Gene Transfer and Rare Diseases Workshop
National Institutes of Health
September 13, 2012
Rockville Hilton, Rockville, MD

8:00 AM Welcome and Opening Remarks
Jacqueline Corrigan-Curay, J.D, M.D., Office of Biotechnology Activities, Office of Science Policy, National Institutes of Health (NIH)
Stephen Groft, Pharm.D., Office of Rare Diseases Research, National Center for Advancing Translational Sciences (NCATS), NIH
Yuman Fong, M.D., Chair, NIH Recombinant DNA Advisory Committee

Session I: Clinical Experience

Gene Transfer for Rare Diseases: What Are the Challenges and Keys to Success?

8:15 AM Hemophilia
Katherine A. High, M.D.
University of Pennsylvania and The Children’s Hospital of Philadelphia
Philadelphia, PA
Slide Presentation

8:35 AM Leber Congenital Amaurosis and Other Eye Disorders
Samuel G. Jacobson, M.D., Ph.D.
Scheie Eye Institute
University of Pennsylvania
Philadelphia, PA
Slide Presentation (To Be Posted)

8:55 AM Blood Cell Disorders
Donald B. Kohn, M.D.
University of California, Los Angeles
Los Angeles, CA
Slide Presentation

9:15 AM Lipoprotein Lipase Deficiency: European Union Development and Regulatory Experience
Carlos R. Camozzi, M.D., Ph.D.
uniQure B.V.
The Netherlands
Slide Presentation
9:40 AM  Panel Discussion

Moderator: Donald B. Kohn, M.D.

Questions

1. What are the key scientific challenges in developing clinical protocols for a rare disease?

2. How frequently were disease-specific animal models available for these diseases? If there was no appropriate animal model, was this a rate-limiting step?

3. Once you have had a clinical success, how do you most efficiently transfer those successful elements into other studies for diseases with a similar phenotype?

10:00 AM  BREAK

Session II: Resources

What NIH Resources Are Available, and How Are They Being Used?

Co-Chairs: Jacqueline Corrigan-Curay, J.D., M.D., Office of Biotechnology Activities, Office of Science Policy, NIH
             Philip J. Brooks, Ph.D. Office of Rare Diseases Research, NCATS, NIH

10:15 AM  Gene Therapy Resource Program (GTRP)
           Sonia I. Skarlatos, Ph.D., F.A.H.A.
           National Heart, Lung, and Blood Institute, NIH
           Slide Presentation

10:35 AM  Bridging Interventional Development Gaps (BrIDGs)
           John McKew, Ph.D.
           Therapeutic Development Branch
           NCATS, NIH
           Slide Presentation

10:50 AM  Genetic Modification Clinical Research Information System (GeMCRIS)
           Robert Jambou, Ph.D.
           Office of Biotechnology Activities, NIH
           Slide Presentation
11:00 AM  Rare Diseases Clinical Research Network (RDCRN)
Rashmi Gopal-Srivastava, Ph.D.
Office of Rare Diseases Research
NCATS, NIH
Slide Presentation

11:10 AM  National Gene Vector Biorepository (NGVB)
Kenneth Cornetta, M.D.
Indiana University
Indianapolis, IN
Slide Presentation

Session III: Defining Opportunities for Data Sharing Across Protocols

11:30 AM  Preclinical Studies To Support Clinical Applications of Gene Therapy Products
Mercedes Serabian, M.S., D.A.B.T.
U.S. Food and Drug Administration
Rockville, MD
Slide Presentation

11:50 AM  LUNCH

12:50 PM  Panel I Discussion
Moderator: Yuman Fong, M.D.
Chair, NIH Recombinant DNA Advisory Committee
Memorial Sloan-Kettering Cancer Center
New York, NY

Lead Panelists

Ronald G. Crystal, M.D.
Department of Genetic Medicine
Weill Cornell Medical College
New York, NY

Barry Byrne, M.D., Ph.D.
University of Florida
Gainesville, FL

Daniel Takefman, Ph.D.
U.S. Food and Drug Administration
Rockville, MD
Janet Benson, Ph.D., D.A.B.T.
Lovelace Respiratory Research Institute
Albuquerque, NM,

Kenneth Cornetta, M.D.

Questions

1. Are there common studies or assays that could produce data that can be shared across different trials involving similar diseases or vectors?
   a. What types of preclinical data could be useful for sharing?
   b. What are the FDA’s and other regulatory agencies’ considerations regarding sharing data (e.g., cross-reference letters, platforms)?
   c. What are possible mechanisms for sharing? What are the tolerance and limitations for sharing in drug development for academic researchers and biotech/pharma?

2. What factors must the studies have in common for shared data to be useful?
   a. For example, would data from biodistribution studies using the same vector backbone still be applicable if the promoter or transgene were changed in the subsequent study but the route of administration was similar?
   b. For studies involving integrating vectors, what factors would need to be considered in determining whether genotoxicity data could be shared?
   c. How useful have the current Ad-5 and AAV-2 reference standards been to the field? Would the development of additional standard reagents be helpful for the field in terms of regulatory review and sharing of data across preclinical studies?

3. How is the NGVB toxicology database currently being used? What improvements might encourage increased use of pharm/tox databases that are detailed, readable, and searchable?

4. How could the NIH foster data sharing?

2:00 PM Panel II Discussion

Lead Panelists

Brian P. Sorrentino, M.D.
St. Jude Children’s Research Hospital
Memphis, TN
Questions

1. Is there a role for developing therapeutic platforms to be used for multiple diseases to maximize the sharing of data and efficiencies in developing new gene transfer studies for rare diseases?
   a. What common characteristics of diseases allow one to develop platforms?
   b. What are the considerations for designing a platform for multiple trials involving similar vectors, diseases, and transgenes (e.g., lentivectors for different immunodeficiencies)?
   c. Are some of the AAV and lentiviral vectors being used across the field sufficiently similar to be included in a platform?
   d. When is the time to consider vector platforms versus continued refinement?

3:00 PM  PUBLIC COMMENT
3:15 PM  BREAK

Session IV: Mechanisms for Advancing Gene Transfer for Rare Diseases

3:30 PM  Panel Discussion

Moderator: Yuman Fong, M.D.

Questions

1. How are current resources being used, and are there ways they might be improved to make them more useful to investigators developing protocols for rare diseases?
   a. RDCRN
   b. BrIDGs
   c. GeMCRIS
   d. NGVB
   e. GTRP
2. Are there particular gaps in available programs that hinder the development of protocols for rare diseases?

3. What are the challenges to obtaining funding for preclinical studies to support IND applications in gene transfer for rare diseases?

4. Are there regulatory policies that can facilitate data sharing?

5. What are the operational needs in data sharing?

6. How can the publication of safety data and negative results be encouraged for both authors and journals?

7. What are our conclusions from this workshop?

5:00 PM PUBLIC COMMENT
5:15 PM ADJOURN