Executive Summary
October 6-7, 2008
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Introduction

Mitochondrial research is gaining momentum in many areas of medicine. There has been a resurgence of investigation into the biology of mitochondria. In particular, recent advances in proteomics and imaging technologies have markedly enhanced our understanding pertaining to the molecular and biochemical functioning of mitochondria. This knowledge has, in turn, lead to the realization that the regulation of mitochondrial function, turnover, and content affects various physiological systems. Many groups, here and abroad, have been working on disparate aspects of mitochondrial research. As the number of studies grows and results raise new possibilities and questions, the ever-present need for exchange of information and expertise among researchers in the field becomes more pressing. This conference at the National Institutes of Health brought together leading thinkers in the field of mitochondrial biology to review the most current knowledge of the mitochondrial regulatory program and its role in cardiovascular health and disease.

Sponsors

National Heart, Lung, and Blood Institute, NIH
Office of Rare Diseases, Office of the Director, NIH
Society for Heart and Vascular Metabolism

Chair- Organizing Committee

Michael Sack, MD, PhD
Conference Design and Content

This conference consisted of eight plenary sessions over the course of two days; it featured thirty-three distinguished speakers, eight session chairs, four oral podium presenters, and the presentation of posters. These latter promote the one-on-one discussions between presenters and participants that distinguish this meeting and reinforce its objectives.

This conference brought together participants from the many walks of mitochondrial research to discuss the state of the art. Featured speakers included experts in mitochondrial function in cardiovascular disease, mitochondrial homeostasis, mitochondrial dysfunction and genetic diseases, and the mitochondrial role in increasing cardiovascular risk. Investigators presented posters and twenty five received Poster Awards and or travel funds. During lunches and after plenary sessions, participants viewed nearly 150 poster topics with their colleagues.
Participant Demographics

Participants: Registration for the 2008 conference meeting exceeded expectations with a total of 522 pre-registered attendees, additionally 92 participants registered on site. Fourteen percent of attendees were international participants. Out of all participants, 311 participants reported their profession as Researcher (approximately 51%) while 53 reported themselves as physicians (about 9%). About 36 participants were listed as with an “other” profession (6%)

Poster: One hundred forty-eight posters were submitted. Twenty percent of the abstracts submitted received awards: Oral Podium Presentation (4), Scientific Poster Award (15) or Travel Award (11). Lunches featured poster sessions for the poster researchers.

CME: Thirty-three physicians that attended the conference claimed a maximum of 13 credit hours for their continuing medical education.
Response to the 2008 Conference

We received a highly gratifying response to the meeting: forty six participants responded to the exit survey. Numerous participants gave enthusiastic answers regarding the quality of presentations and course content. Also, 99% of the respondents rated the meeting as considerably promoting scientific exchange of ideas.

Question 1: Were the Activity Objectives (Explaining current advances, exploring the application of novel therapeutics, proposing collaborative relationships) met?
The participants felt the activity objectives were sufficiently met. Advances in mitochondrial biology and their function at molecular and biochemical levels were satisfactorily discussed and the application of novel therapeutics targeting mitochondrial function to modulate cardiac risk factors and treat cardiovascular disease adequately explored; all those surveyed strongly agreed or agreed with these statements. However, more collaborative relationships could have been established, as some of those surveyed were more neutral in their response than in agreement.

Question 2: Will you change your practice in any way as a result of attending this course?
Most of those surveyed (42%) responded that they wouldn’t change their practice, while 25% did not respond to the question. This is most likely due to the fact that most of the attendees were researchers, rather than physicians.

Question 3: Please evaluate this activity as a whole:
All of the attendees that responded in the overall evaluation gave the activity ratings of “Good” or higher, and more than half of them rated it as “Excellent.” More than 90% of respondents rated the course organization, course content, quality of presentations and audiovisual aids as “good” or better. Ratings of the course usefulness, conference facilities, and registration process were also generally very good. The range of ratings for syllabus materials was large, as equal numbers of respondents gave “Excellent” or “Fair” ratings.

Question 4: Do you feel the activity was objective, balanced, and free of commercial bias?
The majority (92%) of the respondents felt that the activity was free from bias.

