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YOU ARE INVITED TO ATTEND THE DEFENSE OF THE DOCTORAL DISSERTATION

"Carbonic anhydrase enzymes: regulators of mast cell development and antihelminth immunity"

by

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Infection, Immunity and Inflammation Program

B.S., 2016, Montclair State University, N.J.

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Monday, June 6th, 2022
11:30 A.M.

Join in-person: Cancer Center, G1196
Join Webex presentation:
https://rutgers.webex.com/rutgers/j.php?MTID=me1d73efca410e2f4aa1f541585605cde
Meeting ID: 2624 927 4240
Password: Graduation

ABSTRACT

Antihelminth responses require robust type 2 cytokine production that simultaneously promotes worm expulsion and initiates the resolution of helminth-induced wounds. However, how infection-induced changes in hematopoiesis contribute to these seemingly distinct processes remains unknown. Recent studies have suggested the existence of a hematopoietic progenitor with dual mast cell/erythrocyte potential. Nonetheless, whether and how these progenitors contribute to host protection during an active infection remains to be defined. Here, we employed single cell RNA-sequencing and identified that the metabolic enzyme, carbonic anhydrase (Car) 1 marks a predefined bone marrow-resident hematopoietic progenitor cell (HPC) population. Next, we generated a Car1-reporter mouse model and found that Car1-GFP positive progenitors represent bipotent mast cell/erythrocyte precursors. Finally, we showed that Car1-expressing HPCs simultaneously support mast cell and erythrocyte responses during *Trichinella spiralis* infection. Collectively, these data suggest that mast cell/erythrocyte precursors are mobilized to promote type 2 cytokine responses and alleviate helminth-induced blood loss, developmentally linking these processes.

Despite these substantial advances, the relative contributions of Car1-expressing progenitors to the infection-induced increases in mast cells and erythrocytes remain unknown. To address this, we have developed a novel Car1-Cre mouse to perform important fate-mapping studies. Here we demonstrate that our novel mouse model can be used to selectively label *Trichinella*-induced mast cells with a history of Car1-expression. Further, we demonstrate that Car1-Cre mice can also be employed to selectively delete Car1-expressing progenitors. This novel tool will allow us, for the first time, to evaluate the developmental origins of infection-induced mast cells. Further, this newly generated mouse model will enable loss-of-function studies to test the contributions of this specific progenitor cell to antihelminth immunity and host protection. Collectively, this work reveals unappreciated hematopoietic events initiated by the host to combat helminth parasites and provide insight into the evolutionary pressure that may have shaped the developmental relationship between mast cells and erythrocytes.