Hydrogel Based Dendritic Cell Recruitment for Induced Protein Production

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Purpose: Current anti-cancer adoptive cell immunotherapies have three major hurdles: extraction and preservation of autologous cells; engineering, expansion, and activation of cells ex vivo; and subsequent re-infusion of engineered cells to the patient. To reduce the resources and time needed to produce engineered autologous cells and bypass the need for extraction and reinfusion, an in-situ, hydrogel-based reprogramming environment was investigated for its viability to recruit and modify dendritic cells to overexpress a protein of interest. Procedure: Macroporous alginate hydrogels were fabricated using a calcium sulfate crosslinking agent. A transwell cell migration assay was used to verify dendritic cell recruitment and transduction by lentiviral particles encoding for interleukin-10. Sustained protein of interest production from recruited cells was measured. Results: Dendritic cells were found to effectively migrate into macroporous alginate hydrogels with granulocyte macrophage colony-stimulating factor-saturated media, and recruited dendritic cells were successfully transduced, exhibiting surface-expressed interleukin-10. Recruited cells also showed sustained interleukin-10 production over three days. Conclusion: Alginate-based hydrogels loaded with lentiviral particles were verified as a platform for dendritic cell recruitment and modification in the context of adoptive cell therapies. The hydrogel scaffold also shows promise as an in situ protein factory platform. Further experimentation will determine optimal formulations of hydrogels and chemoattractants for maximized dendritic cell recruitment, transduction, and retention. Co-culture experimentation with CD8+ T lymphocytes will determine the efficacy of induced dendritic cell priming.

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Fourth Award of $600

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