

THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

Fauziyya Y. Muhammad

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
GRADUATE COLLEGE

Department of Microbiology and Immunology

Monday, July 20, 2020 | 10:00 am

Meeting Location: <https://ouhsc.zoom.us/j/96762460723>

Password: **56923316**



PHENOTYPIC CHARACTERIZATION OF REGULATORY T CELLS NECESSARY FOR SUPPRESSION OF UVEITIS

COMMITTEE IN CHARGE: Darren J. Lee, PhD, Chair;
Michelle Callegan, PhD, Daniel J.J. Carr, PhD;
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ABSTRACT: Autoimmune uveitis is a leading cause of blindness worldwide. The immunological mechanisms that limit ocular inflammation are poorly understood. Current treatments for uveitis do not lead to induction of regulatory immunity and hence fail to prevent relapsing uveitis. Accordingly, we used molecular and immunology techniques to investigate the role of regulatory T cells in the suppression of uveitis. Regulatory T cells constitute heterogeneous populations that utilize different mechanisms to suppress inflammation. During experimental autoimmune uveitis (EAU), which manifests with pathology that recapitulates human autoimmune uveitis, mice recover spontaneously.

Recovery is marked by the presence of regulatory T cells (post-EAU regulatory T cells) in the spleen as a component of the melanocortin-adenosinergic (M-A)-induced systemic regulatory immunity. The post-EAU regulatory T cells show therapeutic potential when transferred into mice immunized for uveitis. The primary objectives of this work were to identify, characterize, and define the suppressive mechanism of post-EAU regulatory T cell subsets necessary for the suppression of ocular inflammation.

Our results show that the post-EAU regulatory T cells stably express FoxP3. These regulatory T cells express unique markers that include TIGIT, PD-1, 2B4, and LAG 3. These suppressive regulatory T cell populations are enriched in the eyes, draining lymph node and spleen during recovery of EAU. We provided for the first-time evidence of the FoxP3 regulatory T cells emerging and persisting in the eyes following recovery of uveitis. Furthermore, we identify unique post-EAU regulatory T cell subsets based on the PD-1 and TIGIT expression. These regulatory T cell subsets are induced through MC5R or A2AR in healthy controls but not in uveitis patients. Also, the PD-1 and TIGIT regulatory T cells are necessary for the suppression of uveitis, and the emergence of regulatory T cells in the eyes at uveitis onset is dependent on A2AR expression.

Collectively, these studies demonstrate the unique phenotype and mechanisms of the regulatory T cells necessary for the suppression of uveitis. Absence of A2AR impacts the suppressive activity of post-EAU regulatory T cells and the lack of stable FoxP3, TIGIT and PD-1 result in the inability of the regulatory T cells to function. In conclusion, our findings provide a mechanistic insight of regulatory T cell function during uveitis, and provide a strong basis for the identification of powerful regulatory T cells. They further suggest the potential utilization of regulatory T cell-based therapy for autoimmune diseases, including uveitis.