma and lymphoma cancers, respectively. If successful, encapsulated cells will deliver constant, sustained clinically relevant amounts of functional MAb, making antibody delivery cost-effective. This novel strategy could have wide applications in the treatment of medical conditions such as various types of cancer and autoimmune diseases, which are already treated with monoclonal antibodies.