IL-4/IL-10 Induced Alterations in Gene Expression Profiles of Rodent Wound Macrophages

Statement of purpose: Alteration and activation of macrophages has emerged as a key area in the fields of biomaterials and regenerative medicine. IL-4 and IL-10 both are anti-inflammatory cytokines and have been implicated in the progression of FBR. In recent studies, IL-10 has been implicated as a potential candidate to alleviate fibrosis. In vitro macrophage activation in response to IL-4 and IL-10 represent different phenotypes that are implicated in wound healing and tissue remodeling.

Our long term research objective is to reduce the fibrosis and enhance the longevity of the implants especially in the context of continuous glucose sensor where problem of fibrosis is severe limiting the implant use to no more than 7-10 days. Thus, the aim of the study was to evaluate the effects of in vivo delivery of IL-4 and IL-10 on macrophage phenotypes using PVA sponge wound models in rats and to understand in vitro to in vivo translation of IL-4/IL-10 effects.

Materials and Methods: IL-4 or IL-10 (200ng/mL in PBS) loaded sterile pva-sponges were implanted in subcutaneous tissue of male Sprague-Dawley rats. Control sponges were soaked in PBS alone. On day 3, a booster dose of IL-4 or IL-10 (200 ng/mL) was given. On day 7 sponges were explanted and processed to collect wound fluid and macrophages. Gene expression analysis was performed on extracted macrophages.

Results: Figure 1 & 2 show the gene expression profile of macrophages from IL-10 treated and IL-4 treated sponges.

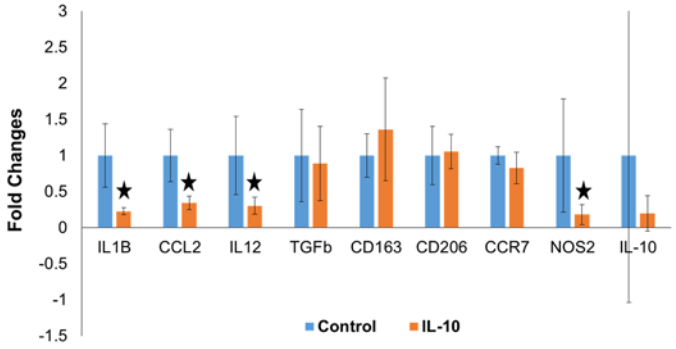

Figure 1: Gene expression profile of macrophages extracted from IL-10 treated sponges.N=4 (Mean±SD)

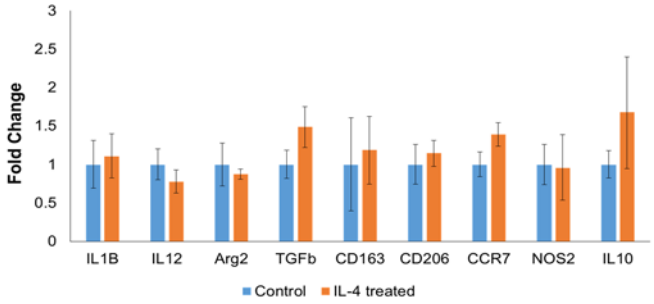

Figure 2: Gene expression profile of macrophages extracted from IL-10 treated sponges.N=4 (Mean±SD)

IL-10 has resulted in significant down-regulation of IL-1β, CCL2, IL-12 and NOS. Data has not reached any significant value in IL-treated sponges.

Conclusions: IL-10 seems to down-regulate the inflammatory cytokine genes but changes in CD163 and CD206 have not reached any statistical significant value which represent the hallmark of IL-10 and IL-4 macrophage activation in vitro.