

**NATIONAL INSTITUTES OF HEALTH
RECOMBINANT DNA ADVISORY COMMITTEE (RAC)**

108th Meeting

**NIH Campus
Building 31, Sixth Floor, C Wing, Room 10**

**June 19-21, 2007
Agenda**

Tuesday, June 19, 2007

8:30 AM Call to Order and Opening Remarks

Howard Federoff, M.D., Ph.D., Chair, NIH RAC

Tab 2449 For Your Information
Notice of Meeting
Conflict of Interest Guidance

8:35 AM Minutes of the March 14, 2007, RAC Meeting

RAC Reviewers: Nicholas Muzyczka, Ph.D.
Lee-Jen Wei, Ph.D.

Tab 2450 Minutes of the March 14, 2007, RAC Meeting

8:40 AM Gene Transfer Safety Assessment Board Report

Tab 2451 Response to M-I-C-1
Protocol List
Protocols Not Selected for RAC Public Review

RAC Reviewers: Steven Albelda, M.D.
Howard Federoff, M.D., Ph.D.
Helen Heslop, M.D.

9:00 - 9:30 AM Immune Responses to Adeno-Associated Virus (AAV) Vectors

9:00 AM Welcome and Introduction

Howard Federoff, M.D., Ph.D., Chair, NIH RAC

RAC Moderators: Hildegund Ertl, M.D.
Nicholas Muzyczka, Ph.D.

Tuesday, June 19, 2007 (continued)

- 9:20 AM **AAV Vectors for Gene Transfer**
- Presenter: Marina O'Reilly, Ph.D.
Office of Biotechnology Activities
- 9:30 - 10:20 AM Session I AAV Virology and Immunology**
- Tab 2466 Background Materials
- 9:30 AM **Biology of AAVs**
- RAC Presenter: Nicholas Muzyczka, Ph.D.
- 10:00 AM **Overview of Immune Responses to AAV Capsid**
- RAC Presenter: Hildegund Ertl, M.D.
- 10:20 AM **BREAK**
- 10:30 - 11:45 AM Session II Immune Responses in Clinical Studies Using AAV Vectors**
- 10:30 AM **CD8+ T-Cell Responses to AAV Capsid in Normal and AAV-Infused Human Subjects**
- Presenter: Katherine High, M.D., The Children's Hospital
of Philadelphia, Philadelphia, PA
- 11:00 AM **Immune Responses in a Lipoprotein Lipase Deficiency Study Using AAV1-LPLS447X**
- Presenter: Janneke Meulenberg, Ph.D., Amsterdam Molecular
Therapeutics, Amsterdam, The Netherlands
- 11:30 AM **Immunological Response to Alpha-1-Antitrypsin in a Phase I Trial Using AAV2 Vector Delivered Intramuscularly**
- RAC Presenter: Nicholas Muzyczka, Ph.D.
- 11:45 AM **LUNCH**
- 12:30 - 2:10 PM Session III Animal Models of AAV Immune Responses**
- 12:30 PM **AAV Gene Transfer and Vaccine Studies of T-Cell Responses in Mice**
- RAC Presenter: Hildegund Ertl, M.D.

Tuesday, June 19, 2007 (continued)

- 1:10 PM **Impact of AAV Capsid Structure on T-Cell Responses in Mice and Monkeys**
- Presenter: James Wilson, M.D., Ph.D., University of Pennsylvania, Philadelphia, PA
- 1:40 PM **Immune Liver Injury in Response to AAV2 in Mice**
- Presenter: Nicholas Crispe, MB BS, Ph.D., University of Rochester, Rochester, NY
- 2:10 - 3:10 PM Session IV AAV Vector Preparation**
- 2:10 PM **Recombinant AAV Generation and Purification: Strategies to Reduce Vector Immunogenicity**
- Presenter: J. Fraser Wright, Ph.D., The Children's Hospital of Philadelphia, Philadelphia, PA
- 2:40 PM **Potential Contaminants in Certain Types of AAV Vector Preparations: Implications for Immunogenicity**
- Presenter: Jude Samulski, Ph.D., The University of North Carolina at Chapel Hill, Chapel Hill, NC
- 3:10 PM **BREAK**
- 3:20 PM **Discussion Session**
- 5:40 PM **ADJOURNMENT**

