Phenotype and Polarization of Autologous T Cells by Biomaterial-Treated Dendritic Cells

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Introduction: Dendritic cells (DCs) are the most effective professional antigen-presenting cells (APCs) that have a potential role in initiating T-cell mediated immunity. Upon their maturation, DCs bridge the innate immune response with the adaptive immune response by stimulating T lymphocytes. In this way, phenotype changes of DC are essential to T cell activation which might induce to T cell immunity or tolerance, associated with T helper (Th) type I response or T helper (Th) type II response with CD4+CD25+ T regulatory cells, respectively. Dendritic cells can control the adaptive immune response by presenting the antigenic peptide to CD4+ or CD8+ T cells, as well as directing cytokine releases into adaptive immunity polarization towards either Th1 (cellular response) or Th2 (humoral response). As such, due to the innate immune response towards the biomaterial component, they have the potential to modulate (inhibit or enhance) the adaptive immune response towards the biological component of a combination product.

Previously, we have shown an adjuvant effect associated with 3-D porous poly(lactic-*co*-glycolic acid) (PLGA) scaffolds in the enhancement of the humoral immune response to associated co-delivered antigen *in vivo*.[1,2] We also have shown differential levels of DC maturation depending on the type of 2-dimensional (2-D) biomaterial films with which immature DCs were treated.[3,4]

To understand the *in vitro* effects of inherently different biomaterials on DC-directed autologous T cell phenotype and polarization, DCs were treated with different biomaterial films in the presence or absence of a model antigen, ovalbumin (OVA), and co-cultured with autologous T cells and their phenotypes assessed.

Methods: Dendritic cells were derived and treated with biomaterial films as previously described.[3,4] Briefly, human peripheral blood monocytes (PBMCs) were collected twice from the same donor on Days 0 and 6. After 5 days (on Days 5 and 11), immature DCs (iDCs) derived from collected PBMCs were treated with different biomaterial films in the absence or presence of model antigen for 24 hours.

On Day 6, after 24 hours of biomaterial/OVA antigen treatment for the first DC culture, DCs were isolated from biomaterials or extracellular antigen and then, co-cultured with autologous non-adherent mononuclear cells (MNCs) which was predominantly composed of CD3+ T cells (1:6.25 of DC:MNC) for another 8 days, combined with additional stimulation of MNCs by another biomaterial/antigen-treated DCs derived from the identical donor on Day 12. Multifunctional effects of these DCs on T cell phenotype and polarization were assessed on Day 14 by examination of T cell marker expression (CD4, CD8, CD25, CD69) and Th1 [interferon (IFN)-γ or interleukin (IL)-12p70) and Th2 (IL-10 or IL-4) cytokine release upon co-culture of biomaterial/antigen treated-DCs & MNCs.

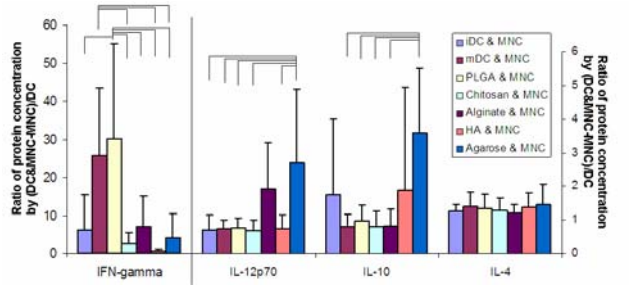

Figure 1. Geometric mean fluorescence intensity (gMFI) of cytometric bead array (CBA) for Th1 (IFN-γ, IL-12p70) and Th2 (IL-10, IL-4) cytokine releases upon co-culture of autologous T cells & DCs treated with different biomaterial films in the presence of model antigen.

Results/Discussion: When autologous T cells were co-cultured with DCs treated with biomaterial film/antigen combinations, different biomaterial films induced differential levels of T cell marker (CD4, CD8, CD25, CD69) expression, as well as differential cytokine profiles of Th1 (IFN-γ, IL-12p70) and Th2 (IL-10, IL-4) in the differential polarizations as shown in Figure 1. Dendritic cells treated with agarose films induced CD4+ CD25+ expression on autologous T cells and IL-10 release at higher levels whereas PLGA film treatment induced release of IFN-γ at higher levels, as compared to DC treatment with other biomaterial films, in the DC-T co-culture system. Interestingly, when DCs were treated with the different biomaterial films, profiles of released cytokines were influenced by the presence of antigen (OVA) or co-culture with autologous T cells.

Conclusions: Differential levels of autologous T cell responses (marker expression and cytokine profiles in Th1/Th2 polarizations) were observed in co-culture of T cells and DCs depending on different biomaterial films used to treat the DCs. This indicate that different biomaterials have the potential to indirectly modulate T cell-mediated immunity and further, these multifunctional effects of different biomaterial-treated DCs on autologous T cells possibly elucidate the type of T cell activation or polarization in the adaptive immune response, which can be expected when those biomaterials are introduced *ex vivo* or *in vivo*.

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References:

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