Question 5: This activity should improve my (practice, procedural or cognitive Skills...)
As most attendees were researchers, many of those surveyed did not comment on how the conference improved their medical knowledge, care attitudes, practice behavior or their patients’ clinical outcomes. The majority of those that did respond felt somewhat agreed with the statement or felt neutral. However, a strong majority agreed that the conference would improve their cognitive skills and research awareness.
Response to the 2008 Conference (con'td)

Question 6: Please evaluate the daily lectures:
Drs Mootha, Shulman, and Spiegelman received the highest percentages and frequencies of excellent ratings. Drs Clarke and Lippincott-Schwartz also had high frequencies of excellent ratings.
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Executive Summary

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Moscow, Russia
## Agenda

### October 6, 2008

<table>
<thead>
<tr>
<th>Start Time</th>
<th>Finish Time</th>
<th>Welcome</th>
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<tbody>
<tr>
<td>8:00 AM</td>
<td>8:05 AM</td>
<td>Michael N. Sack, MD, PhD</td>
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<tr>
<td>8:05 AM</td>
<td>8:15 AM</td>
<td>Elizabeth G. Nabel, MD</td>
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### Session 1
The Regulatory Control of Mitochondrial Homeostasis
Chair: Daniel P. Kelly, MD

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<th>Time</th>
<th>Topic</th>
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<tr>
<td>8:15 AM</td>
<td>Proteolytic Control of Mitochondrial Biogenesis and Dynamics</td>
</tr>
<tr>
<td>8:35 AM</td>
<td>The PGC Family is Master Regulators of Mitochondrial Biogenesis</td>
</tr>
<tr>
<td>8:55 AM</td>
<td>Assembling the Components and Circuitry for Mitochondrial Biogenesis</td>
</tr>
<tr>
<td>9:15 AM</td>
<td>Mitochondrial Gene Expression and Signaling in Disease and Aging</td>
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<td>9:50 AM</td>
<td>Oral Poster - Biological Function of SIRT5 in Metabolism</td>
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### Session 2
Reactive Oxygen Species Biology, Calcium and the Role of Mitochondria in Signal Transduction
Chair: Toren Finkel, MD, PhD

<table>
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<th>Time</th>
<th>Topic</th>
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<tbody>
<tr>
<td>10:25 AM</td>
<td>Mechanisms of Cardioprotection by Nitric Oxide acting at the Mitochondrial Level</td>
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<tr>
<td>10:45 AM</td>
<td>New Perspectives on the Role of Mitochondria in Heart Disease</td>
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<tr>
<td>11:05 AM</td>
<td>Keeping Mitochondria in Shape: A Matter of Life and Death</td>
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<tr>
<td>11:25 AM</td>
<td>Mitochondrial Production of Reactive Oxygen Species</td>
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<tr>
<td>11:45 AM</td>
<td>Mitochondrial Pathways for Reactive Oxygen Species Formation and Myocardial Injury</td>
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### Session 3
Proteomics in Advancing the Understanding of Mitochondrial Biology
Chair: Peipei Ping, PhD

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<tr>
<td>1:35 PM</td>
<td>The Dynamics of the Mitochondrial Proteome</td>
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<td>Analysis of the Effects of Bi-ventricular Pacing on the Mitochondrial Sub-proteome</td>
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<td>2:15 PM</td>
<td>Systems Biology of the Mitochondria</td>
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<tr>
<td>2:35 PM</td>
<td>Oral Poster- Proteomics of Lysine Acetylation in Mitochondrion</td>
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### Session 4
Imaging of Mitochondrial Function
Chair: Robert S. Balaban, PhD

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<tr>
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<td>A Functional Link between Mitochondrial Morphology and Cell Cycle Progression at G1-S</td>
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<td>Mitochondrial Energy Metabolism in the Diabetic Heart and Skeletal Muscle</td>
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<tr>
<td>4:15 PM</td>
<td>Mitochondria from Cradle to Grave</td>
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<td>4:35 PM</td>
<td>Oral Poster- PDGFR β Signaling is an Essential Component of the Cardiac Response to Load Induced Stress</td>
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<td>4:50 PM</td>
<td>Scientific Poster Award Presentation</td>
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## October 7, 2008

