Next-generation sequencing Lecture 6

February 23, 2015

Marylyn D. Ritchie

PENNSTATE

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

PENNSTATE

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

PENNSTATE

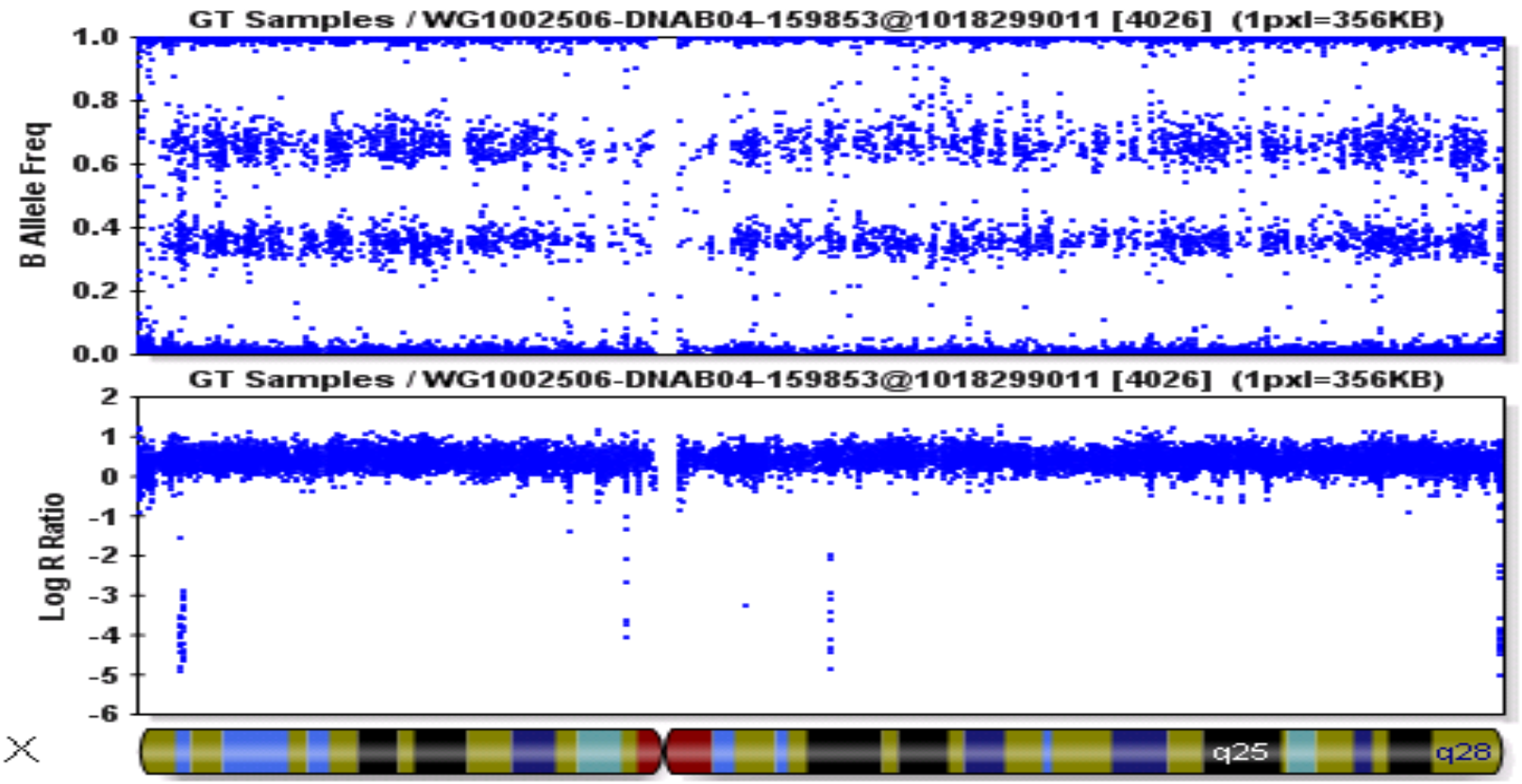
Homer N, et al. (2008) PLoS Genet 4(8): e1000167.

