

Wallace H. Coulter Foundation Biomedical Engineering Seminar Series

VLADIMIR BELJANSKI is a faculty at the Cell Therapy Institute of Nova Southeastern University. He received his Ph.D. at Emory University and post-doctoral training at the Medical University of South Carolina. His expertise covers pre-clinical discovery and development of therapies. The goals of his current research program is to develop cell therapy for regeneration of damaged or diseased tissue. Dr Beljanski's team utilizes stromal cells from various sources and studies factors that limit therapeutic efficacy of such cells. Specifically, he is looking into manipulating cellular self-digestion pathway as a mean to make therapeutic cells more effective.



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Autophagy Modulators Enhance Immunoregulatory Properties Of Miami Cells

ABSTRACT: Mesenchymal stromal cells (MSCs), adult stromal cells most commonly isolated from bone marrow (BM), are being increasingly utilized in various therapeutic applications including tissue repair via immunomodulation, which is recognized as one of their most relevant mechanism of action. The promise of MSC-based therapies is somewhat hindered by their apparent modest clinical benefits; highlighting the need for approaches that would increase the efficacy of such therapies. Manipulation of cellular stress-response mechanism(s) such as autophagy, a catabolic stress-response mechanism, with small molecules prior to or during MSC injection could improve MSCs' therapeutic efficacy. Unfortunately, limited information exists on how manipulation of autophagy affects MSCs' response to inflammation and subsequent immunoregulatory properties. Methods: In this study, we exposed BM- MSC precursor cells, "marrow-isolated adult multilineage inducible" (MIAMI) cells, to autophagy modulators tamoxifen (TX) or chloroquine (CQ), together with IFN-g. Exposed cells then underwent RNA sequencing

(RNAseq) to determine the effects of TX or CQ co-treatments on cellular response to IFN-g at a molecular level. Furthermore, we evaluated their immunoregulatory capacity using activated CD4+ T cells by analysing T cell activation marker CD25 and the percentage of proliferating T cells after co-culturing the cells with MIAMI cells treated or not with TX or CQ. Results: RNAseq data indicate that the co-treatments alter both mRNA and protein levels of key genes responsible for MSCs' immune-regulatory properties. Interestingly, TX and CQ also altered some of the microRNAs targeting such key genes. In addition, while IFN-g treatment alone increased the surface expression of PD-L1 and secretion of IDO, this increase was further enhanced with TX. An improvement in MIAMI cells' ability to decrease the activation and proliferation of T cells was also observed with TX, and to a lesser extent, CQ co-treatments. Conclusion: Altogether, this work suggests that both TX and CQ have a potential to enhance MIAMI cells' immunoregulatory properties. However, this enhancement is more pronounced with TX co-treatment.



Through the generous support of the Wallace H. Coulter Foundation the Department of Biomedical Engineering facilitates weekly lectures each year during academic terms. Experts in all areas of Biomedical Engineering are invited to campus to provide a research seminar and to meet with faculty and students and to tour our academic and research facilities.

Friday, January 10th, 2020
9:00AM-10:00AM Room EC 2300