C3G is a complex disease that develops in the renal glomerulus.

Every person with C3G has a different combination of antibodies, genetic variants, and course of disease. Our goal is to use this information to understand C3G and develop effective treatment strategies. Some important questions we are currently asking in our research include:
1. Are there other disease drivers that we have not yet identified?
2. Because C3G is a disease that affects the kidney, are there genetic variants in the genes associated with the glomerulus that affect disease development and/or progression?
3. If many disease drivers exist, is it possible that some drivers are more common than others?

The glomerular microenvironment is very complex and highly specialized.

The glomerular microenvironment is responsible for the selective filtration of our blood. This image represents the cross-section of a glomerular capillary. In the lumen of the capillary where blood flows, you can see the capillary walls coated with fenestrated endothelial cells. On top of the cells is a blanket of glycoproteins and other components, which we call the glycocalyx. Together, we call the glycocalyx and the glomerular basement membrane the "glycomatrix". In C3G, the glycocalyx is the location where complement proteins are damaging the kidney.

What have we learned about the glycomatrix in C3G?
1. The C3G patient cohort is enriched for genetic variation in several genes that are associated with the glycomatrix structure and function.
2. The enrichment we see comes from both rare and common genetic variants and is gene-dependent.
3. The genes we have identified play important roles in the glycomatrix structure and function and support our hypothesis that the glycomatrix may be vulnerable to complement damage in C3G.

What are the next steps in this research study?
1. Develop experiments which will test the function of the genes with significant enrichment in C3G. This will help us understand if the genetic variants we found are disrupting the gene's normal function.
2. Work with our collaborators to test other C3G cohorts to determine if we can replicate our findings in a separate population. If we can, this data will provide more evidence to support our hypothesis.
3. Understand how we can use this information to better inform clinical decisions and patient care for C3G.