Welcome/Opening Remarks
Thursday, December 3, 2009

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

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

GENEQOL Consortium Meeting
Amsterdam, December 2 - 3, 2009
Housekeeping: Facilities

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

• Lunch at 13:00 in this room
• If you need help with transport to airport, let us know
• Go home
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
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
"Your DNA test shows you're predisposed to sue doctors."
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!
Examples of submitted grants

Jeff Sloan: Challenge NIH grant
Examples of submitted grants

Jeff Sloan: TR01 NCI grant: discussion
Examples of submitted grants

Koos Zwinderman: Dutch Cancer Society grant
Identify granting agencies

- NIH
- NCI
- National Science Foundation
- Dutch Cancer Society (KWF)
- Swedish Cancer FUNDEN
- EU
- Mayo Foundation
- Robert Wood Johnston/Eagles/Komen
Identify granting agencies, continued
Identify basic requirements of data sets

- Research question is key
- Design
- Sample size
- Phenotyping quality of life
- Genetic data
- ...

Research questions

• What are the genetic variables associated with deficits in overall QOL which has been demonstrated to be prognostic for survival?
Designs to study genetic contributions, example of depression

<table>
<thead>
<tr>
<th>Target population</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Twin study</strong></td>
<td>Heritability account for depression (i.e., 30-40%)</td>
</tr>
<tr>
<td>Monozygotic twins</td>
<td></td>
</tr>
<tr>
<td>Dizygotic twins</td>
<td></td>
</tr>
<tr>
<td><strong>Linkage study</strong></td>
<td>Gene locations related to depression, e.g. chromosomes 15q, 17p, 8p</td>
</tr>
<tr>
<td>Family</td>
<td></td>
</tr>
<tr>
<td><strong>Candidate gene association study</strong></td>
<td>Genetic variants related to depression, e.g. APOE, GNB3, MTHFR, SLC6A3, SLC6a4</td>
</tr>
<tr>
<td>Unrelated individuals (hypothesis driven genetic marker selection)</td>
<td></td>
</tr>
<tr>
<td><strong>Genome wide association study (GWAS)</strong></td>
<td>Genetic variants related to depression, e.g. rs2522833 in PCLO</td>
</tr>
<tr>
<td>Unrelated individuals (examine genetic variants across the whole genome)</td>
<td></td>
</tr>
</tbody>
</table>
Identify basic requirements of data sets
Design and sample size

<table>
<thead>
<tr>
<th>Design</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Twin studies:</td>
<td>?</td>
</tr>
<tr>
<td>• Linkage studies:</td>
<td>?</td>
</tr>
<tr>
<td>• Candidate Gene studies:</td>
<td>100s</td>
</tr>
<tr>
<td>• GWAS:</td>
<td>1000s</td>
</tr>
</tbody>
</table>
Identify basic requirements of data sets
Phenotyping Quality of Life

• Internationally validated measures/scales
• One-item measures
• Which domains: ....
• Clinically defined case based on phenotype (e.g. score < 50: deficit in QL)
• ...

...
Identify basic requirements of data sets
Genotyping

<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>
Identify basic requirements of data sets
Genotyping

- Body material
- Which genes
Outline grant (4 types)

• Secundary data analysis: QL and genetic data available
• Collecting additional QL data: genetic data available
• Collecting additional DNA data: QL data available
• Preparing new study
Identify writing team
Research Funding: Infrastructure/meeting
Future Research Agenda
Defining Home Work Tasks
Parting Words

• Thank you, thank you, thank you