FOUNDATION FIGHTING BLINDNESS

FFB-CRI's RUSH2A Study: Gaining Insights into USH2A

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Patient Registry for All Inherited Retinal Diseases

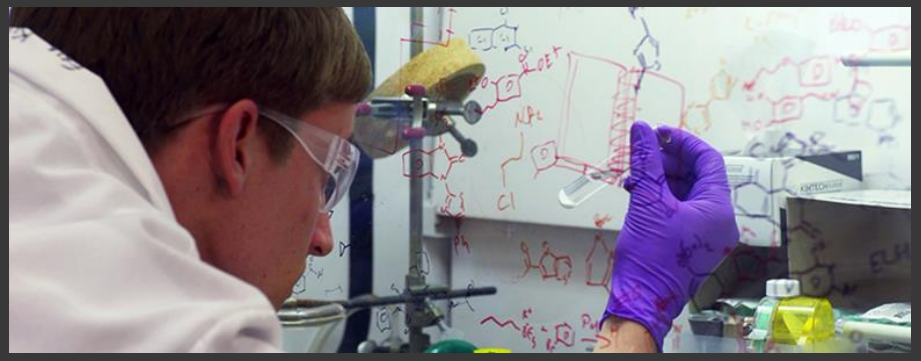
Global, Free, Secure, Easy-to-Use

Patient-Controlled

www.MyRetinaTracker.org

A Natural History Study for People with USH2A Mutations: Goals

- Understand progression rate of vision loss.
- Understand how specific mutations affect vision (genotype-phenotype correlation).
- Identify participants for clinical trials for therapies.
- Identify optimal outcome measures for clinical trials.
- More USH2A knowledge → drive therapy development.



Why USH2A?

- Common retinal-disease gene, large unmet need.
- >400,000 people affected by USH2A mutations[1].
- Leading cause of USH2: 57-63% of cases[2].
- Leading cause of autosomal recessive retinitis pigmentosa in U.S.: 19-23% of cases[2].
- Big gene (15.7 kb coding sequence).
- Hundreds of RP/USH mutations – lots of variation.

1 – Worldwide estimate, Radboud presentation 2015
2 - McGee, et al, J Med Genet. 2010 Jul; 47(7): 499–506
(Study of 188 USH2A patients in U.S.)

Jacque Duncan, M.D., UCSF, Study Chair

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U.S. Study Sites

- Baylor – Houston
- Columbia University – New York City
- National Eye Institute – Bethesda
- Retina Foundation of the Southwest – Dallas
- Medical College of Wisconsin – Milwaukee
- University of California, San Francisco
- Vitreo Retinal Associates – Gainesville
- Massachusetts Eye and Ear Infirmary – Boston
- Kellogg Eye Institute – Ann Arbor
- Moran Eye Center – Salt Lake City
- Emory University – Atlanta
- Wilmer Eye Institute – Baltimore
- Duke University – Raleigh-Durham
- Casey Eye Institute – Portland (Oregon)

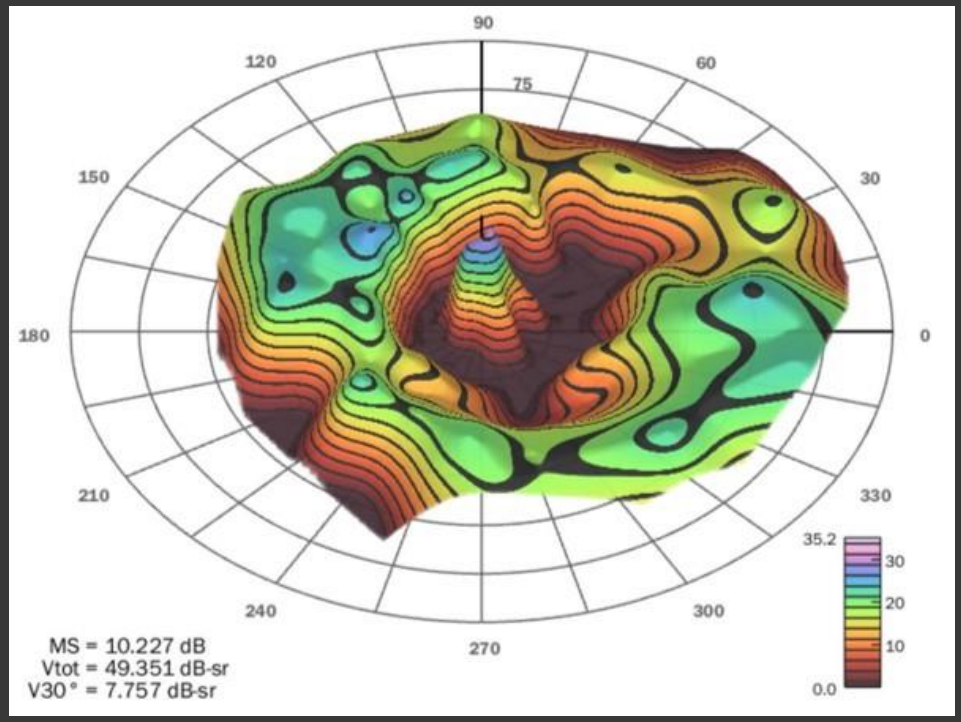
Sites Outside the U.S.

