CD206 Positive Renal Resident Macrophages Facilitate Cyst Progression in a Juvenile-induced Cilia Mutant Mouse Model

Zhang Li[1], Kurt A. Zimmerman[1], Cheng Song[1] and Bradley K. Yoder[1]

[1]Department of Cell, Developmental, and Integrative Biology, University of Alabama at Birmingham

INTRODUCTION

Polycystic kidney disease (PKD) is one of the most common inherited genetic renal diseases. It has been reported that abnormalities in the structure or function of primary cilia result in kidney cyst growth in animal models of PKD and human patients, but the mechanism of how primary cilia regulate cystogenesis is largely undefined. Recent data suggests that macrophages are associated with cyst formation in PKD; however, the contribution of specific macrophage subsets in promoting renal cyst formation and how this is related to ciliary dysfunction is unknown.

METHODS

To address the involvement of cilia and macrophages subtypes in cyst formation, our lab utilized a mouse model of inducible cilia deletion (Caggcre^{ERT2};IFT88$^{f/f}$ mouse) to conditionally disrupt the *Ift88* gene. For these studies, we induced cilia loss by tamoxifen injection at postnatal day 7 (p7), a time point in which cilia disruption leads to rapid cyst formation. Macrophage populations were analyzed in both wild type and cilia mutant backgrounds via immunofluorescence microscopy and flow cytometry at different time points following cilia loss.

RESULTS

Our data indicate that there is a predominant subset of renal resident macrophages expressing CD206 in juvenile WT mice and that the number of CD206+ macrophages decreases rapidly as the mice mature into adulthood. However, in cilia conditional mutant mice, induction of cilia loss in juvenile stages leads to persistently elevated levels of CD206+ macrophages compared to control mice. Moreover, our data show that in the juvenile period the severity of cyst formation is also associated with the time of cilia deletion. Earlier induction of cilia loss (e.g P3), which coincides with the greater number of CD206+ macrophages, results in increased cyst severity in the kidney than induction at later ages (e.g. P7).

CONCLUSION

These data suggest that CD206+ expressing macrophages may be involved in promoting renal cystogenesis. Understanding how loss of cilia on tubule epithelium influence macrophage proliferation, survival, and polarization in the kidney could provide a promising option for PKD therapy.