<table>
<thead>
<tr>
<th>Start Time</th>
<th>Finish Time</th>
<th>Session 5</th>
<th>Mitochondrial Dysfunction and Genetic Diseases</th>
<th>Chair: Paul Hwang, MD, PhD</th>
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<tbody>
<tr>
<td>8:15 AM</td>
<td>8:35 AM</td>
<td>8:15 AM</td>
<td>Metabolic Basis of Hypertrophic Cardiomyopathy</td>
<td>Hugh Watkins, MD, PhD</td>
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<td>8:35 AM</td>
<td>8:55 AM</td>
<td>8:35 AM</td>
<td>Mitochondrial Dynamics in Development and Disease</td>
<td>David C. Chan, MD, PhD</td>
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<td>8:55 AM</td>
<td>9:15 AM</td>
<td>8:55 AM</td>
<td>Mitochondrial Antioxidants as Potential Therapies</td>
<td>Michael P. Murphy, PhD</td>
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<td>9:15 AM</td>
<td>9:30 AM</td>
<td>9:15 AM</td>
<td>Oral Poster - Reduced Fatty Acid Metabolism and Elevated Mitochondrial H202 Emission Are Associated with Decreased PPARα in Diabetic Human Myocardium</td>
<td>Ethan Anderson, PhD</td>
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| 9:30 AM    | 9:55 AM     | 9:30 AM   | Break                                         |                           |

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<thead>
<tr>
<th>Session 6</th>
<th>Mitochondrial Role in Increasing Cardiovascular Risk including Obesity and Type II Diabetes</th>
<th>Chair: Michael N. Sack, MD, PhD</th>
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<tr>
<th>Session 7</th>
<th>Mitochondrial Function in Cardiovascular Disease-Ischemia, Hypertrophy and Heart Failure</th>
<th>Chair: Elizabeth C. Murphy, PhD</th>
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<th>Session 8</th>
<th>The Mitochondria as a Therapeutic Target in Cardiovascular Disease</th>
<th>Chair: Heinrich Taegtmeyer, MD, PhD</th>
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Web Sites

Conference web site: www.mitochondrial2008.com

Organizing Committee Website: www.strategicresults.com/mito_OC/

Speaker Website: www.strategicresults.com/mito_speakers/
Appendixes

Exit Questionnaire
Program Guide (CD)
Exit Questionnaire

Questionnaires were included in the program guide. The participants were asked to complete and leave at the welcome desk. The completed questionnaires were submitted at the end of the second day, along with CME details.
Exit Questionnaire

Question 1
Were the following Activity Objectives Met?

1a. To discuss and explain current advances in the understanding of mitochondrial biology and function at the molecular and biochemical levels
   Strongly Agree 53% (19)
   Agree 44% (16)
   Neutral 0% (0)
   Disagree 0% (0)
   Strongly Disagree 0% (0)
   N/A 4% (1)

1b. To explore the application of novel therapeutics targeting mitochondrial function to modulate cardiac risk factors and treat cardiovascular disease
   Strongly Agree 42% (15)
   Agree 47% (17)
   Neutral 6% (2)
   Disagree 0% (0)
   Strongly Disagree 0% (0)
   N/A 6% (2)

1c. To propose collaborative relationships with other health professionals who share an interest in pursuing novel applications in this emerging field
   Strongly Agree 44% (16)
   Agree 42% (15)
   Neutral 11% (4)
   Disagree 0% (0)
   Strongly Disagree 0% (0)
   N/A 4% (1)

Question 2
Will you change your Practice in any way as a result of attending this course?
   Yes 33% (12)
   No 42% (15)
   N/A 25% (9)

Question 3
Please Evaluate this activity as a whole:

3a. Overall Evaluation
   Excellent 56% (20)
   Very Good 28% (10)
   Good 14% (5)
   Fair 0% (0)
   Poor 0% (0)
   N/A 3% (1)
### Exit Questionnaire (cont'd)

#### 3b. Course Organization
- Excellent: 53% (19)
- Very Good: 28% (10)
- Good: 14% (5)
- Fair: 3% (1)
- Poor: 0% (0)
- N/A: 3% (1)

#### 3c. Course Content
- Excellent: 42% (15)
- Very Good: 42% (15)
- Good: 14% (5)
- Fair: 0% (0)
- Poor: 0% (0)
- N/A: 3% (1)

