Next-generation sequencing
Lecture 6

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DISCUSS THE IMPORTANT ASPECTS OF GWAS AND NEXT-GENERATION SEQUENCING FOR PATIENT CARE PROVIDERS AND PATIENTS
Privacy Concerns

• All NIH funded GWAS must be deposited into dbGaP (also sequence data)
  – Can be a consent issue
    • Re-consent required for some studies
  – De-identified genotypes and phenotypes deposited
    • Concerns about the re-identification potential even in de-identified data
    • Homer et al. (2008) suggests that “it is straightforward to assess the probability that a person or relative participated in a GWA study” still a matter of debate

Incidental Findings

• Due to the enormous wealth of data and information that GWAS provides, the probability of finding unexpected results is increased
  – Non-paternity (as with most genetic studies)
  – Ancestry
  – Sex chromosome anomalies
  – Presence of disease-associated polymorphisms
    • SNPs in LD with APOE are on GWAS platforms
Sex Chromosome Anomalies

XXY/XY mosaic
Sex Chromosome Anomalies

XXY/XY mosaic
Sex Chromosome Anomalies

XXY
Sex Chromosome Anomalies

XX/XO mosaic
Incidental Findings:

• Usual practice in genomic research - no disclosure of individual research results, including incidental findings.

This procedure under recent scrutiny - genomic research produces a vast quantity of health-related data and information that may be beneficial to participants.

Potential for disclosure of results raises new issues - who might be responsible for dealing with any incidental findings - use of samples in multiple studies and the absence of defined limits for their use.

http://www.phgfoundaion.org/news/4269/
Return of results

- **Pros**
  - Investigators often want to return them
  - Research participants often want/expect to receive them
  - Promotes trust in research

- **Cons**
  - Some participants do not want them
  - Typically results are not obtained under clinical conditions
  - Blurring of line between research and clinical care
  - History of not returning some types of results

Courtesy of Ellen Clayton
Return of results

• Unresolved issues
  – What kinds of information warrant disclosure?
    • Personal health, reproductive planning, interest?
  – Does the investigator need to conduct research under clinical conditions?
  – How hard does the investigator have to look for potentially reportable results?
  – What issues arise for third-party discovered incidental discoveries?
  – What threshold? What process?
Direct-to-Consumer GWAS

• Several companies are providing a GWAS service for interested customers
  – Affordable, easy

1. Order a kit ($399 USD) from our online store.
2. Claim your kit, spit into the tube, and send it to the lab.
3. Our CLIA-certified lab analyzes your DNA in 2-4 weeks.
4. Log in and start exploring your genome.

23andMe  deCODEme $985
Direct-to-Consumer GWAS

- Recreational genomics can be dangerous
- 23andMe includes genetic analysis of 33 clinical reports and 86 research reports
  - FDA put a stop to this for now
- Most of these associations are from GWAS
  - Teensy odds ratios
  - Explain small % of heritability
  - Only investigated in European-American populations
Direct-to-Consumer GWAS

• What does this mean for you?
  – Many individuals will have all results returned
  – Many individuals will not understand their results
  – Many individuals will wonder if their family members need to have their own GWAS performed
  – Many individuals will look to their physicians for advice
    • Many physicians will refer them to genetic counselors
DTC Whole Exome/Genome Sequencing Services Are Now Available

http://www.knome.com/

http://www.everygenome.com/
Questions???