“Cutting Edge Genomic Research”
(In the Psychiatric Clinic)

John Tierney, MD
Adjunct Associate Professor
UTHSC Medical School
San Antonio
South Texas Psychiatric PBRN
“In Search of Alcoholism Genes”

- Humble Beginnings
  - Can we return cards?
  - How do we feel about our patients?
  - A Publication!
- Social Network of Science
  - Dr. John Roache approaches with an idea
- Translational Research
- Genomic Research
  - Dr. Johnson-Pais of the Genomics Core Lab has the equipment
- Personalized Medicine
**HIDDEN RISKS** | Variations in DNA, along with environmental factors, may play a role in drinking.

- A rare gene found mainly in Finnish people leads to severe impulsivity and alcoholism.
- Dopamine-receptor gene boosts pleasure from alcohol; friends often choose friends with the same variation.
- If one identical twin is an alcoholic, the other has a 76% risk of alcoholism, too, according to a 1960 study.

- Genes regulating Neuropeptide Y are linked to stress and withdrawal symptoms from alcohol.
- Sons of alcoholic fathers have nine times the usual risk of becoming alcoholic themselves.
- People with a ‘U型’ gene get inebriated on just one or two drinks, discouraging alcoholism.
- Children of alcoholics have a high risk of alcohol dependence—even if they’re raised in nonalcoholic homes.
- ‘Asian flush’ genes metabolize alcohol quickly, causing nausea and rapid heart beat, making alcoholism unlikely.
Alcoholism

- Children of Alcoholic Parents carry 4X Risk
- Sons of Alcoholic Fathers carry 9X Risk
- Babies of Alcoholics raised in non-alcoholic adoptive homes carry same Risk
- 1 in 10 Americans meet criteria for Alcohol Dependence
Alcoholism Subtypes

- **Type A**
  - Later age of onset (>25y/o)
  - Low Family Loading for Alcoholism
  - Preponderance of Psychosocial Morbidity

- **Type B**
  - Early age of onset (<25y/o)
  - Low Family Loading for Alcoholism
  - Broad range of Impulse-Control Traits
Type B
(Early Onset Alcoholism)

○ Homozygous for Long Form; “L”
  ▪ INS/ DEL polymorphism
  ▪ 5’-promoter region SLC6A4 gene
  ▪ Chromosome 17q11.1-q12

○ Homozygous shown to drink more when given SSRIs (Kranzler et al 2010)

○ Shown to drink less when given Serotonin Antagonist (Johnson et al 2011)
Translational Research

- Type A Alcoholics may benefit from SSRIs
- Type B Alcoholics may do worse with SSRIs
- Aim 1: Card Study to identify subgroups
- Aim 2: Longitudinal Assessment of subgroup responses
  - Does Type B do worse with SSRIs?
Genomic Research

- Genetic biomarkers of alcoholism
- Stop the Study!!!
- Let’s Add a Pilot Study
  - Collect saliva samples to analyze for biomarkers
  - INS/ DEL polymorphism
  - 5’-promoter region SLC6A4 gene
  - Chromosome 17q11.1-q12
Abundance

- J Craig Venter
  - Won race with government to map Human Genome 2004

- Technophilanthropy (eg Bill Gates)

- Personalized Medicine based on Genetics
  - Industry didn’t exist 10 years ago
  - Now growing at 15%/year
  - Estimated $452 Billion industry by 2015
  - Centenarian pop is doubling every decade; estimated 4 million by 2050
Personalized Medicine

- New line of Translational Research venue for Dr. Roache’s interest in serotonergic vulnerabilities
- Advance scope and breadth of PBRN research
- Preliminary data for future NIH applications
- Test whether phenomenological subtyping can make clinically important predictions with a serotonin-biological basis
- Will Clinicians personalize SSRI/SNRI use in Alcohol subtypes based upon this study?
Conclusion

- Clinicians in a PBRN can contribute to cutting edge Research
- Translational Research is the Future
- Genomic Research can occur simultaneously
- Personalized medicine can evolve from PBRNs