ABSTRACT NUMBER: 1774

Bone Marrow Derived Dendritic Cells Modified By Lentiviral-Mediated RelB shRNA Possess Tolerogenic Phenotype and Functions on Lupus Splenic Lymphocytes

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Meeting: 2015 ACR/ARHP Annual Meeting

Date of first publication: September 29, 2015

Keywords: Dendritic cells, immune tolerance and systemic lupus erythematosus (SLE)

SESSION INFORMATION

Date: Monday, November 9, 2015

Session Type: ACR Poster Session B

Session Title: Systemic Lupus Erythematosus - Animal Models Poster II

Session Time: 9:00AM-11:00AM

Background/Purpose:

Systemic lupus erythematosus (SLE) is an autoimmune disease that is characterized by high morbidity and mortality and remains challenging in treatment. Dendritic cells (DCs) have been shown to participate in the initiation and perpetuation of lupus pathogenesis. DCs that can induce tolerogenicity appear as potential cell-based therapy in this condition. In this study, we examined the *in vitro* tolerogenic properties of bone-marrow derived DCs (BMDCs) in the murine lupus setting.

Methods:

We used lentiviral transduction of RelB-silencing shRNA to modify expression of RelB, a key transcription factor regulating DC maturation, in BMDCs from MRL/MpJ mice. Tolerogenic properties of RelB-modified DCs were compared to scrambled control (SC)-modified DCs.

Results:

RelB expression was found to be significantly reduced in RelB-modified DCs derived from MRL/MpJ mice, wild type of the same genetic background as MRL/lpr lupus-prone mice. These MRL/MpJ RelB-modified DCs displayed semi-mature phenotype with expression of lower levels of co-stimulatory molecules compared to SC-modified DCs. RelB-modified DCs were found to be low producer of IL-12p70, can induce hyporesponsiveness of splenic T cells from MRL/MpJ and lupus-prone MRL/lpr mice. Furthermore, they downregulated IFN-γ expression and induced IL-10 producing T cells in MRL/MpJ splenocytes, and attenuated IFN-γ and IL-17 expression in MRL/lpr splenic CD4+ lymphocytes. Splenocytes primed by RelB-modified DCs demonstrated antigen-specific suppressive effect on allogeneic splenocytes.

Conclusion:

RelB-silencing in DCs generates DCs of tolerogenic properties with immunomodulatory function and appears as potential option of cell-targeted therapy.

Disclosure: H. Wu, None; **Y. Lo**, None; **A. Chan**, None; **M. Y. Mok**, None.

To cite this abstract in AMA style:

Wu H, Lo Y, Chan A, Mok MY. Bone Marrow Derived Dendritic Cells Modified By Lentiviral-Mediated RelB shRNA Possess Tolerogenic Phenotype and Functions on Lupus Splenic Lymphocytes [abstract]. *Arthritis Rheumatol.* 2015; 67 (suppl 10). http://acrabstracts.org/abstract/bone-marrow-derived-dendritic-cells-modified-by-lentiviral-mediated-relb-shrna-possess-tolerogenic-phenotype-and-functions-on-lupus-splenic-lymphocytes/. Accessed December 9, 2015.

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