

**Improving Cellular Therapy for Primary Immune Deficiency Diseases:
Recognition, Diagnosis and Management**

Co-Sponsored by NIAID and the Office of Rare Diseases Research, NIH

Thursday May 21 and Friday May 22, 2009

Executive Plaza North, 6130 Executive Boulevard, Rms. C, D, E, F, Bethesda, MD

The primary objectives of this workshop are to critically review current practice, and propose guidelines for the recognition and care of patients with primary immune deficiency (PID) diseases. Current US and European data in allogeneic HCT and gene therapy for PID will be evaluated, as a basis for development of guidance. Key steps in the timeline for patient management will be addressed. These will include clinical evaluation, diagnostic testing and therapeutic options, and best practices both before and after definitive treatment. Both severe combined immune deficiency (SCID) and non-SCID diseases will be reviewed. Working groups will consider these issues in advance, and consensus documents will be presented for discussion at the workshop. The proceedings will be submitted to a peer reviewed journal for publication. This workshop should provide guidelines for clinical management of patients with immune deficiency diseases.

Thursday May 21

8:00 am – 8:05 am Introduction

Linda Griffith, DAIT, NIAID, NIH

8:05-8:15 am Opening Remarks, Office of Rare Diseases Research

Henrietta Hyatt-Knorr, Director, Policy and Program Planning and Analysis,
Office of Rare Diseases Research, NIH, Bethesda, MD

**8:15 am – 12:30 pm Session I: Current Data and Emerging Strategies
for PID Management**

Chair: Thomas Fleisher

8:15 – 8:35 European updates, including HCT for ADA and leaky SCID – H. Bobby Gaspar, Institute of Child Health University College London, London, England, UK

8:40 – 9:00 Novel approaches in highly purified stem cell transplantation for SCID – Judith Anne Shizuru, Stanford University School of Medicine, Stanford, CA

9:05 – 9:25 HCT for Artemis and RAG SCID – a comparative study – Christopher Dvorak, Children's Hospital University of California, San Francisco, CA

9:30 – 9:40 HCT for WAS, a European and US collaborative study, including relation of chimerism to outcome – Luigi D. Notarangelo, Children's Hospital Harvard Medical School, Boston, MA

9:40-9:50 XLT: long-term follow-up (including European data) – Michael H. Albert, Haunersches Kinderspital, Munich, Germany

9:55 – 10:15 am Break

10:15 – 11:00 Debate: Non-HCT vs HCT for WAS/XLT

Non-HCT therapy: Hans Ochs, University of Washington, Seattle, WA

HCT therapy: Luigi D. Notarangelo, Children's Hospital Harvard Medical School, Boston, MA

Moderator: Jennifer Puck, University of California San Francisco, CA

11:05 – 11:35 Overview: Gene Therapy for PID in the US

Moderator: Fabio Candotti, NHGRI, NIH
(PI for each study to present a 1-2 slide summary)

1) SCID: X-SCID

X-SCID gene therapy study, Great Ormond Street experience

- Bobby Gaspar, University College London, UK

X-SCID self-inactivating (SIN) gamma-retroviral vector clinical trial – Boston, Cincinnati, Children's Hospital Los Angeles, Paris & London - Luigi Notarangelo, Harvard University, Boston, MA

Retroviral gene therapy in older X-SCID boys, previous experience at NIH

- Javier Chinen, Baylor College of Medicine, Houston, TX

Lentivirus vector gene therapy protocol proposed for X-SCID infants, to be conducted at St. Jude

- Mary Ellen Conley, St. Jude Children's Hospital, Memphis, TN

Lentivirus vector gene therapy protocol proposed for “older” X-SCID children,

to be conducted at NIH - Suk See DeRavin, NIAID, NIH, Bethesda, MD

2) SCID: ADA SCID

ADA SCID gene therapy studies, Great Ormond Street experience

- Bobby Gaspar, University College London, UK

ADA SCID, NIH & Children's Hospital Los Angeles study

- Don Kohn, University of California, Los Angeles, CA

3) CGD

CGD gene therapy study at NIH - Elizabeth Kang, NIAID, NIH, Bethesda, MD

11:40 – 12:25 Debate: Gene therapy vs HCT for SCID

Gene therapy: Donald Kohn, University of California, Los Angeles, CA

HCT therapy: Richard O'Reilly, Memorial Sloan Kettering Cancer Center, New York, NY

Moderator: H. Bobby Gaspar, Institute of Child Health University College London, London, England, UK

12:30 – 1:00 pm Lunch

**1:00 pm – 2:50 pm Session II: Current Data and Emerging Strategies
for PID Management, Continued**

Chair: William Shearer

1:00 – 1:20 SCID quality of life study – Barbara Ballard and Marcia Boyle, Immune Deficiency Foundation, Towson, MD

1:25 – 1:45 Emerging approaches in HCT for SCID – Morton J. Cowan, Children's Hospital University of California, San Francisco, CA

1:50 – 2:10 A fuzzy line: overlap between leaky SCID, CID and CVID – Charlotte Cunningham-Rundles, Mount Sinai School of Medicine, New York, NY; **Discussant:** Mary Ellen Conley, St. Jude Children's Research Hospital, Memphis, TN

2:15 – 2:30 pm Break

**2:30 pm – 5:00 pm Session III: Working Groups Draft Documents
Review and Critical Discussion**

Chair: Don Kohn

2:30 – 3:00 Group 1: Timely suspicion for diagnosis & triage for diagnostic workup (including newborn screening)

Co-Chairs: Rebecca H. Buckley, Duke University School of Medicine; Thomas Fleisher, Division of Laboratory Medicine, Clinical Center, NIH, Bethesda, MD; Jennifer Puck, University of California, San Francisco, CA.

