ADNI Genetics Update

Steering Committee Meeting
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Genetics Working Group

- Bryan DeChairo (Pfizer, ISAB Representative)
- Lindsay A. Farrer (BU)
- Tatiana M. Foroud (Indiana U, NCRAD)
- Steven Potkin (UCI)
- Andrew J. Saykin (Indiana U) – Chair *
- Gerard D. Schellenberg (U Washington)
- Rudolph E. Tanzi (MGH)
- John Q. Trojanowski (U Penn, Biomarker PI)
- Christopher van Dyck (Yale)
- Michael W. Weiner (UCSF, ADNI PI)
- Kirk C. Wilhelmsen (UNC)

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ADNI Genotyping Project

- Developments in the past year
- Initial goal: high density whole genome scan
- Illumina genotyping platform was selected
- TGEN (Phoenix, AZ) selected to run assays
- Funding obtained for genetics projects:
  - Two proposals were submitted to industry and foundations in conjunction with the FNIH
  - The Illumina Human 1M array was initially selected as the preferred platform by consensus of the Genetics Committee & ISAB
  - This was revised to the new Quad 610 array due to cost and a challenge grant deadline

Grant Support: Arrays, Reagents & Processing

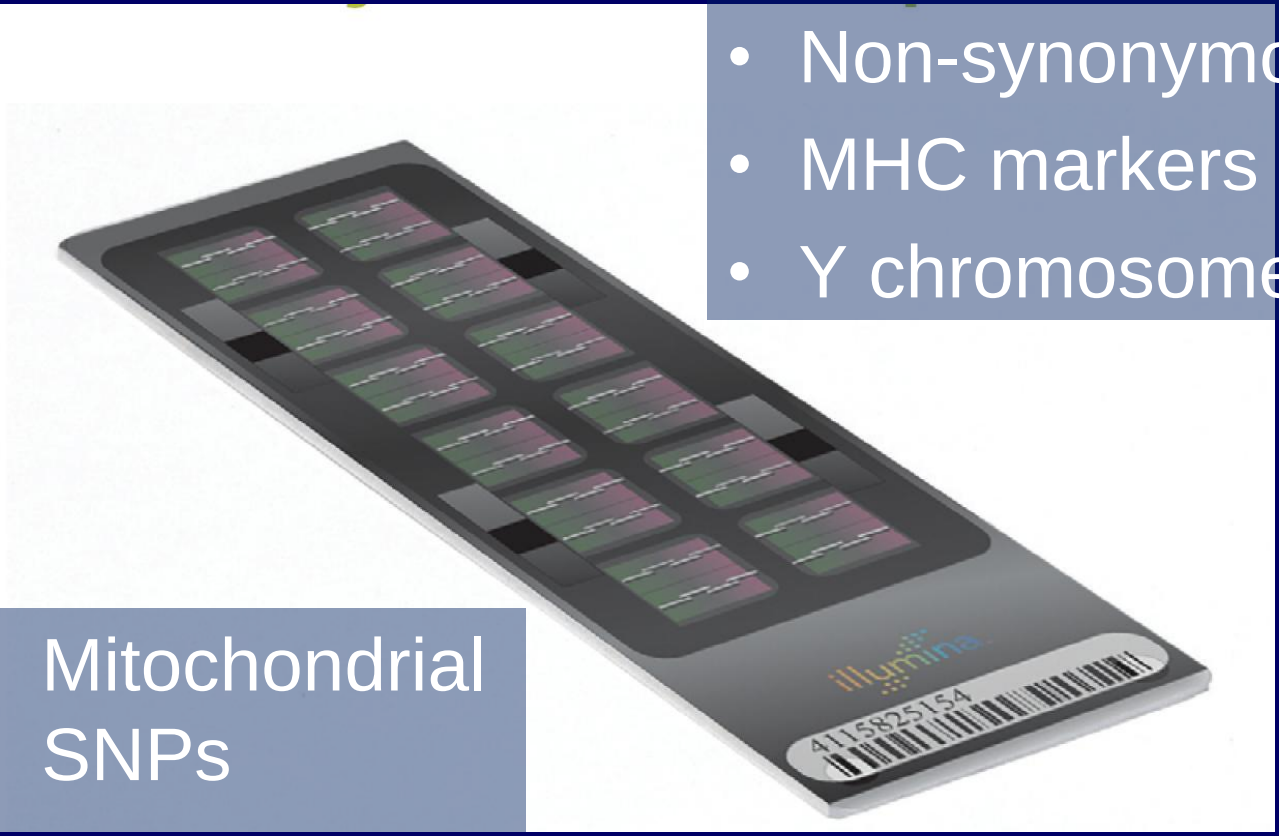
- "Whole Genome Analysis of the Alzheimer's Disease Neuroimaging Initiative Cohort"
  - Goal: High density genome wide scan of the ADNI cohort using advanced single nucleotide polymorphism (SNP) and copy number variation (CNV) arrays. Data to be rapidly made available to the scientific community.
  - PIs: D. Stephan (TGEN) & A. Saykin (IUSM)
  - Total funding: $333,551 via the FNIH
    - Contributors: Anonymous Foundation (Challenge Grant), Merck, Pfizer & Gene Network Sciences
    - Additional assistance from TGEN, IUSM & NCRAD
    - Highly discounted arrays from Illumina for ADNI

Grant Support: Initial Association Analyses

- "Genetic Association Analysis of the Alzheimer's Disease Neuroimaging Initiative Cohort"
  - Goal: Preliminary analyses of genotype/phenotype associations in the ADNI cohort using the results the whole genome SNP array. Data and results will be rapidly made available to the scientific community.
  - PIs: S. Potkin (UCI) & A. Saykin (IUSM)
  - Funding: $167,143 via the FNIH
    - Contributors: Anonymous Foundation (Challenge Grant), Merck, Pfizer & Gene Network Sciences
    - Additional assistance from NIBIB (supplement to UCI)

Illumina Human 610-Quad Coverage

www.illumina.com/infinium



- Non-synonymous SNPs
- MHC markers
- Y chromosome SNPs
- Mitochondrial SNPs

- 620,901 markers (~90% genomic coverage, CEU)
- Combines the contents of the Human Hap550-Duo and Human CNV370-Duo BeadChips

ADNI Genotyping Current Status

- Blood was transferred from the ADNI Biomarker Core (PENN) to Pfizer (B. DeChairo) & DNA was extracted
- DNA was assessed and samples were sent to TGEN
- Where necessary, DNA was extracted from cell line data at NCRAD (T. Foroud)
- Samples are now at TGEN and being further assessed and processed (D. Stephan)
- Assays should be completed by the end of May

Plans

- Next Steps
  - Initial QC of raw data
  - Set up database(s) with standard data format for downloads (Database & Statistics Cores)
  - As projected, SNP data should be available by ~mid 2008
- The genomic scan is just the beginning
  - Numerous genetic follow-up studies will be needed
  - Extensive analyses will be needed to integrate WGA with imaging, clinical and other biomarker data
- Apply for supplement/grants for genomic analyses
  - Facilitate collaborations for integrative data analysis
- Develop Genetics Core for ADNI-2
- Coordinate w/ proposed NIA AD Genetics Consortium