THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

Hannah Berrett

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
GRADUATE COLLEGE
Department of Cell Biology

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10:00 am | Biomedical Research Center, Room 109

The role of E protein activity in effector program differentiation of invariant Natural Killer T cells and Innate Lymphoid Cells

COMMITTEE IN CHARGE

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ABSTRACT: Effector programs allow immune cells to have specialized cytokine responses to different categories of pathogens. While first described in adaptive CD4$^+$ T helper cells, effector programs are now known to define subsets of innate-like lymphocytes as well, including invariant natural killer (iNKT) cells and innate lymphoid cells (ILCs). The type 1 effector program includes T_H1 cells, NKT1s, and ILC1s and is characterized by IFNγ production, TBET expression, and protection against intracellular pathogens. The type 2 effector program includes T_H2 cells, NKT2s, and ILC2s and is characterized by IL-4, IL-5, and IL-13 production, GATA3 expression, and protection against helminths. The type 17 effector program includes T_H17 cells, NKT17s, and ILC3s and is characterized by IL-17 and IL-22 production, RORγt expression, and protection against extracellular bacteria and fungi. While these different cell lineages have many components of their regulatory networks in common for effector program differentiation, important differences exist as well. This work demonstrates that the roles of E protein activity in effector program differentiation differs between iNKT cells and ILCs. In iNKT development, inhibiting E protein activity leads to a shift in subset population frequency from NKT2 cells and toward NKT1 cells. Additionally, we examined T cell receptor (TCR) signal strength as a potential mechanism for modulating E protein activity and found that, indeed, TCR strength and E protein activity had an inverse relationship affecting iNKT effector program development. In ILC development, sustaining E protein activity negatively affects ILC2 cell development and function, with several ILC2-associated genes being downregulated in ILC precursor cells. Therefore, E protein activity affects effector program differentiation in both iNKT cells and ILCs, although its role is distinct in each cell lineage, demonstrating the importance of examining this developmental process in all cell types individually.