Participants: Jack Blessing, Children's Hospital, Cincinnati, OH; Marcia Boyle, Immune Deficiency Foundation, Towson, MD; Linda Griffith, NIAID, NIH, Bethesda, MD; Kimberly Risma, University of Cincinnati, Cincinnati, OH; Jack Routes, Medical College of Wisconsin, Milwaukee, WI (pending availability); William Shearer, Baylor College of Medicine, Houston, TX; Troy Torgerson, University of Washington, Seattle, WA.

3:00 – 3:30 Group 2: SCID, “leaky SCID” & CID issues & management pre-HCT (or pre-gene therapy)

Co-Chairs: Morton J. Cowan, Children’s Hospital University of California, San Francisco, CA; Chaim M. Roifman, Hospital for Sick Children, University of Toronto, Canada (focus on CID).

Participants: Lauri Burroughs, Fred Hutchinson Cancer Research Center, Seattle, WA; Charlotte Cunningham-Rundles, Mount Sinai, New York, NY (focus on “leaky SCID”); Suk See DeRavin, NIAID, NIH, Bethesda, MD; Christopher Dvorak, University of California, San Francisco, CA; H. Bobby Gaspar, Great Ormond Street Hospital, University College, London, England, UK; Naynesh Kamani, Children's National Hospital, Washington, DC; Neena Kapoor, Children's Hospital, Los Angeles, CA; Donald Kohn, University of California, Los Angeles, CA; Joshua D. Milner, NIAID, NIH, Bethesda, MD; Luigi Notarangelo, Children’s Hospital, Harvard Medical School, Boston, MA; Richard O'Reilly, Memorial Sloan-Kettering Cancer Center, New York, NY; Jennifer Puck, University of California, San Francisco, CA; Paul Szabolcs, Duke University Medical Center, Durham, NC.

3:30 – 4:00 Group 3: Non-SCID issues & management pre-HCT (or pre-gene therapy); focus on entities more likely to receive HCT such as: HLH, XLP, WAS

Co-Chairs: Fabio Candotti, NHGRI, NIH, Bethesda, MD; Elizabeth Kang, Laboratory of Host Defenses, NIAID, NIH, Bethesda, MD; Kim E. Nichols, Children’s Hospital of Philadelphia, PA.

Participants: Michael Albert, Haunersches Kinderspital, Munich, Germany; Alexandra (Lisa) Filipovich, Children’s Hospital, Cincinnati, OH; Elie Haddad, Mother and Child Ste. Justine Hospital, Montreal, Quebec, Canada; Steven Holland, Laboratory of Clinical Infectious Diseases, NIAID, NIH, Bethesda, MD; Harry Malech, Laboratory of Host Defenses, NIAID, NIH, Bethesda, MD; Hans Ochs, University of Washington, Seattle, WA; Jordan Orange, University of Pennsylvania, Philadelphia, PA; David Rawlings, University of Washington, Seattle, WA.

4:00 – 4:30 pm Group 4: Post-HCT or post-gene therapy management

Co-Chairs: Mary Ellen Conley, St. Jude Children’s Research Hospital, Memphis, TN; Trudy Small, Memorial Sloan Kettering Cancer Center, New York, NY.

Participants: Javier Chinen, Baylor College of Medicine, Houston, TX; M. Louise Markert, Duke University, Durham, NC; Sung-Yun Pai, Harvard University, Boston, MA; Robertson Parkman, Children’s Hospital Los Angeles, CA; Kirk Schultz, Children's Hospital, Vancouver, BC, Canada; Paul Szabolcs, Duke University Medical Center, Durham, NC; Roy Wu, NCI, NIH, Bethesda, MD.

4:30-5:00 Group 5: Databases / registries

Chair: Luigi Notarangelo, Children’s Hospital, Harvard Medical School, Boston, MA.

Participants: Marcia Boyle, Immune Deficiency Foundation, Towson, MD; Mort Cowan, University of California, San Francisco, CA; Linda Griffith, NIAID, NIH, Bethesda, MD (NIAID PO for CIBMTR); J. Douglas Rizzo, CIBMTR, Milwaukee, WI; Kate Sullivan, Children’s Hospital of Philadelphia, PA; Josiah Wedgwood, NIAID, NIH, Bethesda, MD (NIAID PO for USIDNET); Roy Wu, NCI, NIH, Bethesda, MD (NCI PO for CIBMTR).

Friday May 22

8:00 am – 12:00 noon Session IV: Working Groups Consensus Presentations

Co-Chairs: Luigi Notarangelo and Morton J. Cowan

8:00 – 8:40 Group 1: Timely suspicion for diagnosis & triage for diagnostic workup (including newborn screening)

8:40 – 9:20 Group 2: SCID, “leaky SCID” & CID issues & management pre-HCT (or pre-gene therapy)

9:20 – 10:00 Group 3: Non-SCID issues & management pre-HCT (or pre-gene therapy); focus on entities more likely to receive HCT such as: HLH, XLP, WAS

10:00 – 10:15 am Break

10:15-10:55 Group 4: Post-HCT or post-gene therapy management

10:55 – 11:35 Group 5: Databases / Registries

11:35 – 12:00 Discussion

12:00 noon – 12:30 pm Lunch

12:30 - 1:00 pm Closing Remarks