Microbiology 204
Discussion Session #4 November 2, 2018
1-2:30PM Room: CL220/223
Faculty leader: Ari Molofsky

Rauber et al. IL-9 driven ILC2 activation in inflammation. Nat Med, 8:938, 2017

Everyone should read this paper before coming to class. In this paper, the supplemental data file has some important information that can be mentioned.

LEARNING OBJECTIVES:
To understand mechanisms involved in downregulation of inflammatory stimuli through complex cellular interactions

STUDENT ASSIGNMENTS
1. Discussion leader (see instruction page for advice on leading the discussion).

2. Outline some of the known mechanisms by which inflammatory responses are downregulated. For example, IL-10, TGF-β, resolvins. What are some of the cellular targets for these anti-inflammatory mediators?

3. In Fig 1, the authors demonstrate that IL-9KO mice have prolonged joint inflammation in the AIA model. Explain how AIA is initiated in this model.

4. In Fig. 2, the authors demonstrate that IL-9KO mice have prolonged joint inflammation in the KxB/N serum transfer model. How does this model differ from the AIA model and what does it specifically test?

5. Discuss Fig. 3a, 3c and 3f/e. The Treg suppression assay primary data is shown in Fig. 3f but the summed results are Fig3e. This type of suppression assay is a difficult and variable assay. Fig 3g suggests that IL-9KO Treg have different surface marker expression, correlated with function. They are missing two other surface markers that correlate with Treg function – CD25 and CTLA-4. Finally, Fig 3i shows that WT Treg can suppress cytokine production from Teffectors; shouldn't this figure also include IL-9KO Tregs?

6. The authors use IL-9citrine reporter mice to define the IL-9 producing cells in the joint. What are these mice? Discuss results in Fig. 4b and Fig 4d. It would seem important to have examined GITRL and ICOSL expression on ILC2s from IL-9KO mice. Not sure why that experiment is missing. Discuss the potential ratio of ILC2 cells in the joint to Tregs (data shown from spleen).

7. Fig. 4e and f are key in vitro experiments. Please explain these results. Though not stated in Fig. legends or methods, presumably these experiments were done the ILC2s that had been stimulated with IL-9 for 72 hrs.

8. Fig. 4g and 4h provide nice in vivo data. Please explain these experiments. But what key control is missing (evidence that the adoptively transferred cells are still persistent through the 40 day experiment).

9. Fig. 5 provides nice correlative human data, indicating presence of ILC2s in joints of patients with low inflammation. However, this could be an effect of resolution of inflammation, not a cause. Discuss these results.

1. Discussion leader can summarize using the Figure from the news/views that accompanies this article.

Student assignment #s

1. Julie Cole
2. Ki Hyun Kim
3. Brian J Woo
4. Iowis Zhu
5. Marissa Chou
6. Cody Mowery
7. Jennifer Umhoefer
8. Adam Wade-Vallance
9. Benjamin Wheeler
10. Darwin Kwok
11. Suraj Makhija
12. Nick Mroz
13. Rachel DeBarge
14.

(NOTE : if you will miss a discussion session, inform Dr. Lowell in advance and you won't be given an assignment that week; if assignments have already been made, you should make a trade with one of your classmates who does not have an assignment that week so that your assignment is covered).