



Lucia Sobrin, M.D., M.P.H.
*Charles Edward Whitten Professor of Ophthalmology, Harvard Medical School
Retina and Uveitis Services, Massachusetts Eye and Ear*

Dr. Sobrin and her colleagues at the Massachusetts Eye and Ear Infirmary are committed to research to further understand and better treat birdshot uveitis through the following projects.

1. Fluorescein angiography leakage patterns in birdshot uveitis

One risk factor for vision loss in birdshot uveitis is that there is often a delay in making the diagnosis. This occurs because some of the signs of the disease are not always obvious on the examination and because findings on imaging tests are not readily recognized as being indicators of birdshot uveitis. Delay in diagnosis can lead to vision loss so it is important to increase awareness of clues to the birdshot uveitis among ophthalmologists. Dr. Sobrin and her colleagues have published a study showing that a pattern of leakage of the retinal vessels as they exit the optic nerve is a common sign of birdshot uveitis that is often overlooked. In the published journal article, if this pattern was present, the chances of birdshot uveitis being the diagnosis were 82%. Dr. Sobrin regularly shows this finding when she gives lectures at regional, national and international ophthalmology meetings.

Article: Li A, Apivatthakakul A, Papaliadis GN, Sobrin L. High positive predictive value of fluorescein angiography contiguous, perineural retinal vascular leakage pattern for birdshot chorioretinopathy. *Ocul Immunol Inflamm* 2022.

2. Genetic risk factors for birdshot uveitis

Most, if not all, patients with birdshot uveitis have one copy of the *HLA-A29* gene. However, the majority of people who have at least one copy of the *HLA-A29* gene (somewhere between 1-10% of the general population, depending on the region in the world) never develop birdshot uveitis. That is, having an *HLA-A29* gene is felt by most ophthalmologists to be necessary for developing birdshot uveitis, but it is certainly not sufficient to lead to the disease.

There are a few possibilities as to what leads only a small proportion of people with the *HLA-A29* gene to develop birdshot chorioretinopathy. One is that there is something that birdshot uveitis patients come into contact with in their environment that somehow triggers birdshot uveitis and that environmental trigger is potentiated to cause disease because of the presence of the *HLA-A29* gene. Another possibility is that there are other genes that patients with birdshot uveitis have that interact with the *HLA-A29* gene and lead to the disease. There have already been some genetic studies in this field that have identified the *ERAP* gene as likely being one of these genes, but it does not explain all of the disease risk on its own. Dr. Sobrin and her colleagues would like to help identify additional genes that may be interacting with the *HLA-A29* gene to cause birdshot uveitis. To this end, they have collected DNA samples from patients who have *HLA-A29* – including both patients who have developed birdshot uveitis and those who have not. They will compare the genetic sequences of patients with birdshot uveitis (all carriers of the *HLA-A29* gene) to those *HLA-A29* positive patients who never develop birdshot uveitis to identify genes that are commonly or exclusively present in the birdshot uveitis patients. By comparing the genetic profile of

these two groups, they hope to identifying these additional genes and gain further insights to how the disease develops and thus into treatment strategies to address the underlying disease processes.

Dr. Sobrin's study protocol allows patients from outside of Mass. Eye and Ear to provide a blood sample for DNA extraction for this study. If you are interested in participating in the study, please see the message below:

Do you have birdshot chorioretinopathy? Are you interested in participating in research to further our understanding of this disease? Dr. Lucia Sobrin at the Mass. Eye and Ear Infirmary is leading a study to identify genetic markers, beyond HLA-A29, that increase the risk of birdshot chorioretinopathy. The study involves a one-time blood draw and signing a form to allow the notes and eye images from your eye doctor's office to be shared with Dr. Sobrin. If you are interested, please contact our Mass. Eye and Ear Research office: Email: tony_succar@meei.harvard.edu Phone: 617-573-6060.