Welcome/Opening Remarks
Wednesday, December 2, 2009

Mirjam A.G. Sprangers
Academic Medical Center, University of Amsterdam, the Netherlands

Jeff A. Sloan
Mayo Clinic Comprehensive Cancer Center
Rochester, MN, US

GENEQOL Consortium Meeting
Amsterdam, December 2 - 3, 2009
Welcome to Amsterdam!
Welcome to Amsterdam!
Welcome to the Academic Medical Center

- 25,000 clinical admissions
- 155 professors
- 2,200 medical students
- 7,000 employees
- 256,000 outpatient visits
- 30,000 day care admissions
- 1,002 beds
- 3,000 publications in scientific journals
- 160 doctorates conferred
Introduction of participants
Introduction of participants

What is the one thing you want to get out of this meeting?
Thanks

• Bert Schadé, Chair Division J/K
• Mayo Foundation
• Ron van Noorden, Department Cell Biology & Histology
• Trees Pierik
• Marieke van Gelderen
• Jessica Hess
Housekeeping: Facilities

- Bathrooms
- Breaks / Meals
- Phones, copier, fax, e-mail
- Emergency phone numbers:
  Room M3-108: +31 20 566 5538
  Wednesday: + 31 20 566 4966
  Thursday: +31 20 566 4661
Housekeeping: Dinner tonight

• Dinner tonight at:

Queen of Holland
Nieuwezijds Voorburgwal 5
Telephone: +31-20 6200 500
Housekeeping: Dinner tonight

- Two menus: who wants meat/fish and who vegetarian?
- We will go by subway; map and tickets available
- This evening is a reward for all the work
- Networking opportunity
Housekeeping: Thursday

- Transport on your own
- Meet in hotel lobby at 8 am; Jeff will guide
- Lunch tomorrow at 13:00 in this room
- If you need help with transport to airport, let us know
- Go home
Brief History
New Initiative: Genetic Research into Quality of Life

Overall objective
To establish strong collaborative and interdisciplinary relationships to translate and plan clinically relevant research to identify and investigate potential genes and genetic variants involved in quality of life
Translational Objective

Results of this work will enable providers to identify which patients are likely to experience symptoms and quality of life deficits from disease and its treatments in order to:

• intervene prophylactically,
• monitor patient well-being,
• improve treatment decision-making, and
• improve outcomes
The Future?

As you can see from your genetic printout you only think you're depressed whereas you are in fact a jolly, happy full of the joys of spring type person!
Clinical Implication

“Doctors will eventually use genetic patterns for several tasks -- to tell whether a cancer will spread, to predict how various therapies such as specific drugs or radiation will work, and perhaps even to see how someone's quality of life will be affected.”

(Sloan and Zhao, 2006)
In other words, is there a quality-of-life gene?
GENEQOL Consortium
The Mayo Clinic/University of Amsterdam International Consortium for Genetics and Quality of Life Research

cellular biology
behavioral genetics
biological psychology
statistical genetics
 genetic epidemiology
medical psychology
clinical psychology
molecular biology
pharmacogenetics
nursing
sociology
psychiatry
oncology
Mayo School of Continuing Medical Education

Genetic Disposition and Patient - Reported Quality of Life Outcomes

February 26, 2009
Leighton Auditorium
Siebens Building
Mayo Clinic
Rochester, MN

Program Directors
Jeff A. Sloan, Ph.D.
Mirjam Sprangos, Ph.D.
genetic Disposition

and patient-reported

quality of life outcomes

February 26-28, 2009, Mayo Clinic, Rochester, MN
Meeting Objectives

• Develop a list of potential biological pathways, genes and genetic variants involved in quality of life domains, by reviewing the state of the art regarding current genetic knowledge.