#### 3d. Usefulness
- Excellent: 44% (16)
- Very Good: 31% (11)
- Good: 14% (5)
- Fair: 8% (3)
- Poor: 0% (0)
- N/A: 3% (1)

#### 3e. Quality of Presentations
- Excellent: 50% (18)
- Very Good: 33% (12)
- Good: 11% (4)
- Fair: 3% (1)
- Poor: 0% (0)
- N/A: 3% (1)

#### 3f. Audiovisual Aids
- Excellent: 47% (17)
- Very Good: 36% (13)
- Good: 14% (5)
- Fair: 0% (0)
- Poor: 0% (0)
- N/A: 3% (1)

#### 3g. Syllabus Materials
- Excellent: 22% (8)
- Very Good: 36% (13)
- Good: 11% (4)
- Fair: 22% (8)
- Poor: 0% (0)
- N/A: 8% (3)
Exit Questionnaire (cont’d)

3h. Conference Facilities
Excellent 50% (18)
Very Good 22% (8)
Good 14% (5)
Fair 6% (2)
Poor 3% (1)
N/A 6% (2)

3i. Registration Process
Excellent 42% (15)
Very Good 36% (13)
Good 11% (4)
Fair 6% (2)
Poor 0% (0)
N/A 6% (2)

Question 4.
Do you feel the activity was Objective, Balanced and Free of Commercial Bias?
Yes 92% (33)
No 3% (1)
N/A 6% (2)

Question 5.
This Activity should Improve my:
Medical or Practice Knowledge
Strongly Agree 25% (9)
Somewhat Agree 25% (9)
Neutral 17% (6)
Somewhat Disagree 3% (1)
Strongly Disagree 8% (3)
N/A 22% (8)

Care Attitudes
Strongly Agree 11% (4)
Somewhat Agree 22% (8)
Neutral 25% (9)
Somewhat Disagree 3% (1)
Strongly Disagree 8% (3)
N/A 31% (11)

Procedural or Cognitive Skills
Strongly Agree 28% (10)
Somewhat Agree 22% (8)
Neutral 22% (8)
Somewhat Disagree 3% (1)
Strongly Disagree 6% (2)
N/A 19% (7)
Exit Questionnaire (cont’d)

**Practice Behavior**

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<tr>
<th>Rating</th>
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<td>8%</td>
<td>(3)</td>
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<tr>
<td>Somewhat Agree</td>
<td>31%</td>
<td>(11)</td>
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<tr>
<td>Neutral</td>
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<td>(8)</td>
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<tr>
<td>Somewhat Disagree</td>
<td>3%</td>
<td>(1)</td>
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<tr>
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<td>8%</td>
<td>(3)</td>
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<td>28%</td>
<td>(10)</td>
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**Patients’ Clinical Outcomes**

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<td>Somewhat Agree</td>
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<td>(9)</td>
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<td>(11)</td>
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<tr>
<td>Somewhat Disagree</td>
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<td>(1)</td>
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<td>8%</td>
<td>(3)</td>
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<tr>
<td>N/A</td>
<td>28%</td>
<td>(10)</td>
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**Approach to my Research/ Public Health Awareness**

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<tr>
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<td>(11)</td>
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<td>Neutral</td>
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**Question 6.**

**Please Evaluate the Daily Lectures:**

**Evan Dale Abel, MD, PhD**

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**Christopher P. Baines, PhD**

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**Robert S. Balaban, PhD**

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### Exit Questionnaire (cont’d)

#### Paul S. Brookes, PhD
- **Excellent**: 28% (10)
- **Very Good**: 28% (10)
- **Good**: 11% (4)
- **Fair**: 3% (1)
- **Poor**: 0% (0)
- **N/A**: 31% (11)

#### David C. Chan, MD, PhD
- **Excellent**: 39% (14)
- **Very Good**: 17% (6)
- **Good**: 11% (4)
- **Fair**: 0% (0)
- **Poor**: 0% (0)
- **N/A**: 25% (12)

#### Kong Y. Chen, PhD
- **Excellent**: 22% (8)
- **Very Good**: 19% (7)
- **Good**: 22% (8)
- **Fair**: 8% (3)
- **Poor**: 0% (0)
- **N/A**: 28% (10)

