A new immunomodulatory drug delivery system based on αlβ2 and αmβ2 aptamers/Alg-PEI

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Abstract

Introduction: Currently, the major concern with biomaterial implantation or tissue grafting is adverse responses of immune system. To remove these barriers, some immunosuppressive drugs are used. But they are associated with adverse effects of systemical delivery. Adhesion of immune cells to foreign body by cell adhesion molecules such as integrins,triggers their activation that leads to immune response. It is demonstrated that this is directed by the ability of dendritic cells (DCs) to drive adaptive immune cells in situ toward adverse reactions and play as a bridge between innate and adaptive immune cells. Thus our focus is on β_2 integrin receptors on DC. This study aims to modulate the immune response by inhibiting $\beta_2$integrins marker on DC.

Methods and Results:to control of DC maturation,αlβ2 and αmβ2 surface markers on DCs should be blocked, hence, the novel aptamer-blocking technique was utilized. For this purpose, immature DCs (iDC) were derived from human peripheral blood monocytes. The antagonist biomolecules (aptamer) that simulated based on inverse of DC markers (αlβ2 and αmβ2) from selex,were embedded into injectable alginate-branched polyethyleneimine by physical entrapment. Then, derived iDCs were treated with synthesized hydrogels in RPMI-1640 media. Interaction of released antagonist aptamers from hydrogels andiDC was analyzed. DC adhesion and subsequently its maturation and potential for adaptive immune cell activation were measured by flowcytometry.When iDCs were treated with hydrogels the levels of DC markers (CD80 and CD86) expression as DC maturation criteria were measured. Expression level ratio for CD80 and CD86 to control sample show significant reduction, about 40 and 50, respectively. Released cytokinesfrom administrated DC by trappedaptamerswithAlg-PEI hydrogel indicate that DC behavior against a chemical foreign body was modulated considering the amount of released cytokines were decreased by10%.

Conclusions: The results of this study demonstrated that this presented drug delivery system based on αlβ2 and αmβ2 aptamers can be used as an immune response modulator in health-related application. αlβ2 and αmβ2 aptamers as a new age of state of the art drug technology could be a good substitute for monoclonal antibody drugs to reduce their side effects and draw backs.

Key words: Immunomodulation, Drugs, Aptamer, Dendritic cell.