• Design a research agenda to investigate and validate those genes and genetic variants of quality of life.
Five Outcomes Under Study

1) Negative emotional states (i.e. depression, anxiety)

2) Positive emotional states (i.e. happiness, life satisfaction, overall quality of life)

3) Perceived or self-rated physical health or functioning

4) Pain

5) Fatigue
We have:

- A great pool of talent
We have:

• A great pool of talent
• A list of genes to chase
List of candidate genes drawn from the literature and GENEQOL consortium work

<table>
<thead>
<tr>
<th>PRO-based Symptom/QOL</th>
<th>Candidate Genes/polymorphisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue, Insomnia</td>
<td>cytokine gene polymorphisms IL1B—511 (C/T) and IL6—174 (G/C), IL8—251 (T/A), IL2—330 (T/G), TNFa—308 (G/A), mu opioid receptor gene OPRM1, folate genes DPYD, MTHFR and TYMS, the -110A &gt; C polymorphism in gene HSP70-1, heat shock protein HSP70 genes (HSPA1A, HSPA1B and HSPA1L)</td>
</tr>
<tr>
<td>Pain</td>
<td>catechol-O-methyltransferase (COMT), monoamino-oxidase A (MAO-A), serotonin transporter gene (SLC6A4/5-HTT), transient receptor potential family A subtype 1 (TRPA1), opioid receptor subtype 1 (OPRD1), fatty acid hydrolase (FAAH), interleukin-1-receptor (IL-1RN), cytochrome P450 enzymes (CYP)</td>
</tr>
<tr>
<td>Nausea, Anorexia</td>
<td>5-hydroxytryptamine type 3B (5-HT3B) receptors, interleukin-1-receptor (IL-1RN), cytochrome P450 enzyme 2D6 (CYP2D6), monoamine oxidase A (MAOA)</td>
</tr>
<tr>
<td>Depressed Mood, Outlook</td>
<td>epsilon4 allele of the apolipoprotein E (APOE) gene, guanine nucleotide-binding protein (GNB3), methylenetetrahydrofolate reductase (MTHFR), dopamine transporters (SLC6A3, SLC6A4), catechol-O-methyltransferase (COMT), monoamino-oxidase A (MAO-A), serotonin transporter gene (SLC6A4/5-HTT)</td>
</tr>
<tr>
<td>Total Symptom Severity, Overall QOL</td>
<td>All of the above</td>
</tr>
</tbody>
</table>
We have:

• A great pool of talent
• A list of genes to chase
• A first collaborative paper
The Establishment of the GENEQOL Consortium to Investigate the Genetic Disposition of Patient-Reported Quality-of-Life Outcomes


Department of Medical Psychology, UMC Utrecht, The Netherlands

The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

Department of Health Sciences Research, Mayo Clinic, Rochester, MN, United States of America

Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, United States of America

Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, United States of America

Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, United States of America

Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, United States of America

Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, United States of America

Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, United States of America

The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, United States of America

Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, United States of America

Department of Medicine, Mayo Clinic, Phoenix, AZ, United States of America

Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, United States of America

Department of Radiation Oncology, Mayo Clinic, Jacksonville, FL, United States of America

Department of Radiation Oncology, Mayo Clinic, Scottsdale, AZ, United States of America

The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

To our knowledge, no comprehensive, interdisciplinary initiatives have been taken to examine the role of genetic variants on patient-reported quality-of-life outcomes. The main objective of this paper is to describe the establishment of an international and interdisciplinary consortium, the GENEQOL Consortium, which intends to investigate the genetic disposition of patient-reported quality-of-life outcomes. We have identified five primary patient-reported quality-of-life outcomes as initial targets: negative psychological affect, positive psychological affect, self-rated physical health, pain, and fatigue. The first tangible objective of the GENEQOL Consortium is to develop a list of potential biological pathways, genes and gene variants involved in these quality-of-life outcomes, by reviewing current genetic knowledge. The second objective is to design a research agenda to investigate and validate these gene and genetic variants of patients reported quality-of-life outcomes, by creating large datasets. During its first meeting, the Consortium had discussed draft summary documents addressing these questions for each patient-reported quality-of-life outcome. A summary of the primary pathways and robust findings of the genetic variants involved is presented here. The research agenda outlines possible research objectives and approaches to examine these and new quality-of-life domains. Intriguing questions arising from this endeavor are discussed.