Wednesday, June 20, 2007

- 8:00 AM **Call to Order and Opening Remarks**
- Howard Federoff, M.D., Ph.D., Chair, NIH RAC
- 8:05 AM **Certificates of Appreciation for RAC Member Service to NIH**
- Presenter: Amy P. Patterson, M.D.
Director, Office of Biotechnology Activities
National Institutes of Health, Bethesda, MD

Wednesday, June 20, 2007 (continued)

8:20 AM **Discussion of Human Gene Transfer Protocol #0704-843:** *A Phase I Study of Autologous T Cells Genetically Modified at the CCR5 Gene by Zinc Finger Nucleases SB-728 in HIV-Infected Patients*

PI: Pablo Tebas, M.D., University of Pennsylvania School of Medicine, Philadelphia, PA

RAC Reviewers: Jeffrey Kahn, Ph.D., M.P.H.
 Nikunj Somia, Ph.D.
 David Weber, M.D., M.P.H.

Ad hoc Reviewer: Toni Cathomen, Ph.D., Charité Medical School Berlin, Germany (*via teleconference*)

Tab 2452 Protocol

Tab 2453 OBA Summary
 OBA Letter to PI on In-Depth RAC Review and Public Discussion
 Reviews from Drs. Kahn, Somia, Weber, and Cathomen
 PI's/Sponsor's Response

9:50 AM **Public Comment**

10:00 AM **BREAK**

10:10 AM **Discussion of Human Gene Transfer Protocol #0704-848:** *A Phase I Study of Intratumoral Administration of Cellular Immunotherapy for Recurrent/Refractory Malignant Glioma Using Alloclone-002 Modified for Glucocorticoid Resistance and Interleukin-2*

PI: Michael Jensen, M.D., City of Hope National Medical Center and Beckman Research Institute, Duarte, CA

RAC Reviewers: Howard Federoff, M.D., Ph.D.
 Eric Kodish, M.D.
 Richard Vile, Ph.D.

Ad hoc Reviewer: Toni Cathomen, Ph.D., Charité Medical School Berlin, Germany (*via teleconference*)

Tab 2454 Protocol

Wednesday, June 20, 2007 (continued)

Tab 2455 OBA Summary
OBA Letter to PI on In-Depth RAC Review
and Public Discussion
Reviews from Drs. Federoff, Kodish, Vile and Cathomen
PI's/Sponsor's Response

11:50 AM **Public Comment**

NOON **WORKING LUNCH**

12:30 PM **Discussion of Human Gene Transfer Protocol # 0704-852: *A Phase I Open-Label Clinical Trial for the Treatment of β -Thalassemia Major with Autologous CD34+ Hematopoietic Progenitor Cells Transduced with ThalagenTM, a Lentiviral Vector Encoding the Normal Human β -Globin Gene***

PI: Farid Boulad, M.D., Memorial Sloan-Kettering Cancer Center,
New York, NY

RAC Reviewers: Helen Heslop, M.D.
Eric Kodish, M.D.
Naomi Rosenberg, Ph.D.

Ad hoc Reviewer: Ellis Neufeld, M.D., Ph.D., Children's Hospital
Boston, Boston, MA (*via teleconference*)

Tab 2456 Protocol

Tab 2457 OBA Summary
OBA Letter to PI on In-Depth RAC Review and
Public Discussion
Reviews from Drs. Heslop, Kodish, Rosenberg, and
Neufeld
PI's/Sponsor's Response

2:00 PM **Public Comment**

2:15 PM **BREAK**

2:30 PM **Consideration of Proposed Major Action: Under Section III-A-1 of the NIH Guidelines: Tetracycline Resistance and *Chlamydia trachomatis***

PI: Daniel Rockey, Ph.D., Oregon State University, Corvallis, OR

RAC Moderator: Louis Kirchhoff, M.D., M.P.H.