- Moorfield's Eye Hospital – London
- University of Tubingen – Germany
- Sick Kids Hospital – Toronto
- Institut de la Vision – Paris
- Radboud University, Nijmegen – Netherlands
- Ghent University Hospital – Belgium

Study Parameters

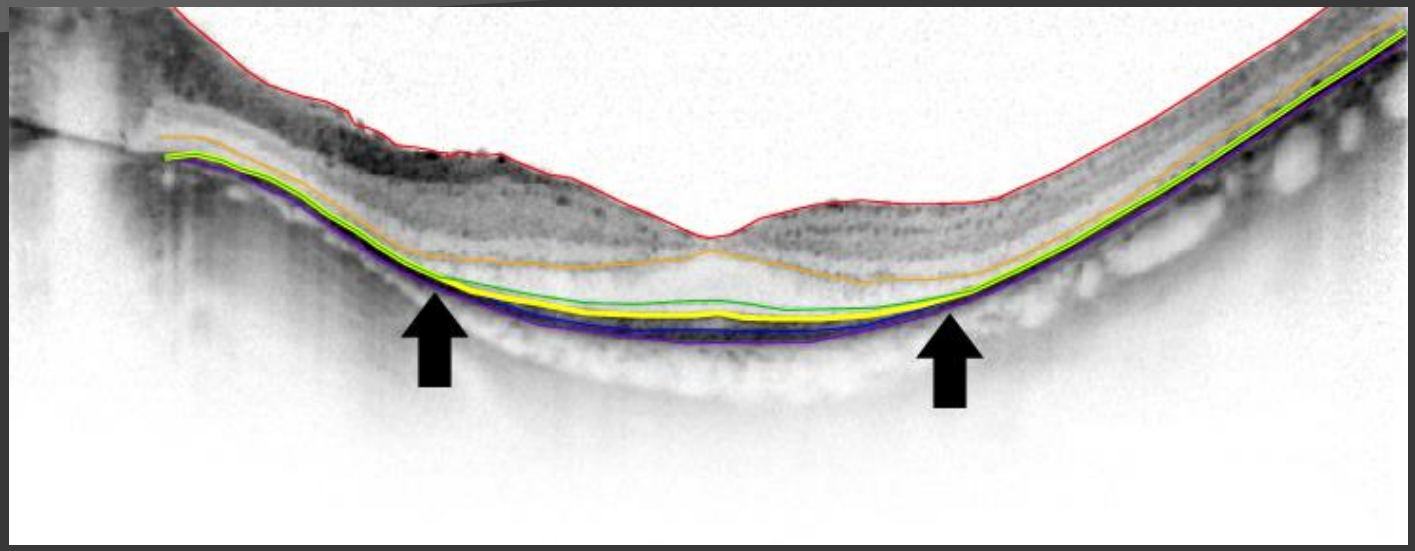
- 120 participants (> or = 8 years old)
- 4-year study – prospective, annual visits
- Outcome Measures:
  - Best corrected visual acuity
  - Visual field (Hill of Vision)
  - Microperimetry
  - Electroretinogram
  - Full-field stimulus testing (FST)
  - EZ Area (from OCT)

Functional Outcome Measure: Hill of Vision



Regions with higher "elevations" correspond to better visual function.

Structural Outcome Measure: EZ Area



- Obtained using optical coherence tomography (OCT)
- Precise and sensitive – quickly capture changes
- Correlates with changes in vision
- Good measure for RP, Usher syndrome
- FDA will accept EZ Area
- FFB-funded

Participant Overview

- Previously diagnosed w/two USH2A mutations
  - ideally, one on each allele (one from each parent)
- Additional genetic testing may be required
- Primary cohort (100 participants):
  - 20/80 or better, visual field > 10 degrees
  - followed for 4 years
- Secondary cohort (20 participants):
  - 20/100 or worse, visual field < 10 degrees
  - only baseline measurements

Recruitment

If you are interested in participating in RUSH2A:

- Go to clinicaltrials.gov, search on "RUSH2A"
- Review inclusion and exclusion criteria
- E-mail or call the contacts
- You will be referred to closest study site

Final Notes

FFB-CRI is investing $8 million in RUSH2A.

Data from study will be published and shared.

But Wait There's More!
Other FFB-Funded Projects for Usher Syndrome

- USH1B dual vector gene therapy (MYO7A)
  - Boye, University of Florida
- USH1B gene-editing (CRISPR/Cas9)
  - Williams, UCLA
- USH1C gene therapy
  - Wolfrum, JGU Mainz
- USH1C mini-pig model
  - Wolfrum, JGU Mainz
- USH2A antisense oligonucleotides
  - Cremers, Radboud (others)
- USH2A, USH1C gene therapies
  - Vandenberghe, MEEI
- USH consortium to study PR structure, function
  - Duncan (UCSF), Carroll (Med College of Wisconsin)

Many cross-cutting therapies for RP may apply to Usher syndrome.

Thank You!

Questions?

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