Albinism and HPS participation in eyeGENE®

National Eye Institute (NEI)
National Institutes of Health (NIH)

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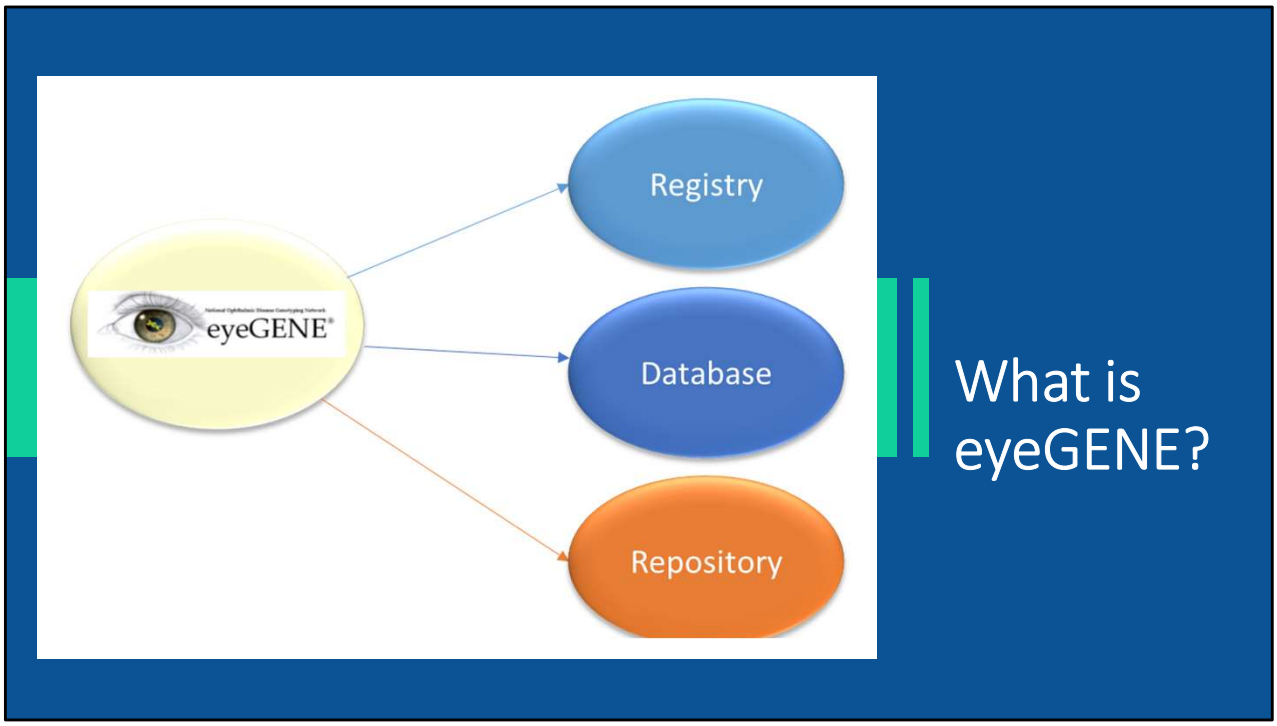
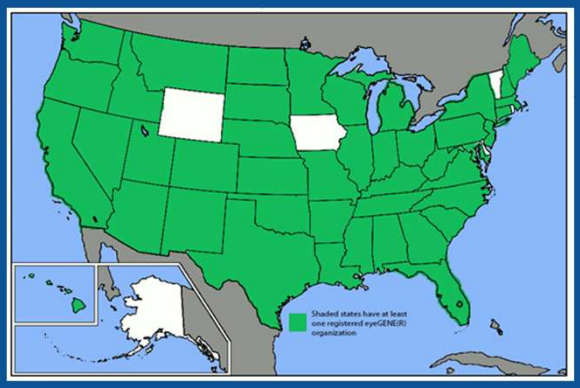
This is a presentation about results from the eyeGENE Program at the National Eye Institute at the National Institutes of Health related to albinism and Hermansky-Pudlak syndrome. Presented by Nia Moore to the 2022 NOAH Conference.

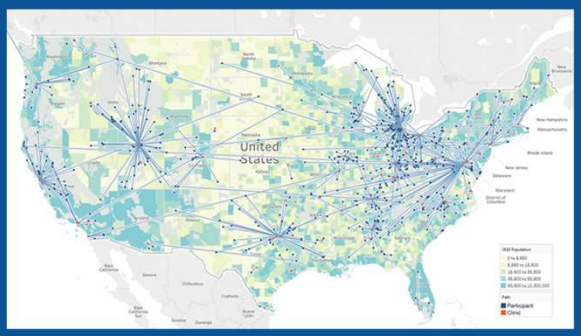


eyeGENE is a multi-site clinical research network created by the National Eye Institute (NEI) at the National Institutes of Health (NIH) in 2007 focused on rare genetic eye disorders. eyeGENE includes data from participants with over 30 inherited eye conditions including albinism. It includes a biorepository for long-term storage of participant DNA samples, a database including eye exam information, ocular images, family history and genetic information.

eyeGENE has become an important data resource for researchers who can apply to access de-identified participant data, DNA samples, and even connect with participants for additional studies. There have been over 30 secondary research projects and over 100 publications using eyeGENE so far

Participants throughout North America





eyeGENE recruited participants from 2007 through the end of 2015. Participants were enrolled through eye care professionals in private practice, academic centers, and the NEI clinic in Bethesda, MD. The map on the left side of the slide shows the states that included clinical referring sites and the map on the right shows the distance that eyeGENE participants traveled to be enrolled in the project.

