The Road to Ocular Gene Therapy: Lessons from the Past

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Eyes to the Past Conference
October 29, 2019
The ultimate application of molecular biology would be when polynucleotide sequences can be grafted by chemical procedures onto a virus DNA....
Gene Therapy for Human Genetic Disease?

Proposals for genetic manipulation in humans raise difficult scientific and ethical problems.

Theodore Friedmann and Richard Roblin
The Good News
1990

Michael Blaese, French Anderson and colleagues: 1990

Ist approved gene therapy for severe combined immune deficiency

1995

Dr. Terence Flotte, 1995
First use of recombinant AAV in humans in Cystic Fibrosis clinical trials
The setback
Jesse Gelsinger, an 18 year old with a relatively mild form of the nitrogen metabolism disorder ornithine transcarbamylase (OT) deficiency, is the first person to die on a gene therapy trial because of vector associated toxicity.
The Return
Novel adeno-associated viruses from rhesus monkeys as vectors for human gene therapy

Guang-Ping Gao, Mauricio R. Alvira, Lili Wang, Roberto Calcedo, Julie Johnston, and James M. Wilson*
You can simply impress your audience and add a unique zing and appeal to your Presentations.

- **2001** Proof of concept in dogs
- **2008** 1st clinical trial
- **2017** FDA approved drug
- **2017** First Treated Patient

First Ocular Gene Therapy Drug
The present
The road ahead
Genetic Testing and Natural History

Mapped and Identified Retinal Disease Genes 1980 - 2019
Delivery route and vehicles

Techniques for Vector delivery

Intravitreal delivery

Subretinal delivery

Pars plana

Intravitreal injection

Subretinal injection

Neural Retina

Retinal Pigment Epithelium

Choroid

Sclera
Delivering large genes

Modeling ocular diseases
AOTC: Advanced Ocular Therapeutics Center
Advanced Ocular Therapeutics Center (AOTC):  
Dr. Shlomit Schaal, Director

**Clinical research:**  
Dr. Johanna Seddon, Director

**Translational Research:**  
Dr. Haijiang Lin, Director

**Basic Mechanisms and Preclinical Research:**  
Dr. Hemant Khanna, Director

**Ocular Research Services:**  
Dr. Claudio Punzo, Director

**Research Focus Areas:**  
- Age-related Macular Degeneration  
- Retinitis Pigmentosa  
- Diabetic Retinopathy  
- Leber congenital amaurosis  
- Stargardt Disease  
- Glaucoma  
- Usher Syndrome  
- Retinal ciliopathies  
- Other ocular conditions
The Team, to date

Dr. Terence Flotte
Dr. Guangping Gao
Dr. Anastasia Khvorova
Dr. Michael Volkert

Dr. Neil Aronin
Dr. Miguel Sena-Esteves
Dr. Robert Kotin
Dr. Heather Gray-Edwards
Mission

• Innovative therapeutic paradigms
• Clinical trials site
• State of the art research services
• Train and recruit exceptional talent