#### Kieran Clarke, PhD
- **Excellent**: 36% (13)
- **Very Good**: 17% (6)
- **Good**: 14% (5)
- **Fair**: 3% (1)
- **Poor**: 3% (1)
- **N/A**: 28% (10)

#### Fabio Di Lisa, MD
- **Excellent**: 22% (8)
- **Very Good**: 28% (10)
- **Good**: 17% (6)
- **Fair**: 6% (2)
- **Poor**: 0% (0)
- **N/A**: 28% (10)

#### Roberta A. Gottlieb, MD
- **Excellent**: 22% (8)
- **Very Good**: 22% (8)
- **Good**: 22% (8)
- **Fair**: 3% (1)
- **Poor**: 0% (0)
- **N/A**: 31% (11)
### Exit Questionnaire (cont'd)

#### Daniel P. Kelly, MD
- Excellent: 28% (10)
- Very Good: 19% (7)
- Good: 11% (4)
- Fair: 6% (2)
- Poor: 0% (0)
- N/A: 36% (13)

#### Thomas Langer, PhD
- Excellent: 33% (12)
- Very Good: 19% (7)
- Good: 6% (2)
- Fair: 3% (1)
- Poor: 0% (0)
- N/A: 39% (14)

#### W. Jonathan Lederer, MD, PhD
- Excellent: 19% (7)
- Very Good: 22% (8)
- Good: 19% (7)
- Fair: 6% (2)
- Poor: 3% (1)
- N/A: 31% (11)

#### Jennifer A. Lippincott-Schwartz, PhD
- Excellent: 36% (13)
- Very Good: 17% (6)
- Good: 17% (6)
- Fair: 0% (0)
- Poor: 0% (0)
- N/A: 31% (11)

#### Gary D. Lopaschuk, PhD
- Excellent: 25% (9)
- Very Good: 11% (4)
- Good: 11% (4)
- Fair: 0% (0)
- Poor: 0% (0)
- N/A: 53% (19)

#### Vamsi K. Mootha, MD
- Excellent: 44% (16)
- Very Good: 17% (6)
- Good: 3% (1)
- Fair: 0% (0)
- Poor: 0% (0)
- N/A: 36% (13)
Exit Questionnaire (cont’d)

Michael P. Murphy, PhD

Excellent 36% (13)
Very Good 28% (10)
Good 8% (3)
Fair 0% (0)
Poor 0% (0)
N/A 28% (10)

Brian O'Rourke, PhD

Excellent 25% (9)
Very Good 22% (8)
Good 22% (7)
Fair 0% (0)
Poor 0% (0)
N/A 33% (12)

Peipei Ping, PhD

Excellent 22% (8)
Very Good 14% (5)
Good 25% (9)
Fair 3% (1)
Poor 0% (0)
N/A 36% (13)

Rainer Schulz, MD, PhD

Excellent 17% (6)
Very Good 25% (9)
Good 28% (10)
Fair 3% (1)
Poor 0% (0)
N/A 28% (10)

Luca Scorrano, MD, PhD

Excellent 33% (12)
Very Good 19% (7)
Good 14% (5)
Fair 0% (0)
Poor 0% (0)
N/A 33% (12)

Gerald S. Shadel, PhD

Excellent 25% (9)
Very Good 28% (10)
Good 8% (3)
Fair 3% (1)
Poor 3% (1)
N/A 33% (12)
Exit Questionnaire (cont’d)

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Exit Questionnaire (cont’d)

Charles J. Steenbergen, JR., MD, PhD
Excellent 25% (9)
Very Good 19% (7)
Good 19% (7)
Fair 0% (0)
Poor 0% (0)
N/A 36% (13)

Rong Tian, MD, PhD
Excellent 22% (8)
Very Good 17% (6)
Good 25% (9)
Fair 0% (0)
Poor 0% (0)
N/A 36% (13)

Jennifer Van Eyk, PhD
Excellent 22% (8)
Very Good 31% (11)
Good 14% (5)
Fair 3% (1)
Poor 0% (0)
N/A 31% (11)

Hugh Watkins, MD, PhD
Excellent 17% (6)
Very Good 28% (10)
Good 8% (3)
Fair 3% (1)
Poor 0% (0)
N/A 44% (16)