The Foundation Fighting Blindness:
Virtual Workshop on Inflammation in Viral Gene Therapy of the Retina
September 14-15, 2020

Day 1: Sept 14
9.00am – 2.00pm EST
Iceberg of Inflammation:
Preclinical data - should we worry?

Overview of the Day:
- Q&A based on pre-recorded presentations
  - Ocular Immunology/Viral immunology
- How preclinical models develop our understanding:
  - What is extent of inflammation and immune activation?
  - What protocols are being used to control inflammation?
  - Do animal models inform appropriately?
  - Modifications of vector, capsid and transgene to reduce inflammation

9.00 – 9.10 am
Welcome and Review of Meeting Goals:
Brian Mansfield

9.10am – 9.40am
Pre-Workshop Survey Results
Brian Mansfield

General Question and Answer on the Pre-meeting Presentations on Retina Immunology and Terminology
Kai Chan, Andrew Dick, and Thomas Langmann
Preclinical Research

9.40am – 10.10am
Moderator: Kai Chan
Presenters: 7 min presentation, 3 min Q&A each
  o Shannon Boye
  o William Beltran
  o Kathryn Pepple

10.10 – 10.40am
  • General Discussion

BREAK  10.40 – 10.50am

10.50am – 11.20am
Moderator: Thomas Langmann
Presenters: 7 min presentation, 3 min Q&A each
  o John Flannery
  o Scott Ellis
  o Bill Merigan

11.20am - Noon
  • General Discussion

Break  Noon – 12.20pm

12.20pm – 1.00pm
Moderator: Paul Sieving

Presenters: 7 min presentation, 3 min Q&A each
  o Jean Bennett
  o Connie Cepko
  o Dominick Fischer
  o Kai Chan

1.00pm – 1.30pm
  • General Discussion
Break 1.30 – 1.35pm

Round Table Discussions
1.35pm – 2.00pm

**Moderators:** Kai Chan, Sara Mary Hall
1. Does gene therapy activate immune responses that do not manifest as clinical inflammation?
2. How does inflammation impact efficacy/activity?
3. How do we subvert immune activation?
4. What is the influence of transgene?
5. What is immune status of degenerative retina? Does this influence approach?

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**Day 2: Sept 15**
9.00am – 2.00pm EST

**Clinical Inflammation:**
What we know and contemporary clinical data

**Clinical Research**

This session will be a discussion of preclinical and clinical data for gene therapies that have been, or still are, in the clinic. The presentations should focus on:

1. Preclinical data that led to dose decisions and toxicology of concern
2. Data that led to immunosuppression protocol
3. Data on immune responses observed
4. Data on clinical inflammation observed

**9.00am - 9.10am**
**Welcome:** Brian Mansfield

**9.10 – 10.20am**
**Moderator:** Joy Cavagnaro

**Presenters:** 7 min presentation, 3 min Q&A each
  o Christine Kay
o Tim Stout
o Jose Sahel
o Kanmin Xue
o Paul Sieving
o Mark Shearman
o Ian MacDonald

Break 10.20 – 10.30am

10.30am - Noon
Round Table Discussion

Discussion of reported observations and trends – are there consensus findings and uncertainties?

**Moderators:** Andrew Dick and Curt Scribner

- Subretinal and intravitreal trials (aim to cover various transgenes, AAV capsids etc)
- Observed inflammation and any adverse events
- Immunosuppressive protocol administered (prophylactic and reactive) and any side effects
- Relationship between dose, inflammation and efficacy
- Comparison between pre-clinical package and clinical data

Break Noon – 12.30pm

12.30pm – 1.30pm
Clinical Summary of Findings

**Moderators:** Tim Stout, Janet Cheetham

Is there a consensus guidance:

- What are the current best clinical practices to control the immune response in gene therapy?
- What are the knowledge gaps in our clinical understanding of controlling the immune system response to gene therapy?
1.30pm – 2.00pm

Meeting Summary

**Moderators:** Kai Chan, Andrew Dick, Sara Mary Hall, Curt Scribner, Brian Mansfield

- Discuss the format of summarizing and disseminating the outcome of the workshop
  - white paper? Publication?
  - Agreement on how to handle process to ensure confidentiality of any sensitive data presented in the workshop
  - Willingness to share findings with regulatory authorities
- Next steps
  - Is there support for a larger conference either sponsored by FFB or with ARVO
  - What would that look like, what content?