Genetic Testing

Samples are shipped to outside CLIA labs for genetic testing

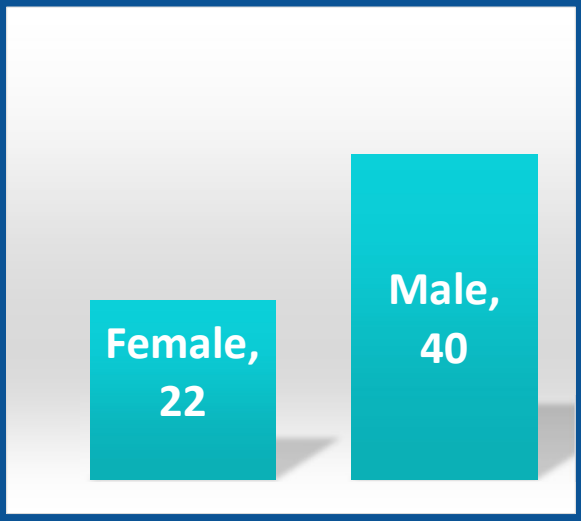
Variant information that is collected in our database is used to increase knowledge on over 30 conditions

When a participant enrolled in eyeGENE they were required to share a blood sample which the eyeGENE lab used to extract a DNA sample to become part of the biorepository. A small portion of the DNA was send to a CLIA (or clinical) diagnostic genetic testing laboratory. The lab would test the sample for genes associated with eye conditions and return a report back to eyeGENE to share with the participant. The genetic information garnered through the testing was also added to the database to allow research insight into the genetic components of the eye condition in the participant.

Almost all participants now have had genetic testing, but not all testing has revealed the genetic component of that person's eye experiences. There are still many research questions and knowledge gaps to be filled, which is why research and data sharing is so important.

Summary of Data for Albinism & HPS

- **Albinism = 59 Participants**
- **Hermansky Pudlak Syndrome = 3 Participants**



Here are some summary details about albinism and HPS data in the eyeGENE program.

Overall, 59 participants had a diagnosis of albinism and 3 were diagnosed with HPS. Of the 62 total, there are 22 females and 40 males.

Summary, cont.

- **Age at diagnosis:**
  - **Min = 0 years old**
  - **Max = 66 years old**
  - **Mean = 8 years old**
- **Age at enrollment:**
  - **Min = 2 years old**
  - **Max = 87 years old**
  - **Mean = 21 years old**
- **Foveal hypoplasia**
  - **Present = 55**
  - **Absent = 5**
- **Iris Transillumination**
  - **Complete = 8**
  - **Moderate = 18**
  - **Mild = 9**
  - **Absent = 25**
- **Fundus hypopigmentation**
  - **Marked = 19**
  - **Moderate = 22**
  - **Mild = 8**
  - **Not significant = 10**

The age of diagnosis was between birth and 66 years old with a mean of 8 years old. The age at enrollment to eyeGENE ranged from 2 to 87, with a mean of 21 years old.
On clinical exam, most participants were reported to have foveal hypoplasia, iris transillumination, and fundus hypopigmentation.

Genetics

Gene	Associated Diagnosis (OMIM)	# of Participants
HPS1	Hermansky-Pudlak Syndrome 1	1
HPS3	Hermansky-Pudlak Syndrome 3	1
TYRP1	Oculocutaneous albinism, Type 3	1
CNGB3	Achromatopsia 3	1
SLC24A5	Oculocutaneous albinism, Type 6	1
GPR143	Ocular albinism, Type 1 (X-linked)	5
OCA2	Oculocutaneous albinism, Type 2	11
TYR	Oculocutaneous albinism, Type 1	26
Inconclusive		12

This table shows the genetic results for the participants with albinism or HPS who have result available in the eyegene database. HPS genes have been noted in 2 participants. The third participant with HPS results are pending. For participants with a diagnosis of albinism, 26 had pathogenic variants in tyrosinase, 11 had variants in OCA2 and 5 had variants in GPR143, which is associated with the ocular-only, X-linked form of albinism. X-linked means that this type of albinism is usually only seen in males, however, one of these participants is female. 12 participants diagnosed with albinism have an inconclusive result after genetic testing, which shows that more research is needed in determining the genetic cause of their diagnosis.

What's next?

- eyeGENE Stage 3
  - Recruit additional participants in
    - Oculocutaneous & ocular albinism, HPS, or other hypopigmentation disorders affecting vision
    - Aniridia
    - Best disease
    - Blue-cone monochromacy
    - Corneal dystrophy
  - DNA sample for genetic testing
  - Contact registry for additional trials
  - Surveys and data collection for research

The NEI is now considering what is next for the eyeGENE program. Concept clearance has just been submitted for what is called eyeGENE Stage 3 to recruit more participants to the program in five diagnosis categories including albinism, HPS, and other hypopigmentation disorders that impact vision. Like the original eyeGENE project, the concept includes collection of DNA for genetic testing, a contact registry, and survey and clinical data collection for research to build on the knowledge of inherited eye conditions and potentially facilitate the development of treatments.

Website and Contact

- **https://eyegene.nih.gov**
- **eyeGENEinfo@nei.nih.gov**

Please reach out to eyeGENE if you have any follow-up questions.