2017 Low Vision Conference: Students with Progressive Vision Loss
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Retinitis Pigmentosa and Inherited Retinal Disorders

Presented by
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Developed for
Texas School for the Blind & Visually Impaired Outreach Programs
Retinitis Pigmentosa and Inherited Retinal Disorders

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Retinitis pigmentosa

- Refers to a group of disorders that are inherited, progressive degeneration and eventual atrophy and loss of retinal cells
- Both rods and cones are affected
- Onset ranges from infancy to late adulthood
- RP may be seen in isolation or associated with other conditions ("syndromic RP")

Clinical features

- Nyctalopia
- Visual field loss
- Central vision loss
  - CME
  - Macular atrophy and/or fibrosis
  - Vascular leakage
- Color vision

Fundus appearance

![Fundus Appearance of Retinitis Pigmentosa](image)

Figure 1 Retinitis pigmentosa with pigmented bone spicules, attenuated vessels, and waxy optic nerve
Figure 2 Retinitis pigmentosa showing retinal pigmentation, thin blood vessels and pale optic disc.

Retinitis pigmentosa

Figure 3 Autofluorescence image of Retinitis Pigmentosa

Current treatment

- Vitamin A (controversial)
- Treatment of macular edema with steroid injection
- Low vision aides

Macular edema treatment

Figure 4 Optical Coherence Tomography showing macular edema

Vitamin A therapy

- Controversial
- One true paper that looked at high dose Vitamin A

Retinitis pigmentosa variants
- Usher syndrome (Type I, II, III)
- Bardet-Biedl
- Refsum disease
- LCA
- Bassen-Kornzweig

**Choroideremia**
- X-linked recessive
- CHM gene is located on X chromosome
- Affects 1 in 50-100,000 people
- Accounts for 4% of blindness

**Clinical features of choroideremia**
- Nyctalopia in the first decade of life
- Slow progressive vision loss
- Tunnel vision

**Choroideremia**

Figure 5  Two retinal images: Left showing early choroideremia and right showing advanced choroideremia
Gyrate atrophy

Gyrate Atrophy

- OAT mutation
- Peripheral, central, night vision affected
- May be associated with cataracts
- Usually normal intelligence
- Muscle weakness may be seen
- Autosomal-recessive inheritance

Clinical trials

Clinical trials for RP

- Stem cell trials
- Gene therapy
- Ocular prosthetic implant
**Stem cell therapy**

Figure 7 Graphic showing how stem cell therapy is done. 1) Culture with growth factors; 2) stem cell division in the culture dish; 3) culture with growth and differentiation factors; 4) cell differentiation into retinal pigment epithelial (RPE) cells; 5) RPE cells injected into the retina of the eye. RPE cells made from human embryonic and iPS cells are at present being investigated for their potential to repair damaged RPE.

**Gene therapy**

Figure 8 Graphic showing gene therapy: 1) new gene inserted into a virus vector; 2) vector binds to cell; 3) vector packaged into vesicle; 4) vesicle injected into the cytoplasm; 5) vesicle breaks down releasing vector; 6) new gene injected into the nucleus.

- Replacing a mutated gene with a healthy copy of the gene
- Inactivating a mutated gene that is functioning improperly
- Introducing a new gene to help fight a disease
Stem cell therapy (Jcyte pharma)

- Jcyte pharmaceuticals
- Phase I/II clinical trial
- 12 month study collaborating with UC Irvine
- Testing safety and efficacy of single intravitreal injection of human progenitor cells (jcells) in patients with advanced RP.
- 18+ years of age
- Vision 20/63-20/200 in worse seeing eye
- 2 different dosing groups
- Goal is to treat before photoreceptor loss and reactivate lost photoreceptors

Stem cell trial #2 (ReNeuron pharmaceuticals)

- Phase I/II dose escalated open label study
- Conducted at Massachusetts Eye and Ear infirmary (Harvard)
- Assessing safety and efficacy of hRPC (human retinal progenitor cell) cell therapy in 15 patients with advanced RP
- Single subretinal injection
- 1 year study
Argus II implant

- Post-approval study
- Argus II retinal implant
- Vision criteria: LP or NLP
- Needs prior history of useful vision
- Needs to have had prior cataract surgery
- Numerous centers around the country

Figure 9 Image of Argus II implant in the retina

Argus II implant: how it works

Figure 10 Image of the parts of the Argus II: Glasses, camera, glasses coil and VPU

Figure 11 Image of the Argus II and a photo of a young woman wearing the device.
Gene therapy for RP

- Spark therapeutics
- RPE65 mutation
- Phase III study closed and awaiting FDA approval
- 93% of patients enrolled in the study (n=31) responded to gene therapy as assessed by mobility testing at 1 Lux

Gene therapy for Choroideremia #1

- Spark therapeutics
- CHM mutation
- Phase I/II
- Subretinal injection of investigational product

Gene therapy for choroideremia #2

- NightStarRx
- AAV to deliver a wild-type copy of REP1
- Requires retinal surgery

Retrosense optogenetics

- Gene therapy technology
- Designed to confer light sensitivity to retinal nerve cells
- Animal studies only to date
- Human Phase I/II is not yet recruiting

Stargardt’s disease

- Variable inheritance
- Autosomal recessive most common
- ABCA4 mutation
Visual transduction pathway

Figure 12 Graphic related to Vitamin A and the Visual Cycle.

Stargardt presentation

- Blurred vision
- Variable presentation
- Vision ranging from 20/30-20/200
- Earlier onset tends to have more severe prognosis
- Abnormal fundus exam usually prompts referral to retina specialist

Stargardt disease

Figure 13 Stargardt disease with yellow flecks and a beaten bronze macular appearance
**Stargardt treatment**

- Currently under investigation to slow visual transduction pathway
- Avoid high dose vitamin A

**“Gene editing”**

- Newest technology
- Published April 21, 2017
- Reprogrammed mutated rod photoreceptors into functional cone photoreceptors restoring vision in two mice models of RP
- CRISPR
- Use AAV vector for gene therapy

**Questions? THANK YOU!!**

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Figure 63 TSBVI logo.

Figure 64 IDEA logo