



Ophthalmology

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Non-infectious uveitis is a heterogeneous group of diseases that are currently defined by clinical features like vascular leakage or vitritis, as well as standard laboratory biomarkers like HLA-A29.

Unfortunately, these aspects of uveitis do not help us understand the actual causes of eye inflammation. Because we do not know which molecules cause disease in individual patients, we must treat all uveitis empirically, basing our therapy plans on what has worked most often in the past. Unfortunately, this approach fails many patients.

Characterization of uveitis based on molecular features, on the other hand, would result in a more precise classification of uveitis that is based on specific key molecules in individual patients. This level of insight could result in a more focused treatment approach, sparing patients unnecessary toxic side effects as well as vision loss due to therapeutic inefficacy.

The goal of the Hassman Uveitis Lab is to characterize patient- and disease-specific mechanisms of eye inflammation so that we can develop precision medicine treatment strategies. Our approach involves partnerships between patients, clinicians and scientists. We

use advanced molecular tools (like single cell RNA-Sequencing) to analyze the immune cells and molecules from our patients. We are working towards:

- 1) understanding the causes of uveitis
- 2) identifying biomarkers that predict treatment response
- 3) developing new therapeutic targets.

Our patients at Washington University in St. Louis have generously partnered with us, sharing their clinical data and biologic samples. This has allowed us to create a uveitis biorepository that currently includes data and biologic samples from 350 patients with uveitis. We are in the process of developing collaborations that would allow us to receive data and samples from other institutions so that we can better understand these rare diseases. We also share our data with other researchers so that we can advance discovery in uveitis. This collection has already fueled 5 collaborative publications.

Currently, we are focused on:

1. An analysis of eye immune cells from 23 patients with diverse types of uveitis, preliminarily entitled: A spectrum of ocular immune responses distinguishes patients with uveitis, in which we identify specific cell types and activation states that differ between uveitis subtypes, including Birdshot chorioretinitis.
2. Clinical and molecular analysis of a small clinical trial for patients with Birdshot chorioretinitis. This study is preliminarily entitled: Remission-associated immunologic remodeling in patients with birdshot chorioretinitis treated with tofacitinib, in which we identify gene and protein expression signatures associated with disease activity and treatment response.

We are in the planning phase for a multi-center clinical study with

investigators at Rush University and the University of Colorado aimed at Identification of clinical and genomic risk factors in Birdshot chorioretinitis.

Finally, we look forward to beginning a clinical study aimed at Identification of clinicomolecular biomarkers predictive of therapeutic response to TNF inhibition in uveitis.