Received 24 March, 2009; accepted 29 April, 2009.

Address for correspondence: Aliko H. Zawadzki, Department of Medical Psychology, UMC Utrecht, P.O. Box 30.001, 3508 TA Utrecht, The Netherlands. Email: zawadzki@umcutrecht.nl
We have:

- A great pool of talent
- A list of genes to chase
- A first collaborative paper
- A website
Overall objective
To establish strong collaborative and interdisciplinary relationships to translate and plan clinically relevant research to identify and investigate potential genes and genetic variants involved in quality of life in response to disease, treatment, and related toxicity.

“Doctors will eventually use genetic patterns for several tasks -- to tell whether a cancer will spread, to predict how various therapies such as specific drugs or radiation will work, and perhaps even to see how someone's quality of life will be affected.”

(Sloan and Zhao, 2006)
We have:

- A great pool of talent
- A list of genes to chase
- A first collaborative paper
- A website
- A series of talks at the International Society of Quality of Life Research, October, 2009
- A series of papers for the journal Quality of Life Research
- A start on a research agenda
We need:

• A great series of grant applications
• A great task force to write grants
• A great set of funding targets
• A great plan for infrastructure
• A great series of small steps to grow
Primary Meeting Goals

- Discussion of progress to date
- Identification of data sets
- Outline of research grant applications
- Identification of targets for infrastructure and research funding
Program Wednesday, December 2, 2009

13:00-13:15: Opening remarks/Welcome/Process
   Mirjam Sprangers and Jeff Sloan

13:15-15:00: Presentation of Data Sets
   Frank Baas (Netherlands)
   Jeff Sloan (USA)
   Gert Wagner (Germany)
   Ruut Veenhoven (Netherlands)

15:00-15:30: Tea Break

15:30-16:30: Presentation of Data Sets, continued
   Hein Raat (Netherlands)
   Juan Ordoñana (Spain)
   Corneel Coens (Belgium)
   Koos Zwinderman (Netherlands)/Pål Klepstad (Norway)

16:30-17:30: Synthesis: capitalizing on the data
   Future Collaboration

17:30-18:15: New ideas

18:15: Leave for Dinner
Program Thursday, December 3, 2009

9:00-10:30: Research Funding: Science
    Jeff Sloan: Challenge NIH grant, TR01 NCI grant: discussion
    Koos Zwinderman: Dutch Cancer Society grant: discussion
    Identify granting agencies
    Identify basic requirements of data sets
    Outline grant
    Identify writing team
    Set out time line

10:30-11:00: Coffee Break

11:00-12:00: Research Funding: Infrastructure/meeting

12:00-13:00: Synthesis
    Future Research Agenda
    Defining Home Work Tasks
    Next Meeting

13:00-14:00: Lunch
Ground Rules

• Brevity is the soul of wit: 1-minute wisdom
• Disagreements are not personal
• Keep to time schedule
• We have a path already chosen, the time for going back to square one has past
• People can be nominated for a walk
• We work hard, but let’s party harder!
Program Wednesday, December 2, 2009

13:00-13:15: Opening remarks/Welcome/Process
   Mirjam Sprangers and Jeff Sloan

13:15-15:00: Presentation of Data Sets
   Frank Baas (Netherlands)
   Jeff Sloan (USA)
   Gert Wagner (Germany)
   Ruut Veenhoven (Netherlands)

15:00-15:30: Tea Break

15:30-16:30: Presentation of Data Sets, continued
   Hein Raat (Netherlands)
   Juan Ordoñana (Spain)
   Corneel Coens (Belgium)
   Koos Zwinderman (Netherlands)/Pål Klepstad (Norway)

16:30-17:30: Synthesis
   Future Collaboration

17:30-18:15: New ideas

18:15: Leave for Dinner
Synthesis: capitalizing on the data
Future collaboration