

NATIONAL INSTITUTES OF HEALTH  
RECOMBINANT DNA ADVISORY COMMITTEE (RAC)

95<sup>th</sup> Meeting

Bethesda Marriott Hotel  
Bethesda, Maryland

March 9-11, 2004  
Meeting Agenda

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*Tuesday, March 9, 2004*

1:00 PM **Call to Order and Opening Remarks**

Diane Wara, M.D., Chair, NIH RAC

Tab 2324 For Your Information  
Notice of Meeting  
Conflict of Interest Guidance

1:05 PM **Minutes of the October 17, 2003, and December 3-4, 2003, RAC Meetings**

Tab 2325

RAC Reviewers: Terry Kwan, M.S.Ed.  
Theodore Friedmann, M.D.

1:15 PM **Discussion of Human Gene Transfer Protocol # 0401-629: *A Phase I Dose-Escalation Trial of vvDD-CDSR (Double-Deleted Vaccinia Virus Plus CD/SMR) Administered by Intratumoral Injection in Patients with Superficial Injectable Tumors***

PI: David L. Bartlett, M.D.  
University of Pittsburgh Medical Center

RAC Reviewers: James Childress, Ph.D.  
David DeMets, Ph.D.  
Philip Johnson, M.D.

*Ad Hoc* Reviewer: Genoveffa Franchini, M.D.  
National Cancer Institute, NIH

Tab 2326 Protocol

**Tuesday, March 9, 2004 (continued)**

Tab 2327                      OBA Summary  
                                    OBA Letter to PI on Indepth RAC Review and  
                                    Public Discussion  
                                    Outcome of Initial Review by RAC Members  
                                    Reviews from Drs. Childress, DeMets, P. Johnson, and  
                                    Franchini  
                                    PI's/Sponsor's Response

2:50 PM            **Public Comment**

3:00 PM            **BREAK**

3:15 PM            **RAC Recommendations**

3:30 PM            **Update on Protocol 0104-469: *Subthalamic GAD Gene Transfer in Parkinson's Disease Patients Who Are Candidates for Deep-Brain Stimulation***

Presenters:    Michael G. Kaplitt, M.D., Ph.D.  
                                    Weill Medical College, Cornell University, Ithaca, NY

                                    Matthew J. During, M.D., Ph.D.  
                                    University of Auckland

4:30 PM            **Public Comment**

4:45 PM            **ADJOURNMENT**

**Wednesday, March 10, 2004**

8:00 AM            **Call to Order and Opening Remarks**  
                                    Diane Wara, M.D., Chair, NIH RAC

8:05 AM            **Introduction of New RAC Members**

8:15 AM            **Discussion of Human Gene Transfer Protocol #0401-624: *A Phase I Trial of Conditionally Replication-Competent Adenovirus (Delta-24-RGD) for Recurrent Malignant Gliomas***

PIs:            Frederick F. Lang, Jr., M.D.  
                                    University of Texas M.D. Anderson Cancer Center, Houston, TX

                                    Charles A. Conrad, M.D.  
                                    University of Texas M.D. Anderson Cancer Center, Houston, TX

**Wednesday, March 10, 2004 (continued)**

RAC Reviewers: Neal DeLuca, Ph.D.  
Madison Powers, J.D., D.Phil.  
Diane Wara, M.D.

*Ad Hoc* Reviewer: Richard G. Vile, Ph.D.  
Mayo Clinic, Rochester, MN

Tab 2328 Protocol

Tab 2329 OBA Summary  
OBA Letter to PIs on Indepth RAC Review and  
Public Discussion  
Outcome of Initial Review by RAC Members  
Reviews from Drs. DeLuca, Powers, Wara, and Vile  
PIs'/Sponsor's Response

9:50 AM **Public Comment**

10:00 AM **BREAK**

10:15 AM **RAC Recommendations**

10:30 AM **Discussion of Human Gene Transfer Protocol #0401-625: A Phase I Study of a Tropism-Modified Conditionally Replicative Adenoviral Vector (Ad5-?24RGD) for Intraperitoneal Delivery in Ovarian and Extraovarian Cancer Patients**

PIs: Ronald D. Alvarez, M.D.  
University of Alabama, Birmingham  
Mack N. Barnes III, M.D.  
University of Alabama, Birmingham  
David T. Curiel, M.D., Ph.D.  
University of Alabama, Birmingham

RAC Reviewers: Maxine Linial, Ph.D.  
Madison Powers, J.D., D.Phil.  
David Sidransky, M.D.

