

Refining the Meeting Charge

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What can we do and what do we want to do

- Develop guidance to NIH for deciding *who*, *when* and *why* to sequence
- Balance four major elements
 1. Technologies
 2. Well-phenotyped studies
 3. How we analyze (call variants)
 4. Availability with *adequate* consent

From general to specific considerations: Mapping diseases and traits

- Start with Pilots??
 - Richness of sample sets-> multiple outcomes
 - Towards answering compelling scientific questions
 - Economy of scale in developing a process
 - Validation
- Larger studies
 - Thresholds (effect/frequency)
 - Pipeline development
 - Genetic
 - Analysis- problems in calling
 - Genotype error 0.01% -> 300,000 errors for WGS....
 - Posting

Strategic Use of Technologies

- Current
 - Exome (~80%) vs WGS (~90%)
- Importance of *revisiting* sample set
 - Supplementary technology for WGS or Exome
 - Increased “coverage of physical map”
 - Target “high-profile” regions
 - Follow-up confirmation
 - New genomics space
 - Detectable mosaicism (sequential testing)
 - Epigenomics
 - RNA Analysis (RNA Seq, miRNA)
 - “ENCODE-driven” targets

Analytical Questions

- Some vs Many questions in a data set?
- Depth vs Breadth
 - Do we ask for a handful of phenotypes in ALL subjects?
 - Survivorship
 - BMI/Height
- Development of Pipelines
 - Reference Sequence
 - Cost of Analysis
 - Central vs Distributed?
- Sequence Data
 - Hard to test agnostically.....
 - Value of laboratory correlation (link to other resources)
- Annotation of results
 - Publication
 - Availability

Long-Term Goals for Same Subjects

- 1,000,000 well sequenced genomes
- 1,000,000 well phenotyped subjects

- Key considerations
 - Recontact
 - Improve lifestyle/environment exposures
- Available to bona fide researchers

Two paradoxes

1. Infer individual insights from large studies
2. Denser data sets can be analyzed by fewer people



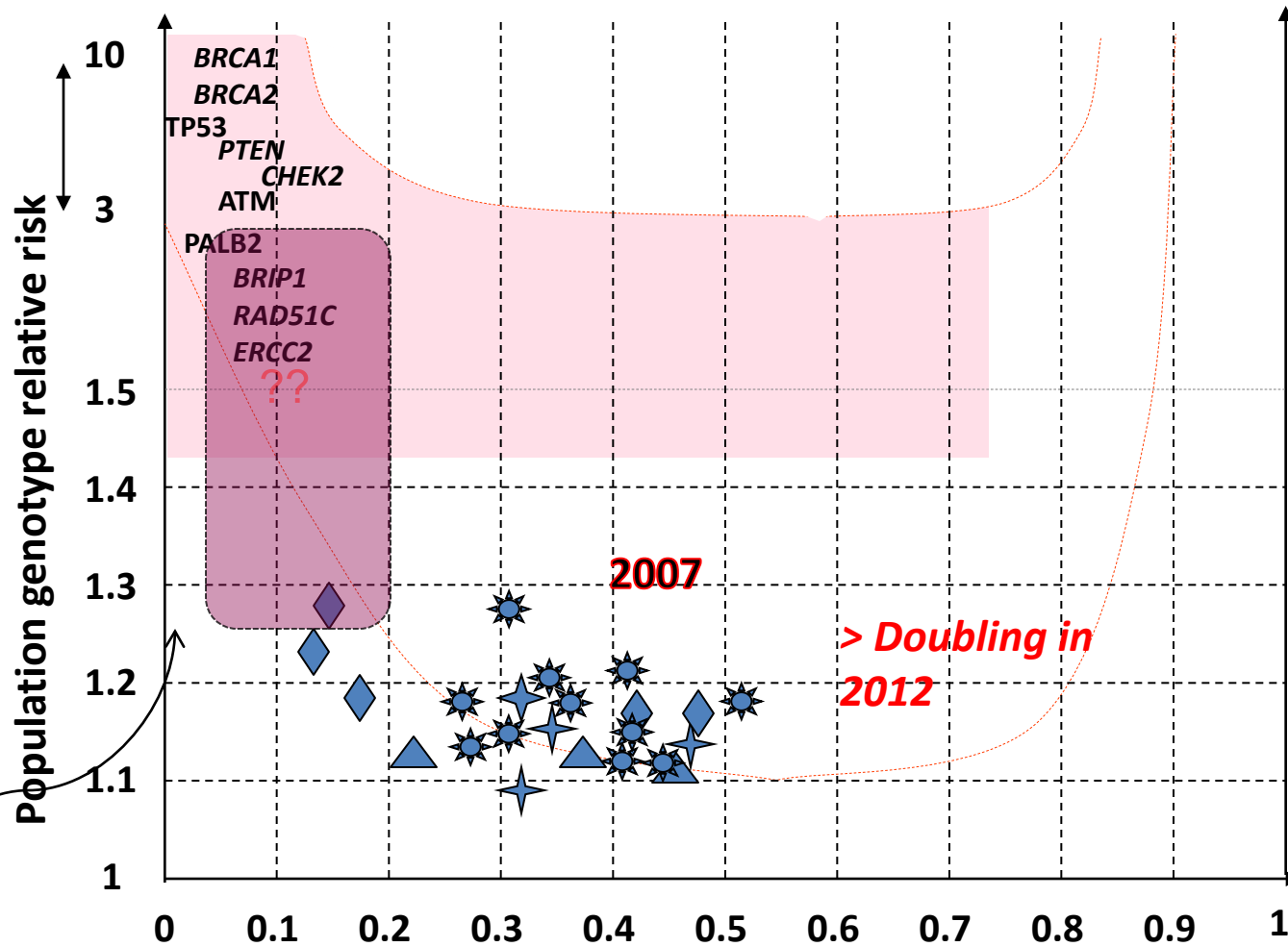
***Advances will be accelerated by
“Collective Intelligence”***

***“I not only use all of the brains
I have, but all I can borrow”***

Woodrow Wilson

Genetic Predisposition to Breast Cancer European Population

1990



**Exome & Whole
Genome Sequencing**

BCAC
 CGEMS/BCAC
 WTCCC
 Other