Investigating CD4 T cells in mouse models of cystic disease and human PKD patients

Kurt Zimmerman, Cheng Song, Nancy-Mize Gonzalez, and Bradley K. Yoder

INTRODUCTION

Polycystic kidney disease (PKD) is caused by mutations in proteins localized to the primary cilia or proteins required for cilia assembly. Despite this knowledge, the mechanism linking cilia dysfunction and renal cystic disease remains unknown. Previous studies from our lab and others show that macrophages promote renal cyst formation. However, the involvement of other immune cells in cystic disease remains unknown.

METHODS

We set out to identify and define the contribution of adaptive immune cells, particularly CD4 T cells, in mouse models of cystic disease (Cagg^{cre} IFT88$^{f/f}$ mice with ischemia reperfusion injury; IFT88^{Orpk} mice) and in human patients with PKD.

RESULTS

Our preliminary data show that CD4 T cell numbers are increased in multiple models of renal cystic disease and that the increase in CD4 T cells occurs prior to the formation of renal cysts. Further subtyping of CD4 T cells shows that IL-17A producing CD4 T cells, termed Th17 cells, represent the major T cell population that is present prior to the formation of renal cysts suggesting that this population of cells may be promoting cyst initiation. Strikingly, deletion of adaptive immune cells (RAG1-/- mouse) significantly reduced renal cyst formation. The data showing accumulation of CD4 T cells in mouse models of cystic disease are paralleled by results from human PKD patients that show increased levels CD4 T cells in regions adjacent to developing cysts. Finally, our preliminary studies show that IL-17A protein levels from serum are greatest in PKD patients between the ages of 20 and 30 suggesting that Th17 cells are most prominent during early stages of the disease.

CONCLUSIONS

Our data identify the presence of CD4 T cells in mouse and human cystic kidneys and suggest that CD4 T cells may be pathogenic in renal cyst formation.