*Ad Hoc* Reviewer: Richard G. Vile, Ph.D.  
Mayo Clinic, Rochester, MN

Tab 2330 Protocol

**Wednesday, March 10, 2004 (continued)**

Tab 2331      OBA Summary  
OBA Letter to PIs on Indepth RAC Review and  
Public Discussion  
Outcome of Initial Review by RAC Members  
Reviews from Drs. Linial, Powers, Sidransky, and Vile  
PIs'/Sponsor's Response

12:05 PM      **Public Comment**

12:15 PM      **BREAK**

12:30 PM      **RAC Recommendations**

12:45 PM      **LUNCH**

1:45 PM      **Discussion of Human Gene Transfer Protocol #0311-614: *First Time in Human Safety Study of Streptococcus mutans Lactic Acid-Deficient Effector Strain (A2JM) Administered in Conjunction with Twice-Daily Dose of D-Alanine Mouthwash in Healthy Adult Male Subjects for Replacement Therapy as an Aid in the Protection Against Dental Caries***

PI:      Constance E. Stone, D.M.D.  
University of Florida, Gainesville, FL

Presenter:      Jeffrey Hillman, D.M.D., Ph.D.  
Oragenics, Inc.

RAC Reviewers:      Emmett Barkley, Ph.D.  
Thomas Gelehrter, M.D.  
Terry Kwan, M.S.Ed.

*Ad Hoc* Reviewer:      Suzanne M. Michalek, Ph.D.  
University of Alabama, Birmingham

Tab 2332      Protocol

Tab 2333      OBA Summary  
OBA Letter to PI on Indepth RAC Review and  
Public Discussion  
Outcome of Initial Review by RAC Members  
Reviews from Drs. Barkley and Gelehrter, Ms. Kwan, and  
Dr. Michalek  
PI's/Sponsor's Response

*Wednesday, March 10, 2004 (continued)*

- 3:20 PM      **Public Comment**
- 3:30 PM      **BREAK**
- 3:45 PM      **RAC Recommendations**
- 4:00 PM      **Update on the RAC Gene Transfer Clinical Trial Design Working Group**
- Presenters:     David DeMets, Ph.D.  
                      NIH RAC  
                      Nancy M.P. King, J.D.  
                      University of North Carolina, Chapel Hill (*via teleconference*)  
                      Cheryl McDonald, M.D.  
                      NIH Office of Biotechnology Activities
- 4:30 PM      **Public Comment**
- 4:45 PM      **ADJOURNMENT**

*Thursday, March 11, 2004*

- 9:00AM      **Call to Order and Opening Remarks**  
                      Diane Wara, M.D., Chair, NIH RAC
- 9:05 AM      **Data Management Report**
- Tab 2334      Protocol List  
                      Protocols Not Selected for RAC Public Review
- RAC Reviewers:     Larry Johnson, M.D.  
                              Robert Simari, M.D.  
                              Diane Wara, M.D.
- Overview of Investigator and Institutional MIC-1 Responses**
- Presenter:         Cheryl McDonald, M.D.  
                              NIH Office of Biotechnology Activities
- 10:00 AM      **Discussion of Human Gene Transfer Protocol #0401-623: *A Phase I/II Dose-Escalating Randomized Controlled Study to Assess the Safety, Tolerability, and Efficacy of CERE-110 [Adeno-Associated Virus (AAV)-Based, Vector-Mediated Delivery of Beta-Nerve Growth Factor (NGF)] in Subjects with Mild to Moderate Alzheimer's Disease***

**Thursday, March 11, 2004 (continued)**

PI: David A. Bennett, M.D.  
Rush University Medical Center, Chicago, IL

RAC Reviewers: Martha Bohn, Ph.D.  
Bernard Lo, M.D.

*Ad Hoc* Reviewers: Steven T. DeKosky, M.D.  
University of Pittsburgh  
Theodore Friedmann, M.D.  
University of California, San Diego

Tab 2335 Protocol

Tab 2336 OBA Summary  
OBA Letter to PI on Indepth RAC Review and  
Public Discussion  
Outcome of Initial Review by RAC Members  
Reviews from Drs. Bohn, Lo, DeKosky, and Friedmann  
PI's/Sponsor's Response

11:35 AM **Public Comment**

11:45 AM **BREAK**

12:00 NOON **RAC Recommendations**

12:15 PM **Discussion of Human Gene Transfer Protocol #0401-622:**  
*Adenylyl Cyclase VI Gene Transfer for Congenital Heart Failure*

PI: H. Kirk Hammond, M.D.  
University of California, San Diego

RAC Reviewers: David DeMets, Ph.D.  
Larry Johnson, M.D.  
Bernard Lo, M.D.  
Robert Simari, M.D.

*Ad Hoc* Reviewers: Walter J. Koch, Ph.D.  
Jefferson Medical College, Philadelphia, PA

Tab 2337 Protocol

*Thursday, March 11, 2004 (continued)*

Tab 2338                    OBA Summary  
                                  OBA Letter to PI on Indepth RAC Review and  
                                  Public Discussion  
                                  Outcome of Initial Review by RAC Members  
                                  Reviews from Drs. DeMets, Johnson, Lo, Simari, and Koch  
                                  PI's/Sponsor's Response

1:50 PM            **Public Comment**

2:00 PM            **BREAK**

2:15 PM            **RAC Recommendations**

2:30 PM            **ADJOURNMENT**