diagnosys

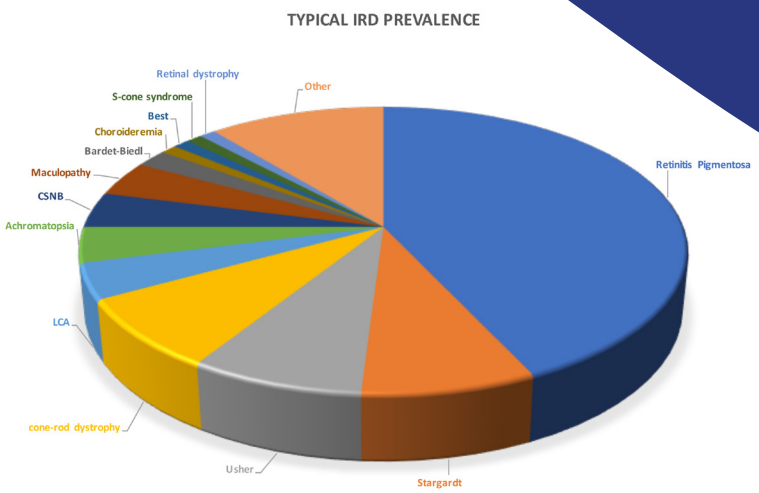
leading the wave

Gene Therapy

Ophthalmic Functional Diagnostic Tests

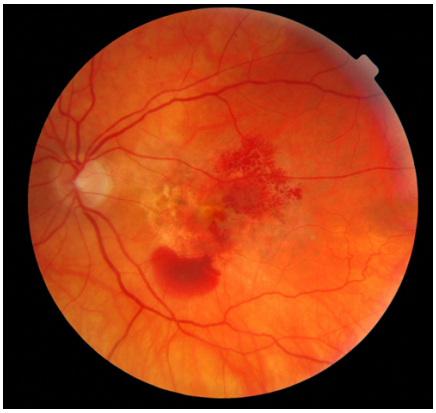
Eye Diseases

There are a rapidly growing number of eye diseases targeted for treatment by gene therapies



Inherited Retinal Diseases (IRD)

- Approximately 4 million people affected worldwide[1]
- As of 2020, over 300 genes have been implicated in the etiology of IRD (sph.uth.edu/retnet)



Age-related Macular Degeneration

- Approximately 200 million people worldwide have wet or dry AMD[2]
- At least 5 gene therapy clinical trials for wet or dry AMD ongoing in the United States, as of 2020[3]

1. Sharon, et al, 'A nationwide genetic analysis of inherited retinal diseases in Israel as assessed by Israeli IIRDC;' 10.1002/humu.23903
2. www.brightfocus.org
3. Clinicaltrials.gov

Therapies and Testing

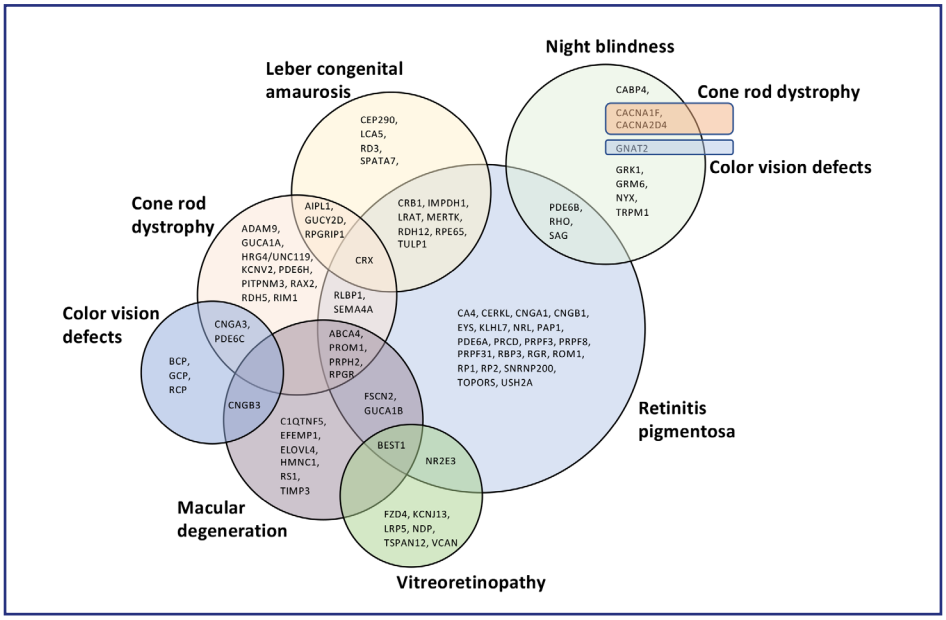
Advanced diagnostics are essential for effective gene therapy clinical trials and clinical implementation

Types of Gene Therapies:

- Gene augmentation: provide genetic material to produce replacement proteins
- Gene inactivation: block production of abnormal protein, e.g. short interfering RNA (siRNA) techniques
- Gene editing: e.g. CRISPR/Cas9
- Neuromodulation: optogenetics, genetically modified light-sensitive RGCs
- Multifactorial: combination of techniques targeting genetically heterogeneous diseases such as AMD

"LUXTURNA™ is the first FDA-approved gene therapy for a genetic disease. Participants who received LUXTURNA showed a statistically significant improvement from baseline to one year in white light FST in the intervention group compared to the control group."[1]

Mutations in the same gene can lead to different phenotypes, making functional testing essential[2]

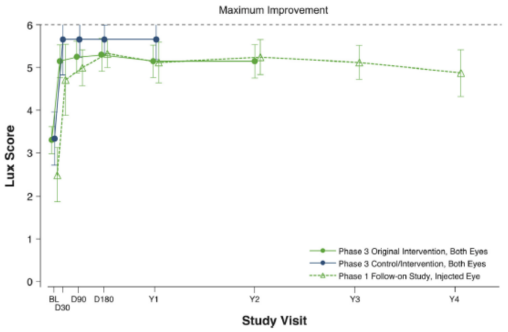


1. Spark Therapeutics press release, December 19, 2017; www.sparktx.com
2. W. Berger, et al; 'Progress in Retinal and Eye Research;' 29 (2010) p335-375

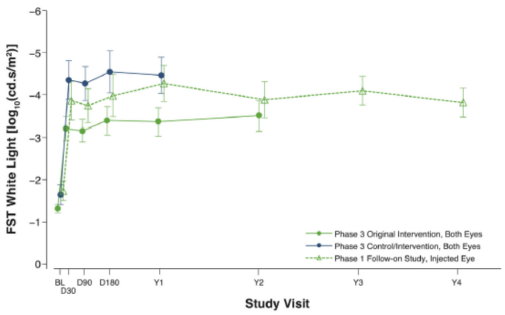
Diagnosys*FST*®: proven in clinical trials

From peer-review paper on the Spark LUXTURNA clinical trial:

Multi-luminance Mobility Test (MLMT)



Diagnosys*FST*



From: Maguire, et al 'Efficacy, Safety, and Durability of Voretigene Neparvovec-rzyl in RPE65 Mutatione-Associated Inherited Retinal Dystrophy,' https://doi.org/10.1016/j.ophtha.2019.06.017, 2019

Select paper list from 100+ clinical trials Diagnosys has supported

- Alejandro J Roman, et al; 'Full-field stimulus testing (FST) to quantify visual perception in severely blind candidates for treatment trials'; Physiol. Meas. 28 (2007) N51–N56.
- William W. Hauswirth, et al; 'Treatment of Leber Congenital Amaurosis Due to RPE65 Mutations by Ocular Subretinal Injection of Adeno-Associated Virus Gene Vector: Short-Term Results of a Phase I Trial'; HUMAN GENE THERAPY 19:979–990 (October 2008).
- M Klein and DG Birch; 'Psychophysical assessment of low visual function in patients with retinal degenerative diseases (RDDs) with the Diagnosys full-field stimulus threshold (D-FST)'; Doc Ophthalmol. 2009 December ; 119(3): 217–224.
- Artur V. Cideciyan, et al; 'Cone photoreceptors are the main targets for gene therapy of NPHP5 (IQCB1) or NPHP6 (CEP290) blindness: generation of an all-cone Nphp6 hypomorph mouse that mimics the human retinal ciliopathy'; Human Molecular Genetics, 2011, Vol. 20, No. 7.
- Katharina Messias, et al; 'Psychophysically determined full-field stimulus thresholds (FST) in retinitis pigmentosa: relationships with electroretinography and visual field outcomes; Doc Ophthalmol (2013) 127:123–129.
- Frederick T. Collison, et al; 'Psychophysical Measurement of Rod and Cone Thresholds in Stargardt Disease with Full-Field Stimuli'; Retina. 2014 September ; 34(9): 1888–1895.
- Samuel G. Jacobson et al; 'Defining Outcomes for Clinical Trials of Leber Congenital Amaurosis Caused by GUCY2D Mutations'; AmJOphthalmol 2017;177:44–57.
- Krunoslav T. Stingl, et al; 'Chromatic Full-Field Stimulus Threshold and Pupillography as Functional Markers for Late-Stage, Early-Onset Retinitis Pigmentosa Caused by CRB1 Mutations'; Trans Vis Sci Tech. 2019;8(6):45.
- Albert M. Maguire, et al; 'Efficacy, Safety, and Durability of Voretigene Neparvovec-rzyl in RPE65 Mutation - Associated Inherited Retinal Dystrophy'; Ophthalmology 2019;126:1273-1285.

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