

International Conference and Exhibition on **Lung Disorders & Therapeutics** July 13-15, 2015 Baltimore, Maryland, USA

Regulatory dendritic cell approaches for asthma immunotherapy

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Asthma affects some 300 million people globally and kills \approx 250,000 annually. While we can manage most asthmatics pharmacologically these therapies are life-long symptom-based approaches and do not address the underlying Th2 immunologic basis of the disease. What we need are therapies that will reverse these Th2 responses such that the treated individual responds to their allergens in the same way as healthy subjects by mounting regulatory T cell (Treg) responses. Tolerogenic dendritic cells (DC) are found in many body compartments but can also be generated in vitro from bone marrow or monocyte precursors by DC differentiation in the presence of mediators like IL-10, dexamethasone or retinoic acid (RA; reviewed in *Front Imm* 5:7, 2014). For example, treatment of severely asthmatic mice with allergen-presenting IL-10-induced DC (DC10) abrogates airway hyper responsiveness (AHR) within 3 week of treatment in an IL-10-dependent fashion and progressively diminishes all other asthma traits to background for at least 8 mo. DC10 induce Th2 effector T cells to trans-differentiate into CD25+Foxp3+Treg. Human monocyte-derived DC10 similarly suppress autologous Th2 cells converting these into CD25+LAG3+Foxp3+Treg. However, given that some inflammatory environments can suppress Foxp3 expression by such Treg and thereby convert the Treg into highly pathogenic Th17 cells, we have also developed protocols to generate RA-induced DC (DC-RA) which in turn can induce Th2 cells to differentiate into CD25+LAG3+CD49b-Foxp3-Treg in an IL-27-dependent fashion. Thus, we have the option of inducing distinct kinds to Treg to suit different pathologies.

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Innovating pulmonary rehabilitation for Chronic Obstructive Pulmonary Disease

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Studies have shown that pulmonary rehabilitation and Tai Chi are beneficial to patients with chronic obstructive pulmonary disease (COPD), which is a major public health problem. Long term effectiveness of exercise interventions at completion of formal pulmonary rehabilitation requires exercise adherence. Tai Chi has also been shown to have proven benefits in improving exercise capacity, physiological status, quality of life health related status, self-efficacy and associated with higher compliance to exercise in COPD patients. The author hypothesized that innovating pulmonary rehabilitation by incorporating Tai Chi elements in the exercise component could have complementary benefits. A single-blind randomized controlled study was conducted from March 2011 to May 2012 with a total of 192 COPD patients recruited from four primary care clinics in Hong Kong. They satisfied the eligibility criteria and consented to randomization to either pulmonary rehabilitation program group (PRP) or the group with Tai Chi elements added to PRP (TC). Both groups received rehabilitation consisting of 2 sessions per week for 6 weeks with totally identical content except that Tai Chi exercises were added to TC group. Data collection was performed at baseline, 2 and 6-month post-intervention. Intention-to-treat analysis was performed for 192 subjects. Both groups did not differ in demographics and baseline variables except for COPD staging, mean FEV1, FEV1%-Pred, Saint George Respiratory Questionnaire SGRQ activity score and COPD-CSES self-efficacy score. Statistical improvements were seen in exercise capacity, health status and self-efficacy within both groups at 6-month post-intervention. Although more favorable improvements in physiological outcomes and health status were demonstrated in Tai Chi group, only the functional exercise capacity showed statistical improvement between groups at 6 months post-intervention ($\beta=12.786$ meters ; 95% CI=3.794, 21.777; $p=0.006$). The adjuvant effect of incorporating Tai Chi in pulmonary rehabilitation showed a modest complementary benefit in exercise capacity.

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