Wednesday, June 20, 2007 (continued)

Tab 2467 Submission by Dr. Daniel Rockey to Oregon State University
IBC
Submission by Dr. Walter Stamm to University of Washington
Environmental Health and Safety Research Project Hazard
Assessment
Review of Proposed Experiments by Biosafety Working
Group
PI's Response

4:00 PM **Public Comment**

4:15 PM **BREAK**

4:30 PM **Discussion of Human Gene Transfer Protocol #0704-849:** *A Phase I Study
Evaluating the Use of Allodepleted T Cells Transduced with Inducible
Caspase 9 Suicide Gene after Haploidentical Stem Cell Transplantation*

PIs: Malcolm K. Brenner, Ph.D., MB, and Helen Heslop, M.D.,
Baylor College of Medicine, Houston, TX

RAC Reviewers: Hildegund Ertl, M.D.
Robyn Shapiro, J.D.
Scott Strome, M.D.

Ad hoc Reviewer: Paul J. Orchard, M.D., University of
Minneapolis, Minneapolis, MN

Tab 2458 Protocol

Tab 2459 OBA Summary
OBA Letter to PI on In-Depth RAC Review and
Public Discussion
Reviews from Drs. Ertl, Shapiro, Strome, and Orchard
PIs'/Sponsor's Response

5:45 PM **Public Comment**

6:00 PM **ADJOURNMENT**

Thursday, June 21, 2007

8:30 AM **Call to Order and Opening Remarks**

Howard Federoff, M.D., Ph.D., Chair, NIH RAC

8:35 AM **Discussion of Human Gene Transfer Protocol #0704-842:** *A Randomized, Controlled Phase III Trial of Replication-Competent Adenovirus-Mediated Suicide Gene Therapy in Combination with IMRT Versus IMRT Alone for the Treatment of Newly Diagnosed Intermediate-Risk Prostate Cancer*

PIs: Svend O. Freytag, Ph.D., Henry Ford Health System, Detroit, MI
 Benjamin Movsas, M.D., Henry Ford Health System, Detroit, MI

RAC Reviewers: Jane Flint, Ph.D.
 Ellen Grant, Ph.D., LCSW-R
 Lee-Jen Wei, Ph.D.

Ad hoc Reviewer: Otis Brawley, M.D., Emory University, Atlanta, GA

Tab 2460 Protocol

Tab 2461 OBA Summary
 OBA Letter to PI on In-Depth RAC Review and Public Discussion
 Reviews from Drs. Flint, Grant, Wei, and Brawley
 PIs'/Sponsor's Response

10:10 AM **Public Comment**

10:20 AM **BREAK**

10:30 AM **Discussion of Human Gene Transfer Protocol #0704-853:** *A Phase I, Open-Label, Dose-Escalation, Multiple-Dose Study of the Safety, Tolerability, and Immune Response of CRS-207 in Adult Subjects with Selected Advanced Solid Tumors Who Have Failed or Who Are Not Candidates for Standard Treatment*

PI: Elizabeth Jaffee, M.D., The Sidney Kimmel Cancer Center at Johns Hopkins University, Baltimore, MD

RAC Reviewers: Stephen Dewhurst, Ph.D.
 Jeffrey Kahn, Ph.D., M.P.H.
 Louis Kirchoff, M.D., M.P.H.

Tab 2462 Protocol

Thursday, June 21, 2007 (continued)

Tab 2463 OBA Summary
OBA Letter to PI on In-Depth RAC Review and
Public Discussion
Reviews from Drs. Dewhurst, Kahn, and Kirchhoff
PI's/Sponsor's Response

12:15 PM **Public Comment**

12:25 PM **LUNCH**

1:15 PM **Discussion of Human Gene Transfer Protocol # 0704-846: *A Phase I, Dose-Ranging Study to Assess Safety and Distribution of GT-111 in Patients with Advanced Metastatic Cancer***

PI: Pierre L. Triozzi, M.D., Cleveland Clinic Foundation,
Cleveland, OH

RAC Reviewers: Steven Albelda, M.D.
Glen Nemerow, Ph.D.
Robyn Shapiro, J.D.

Tab 2464 Protocol

Tab 2465 OBA Summary
OBA Letter to PI on In-Depth RAC Review and
Public Discussion
Reviews from Drs. Albelda, Nemerow, and Shapiro
PI's/Sponsor's Response

3:00 PM **Public Comment**

3:15 PM **ADJOURNMENT**