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

PENNSTATE

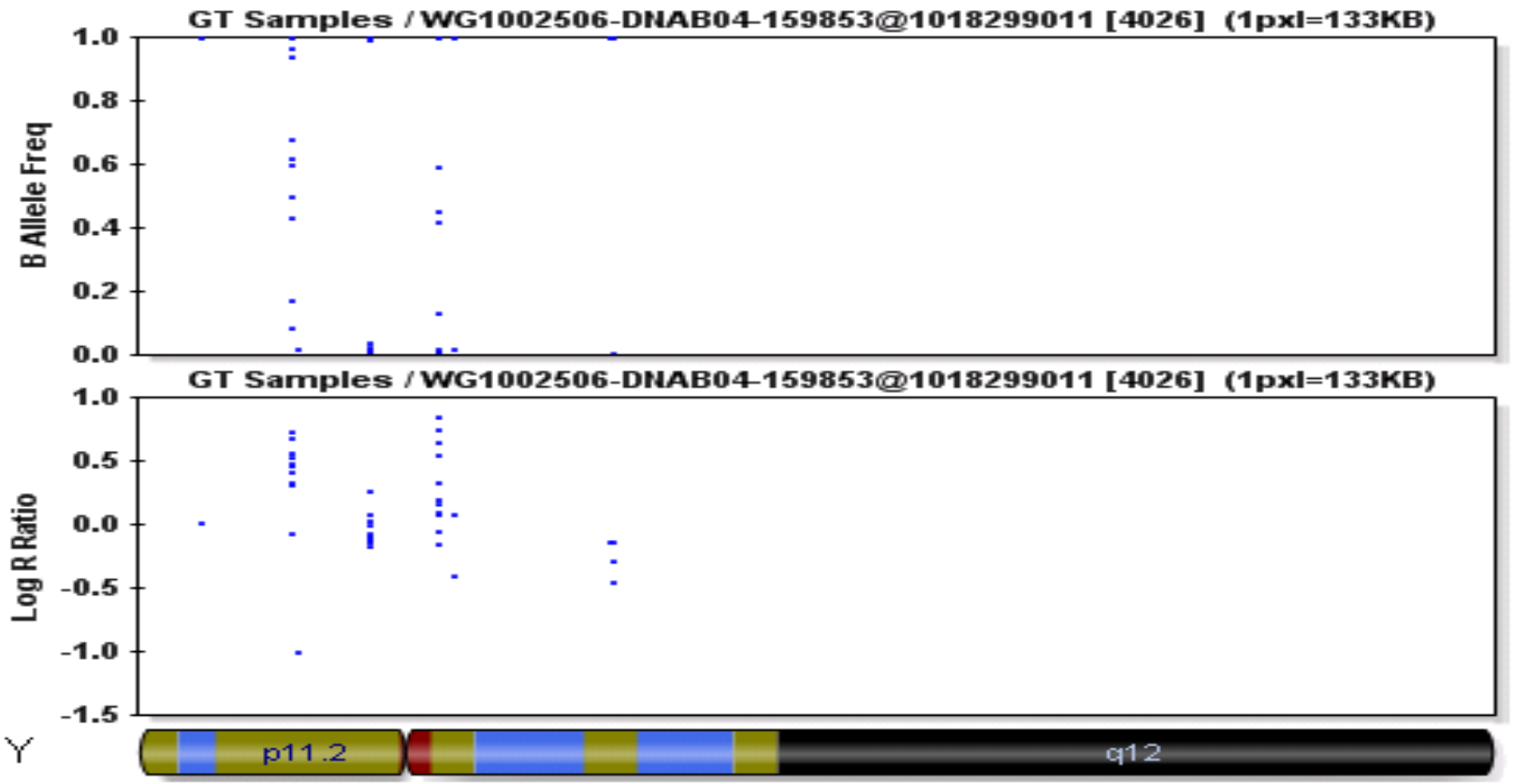
Sex Chromosome Anomalies



XXY/XY mosaic

PENNSTATE

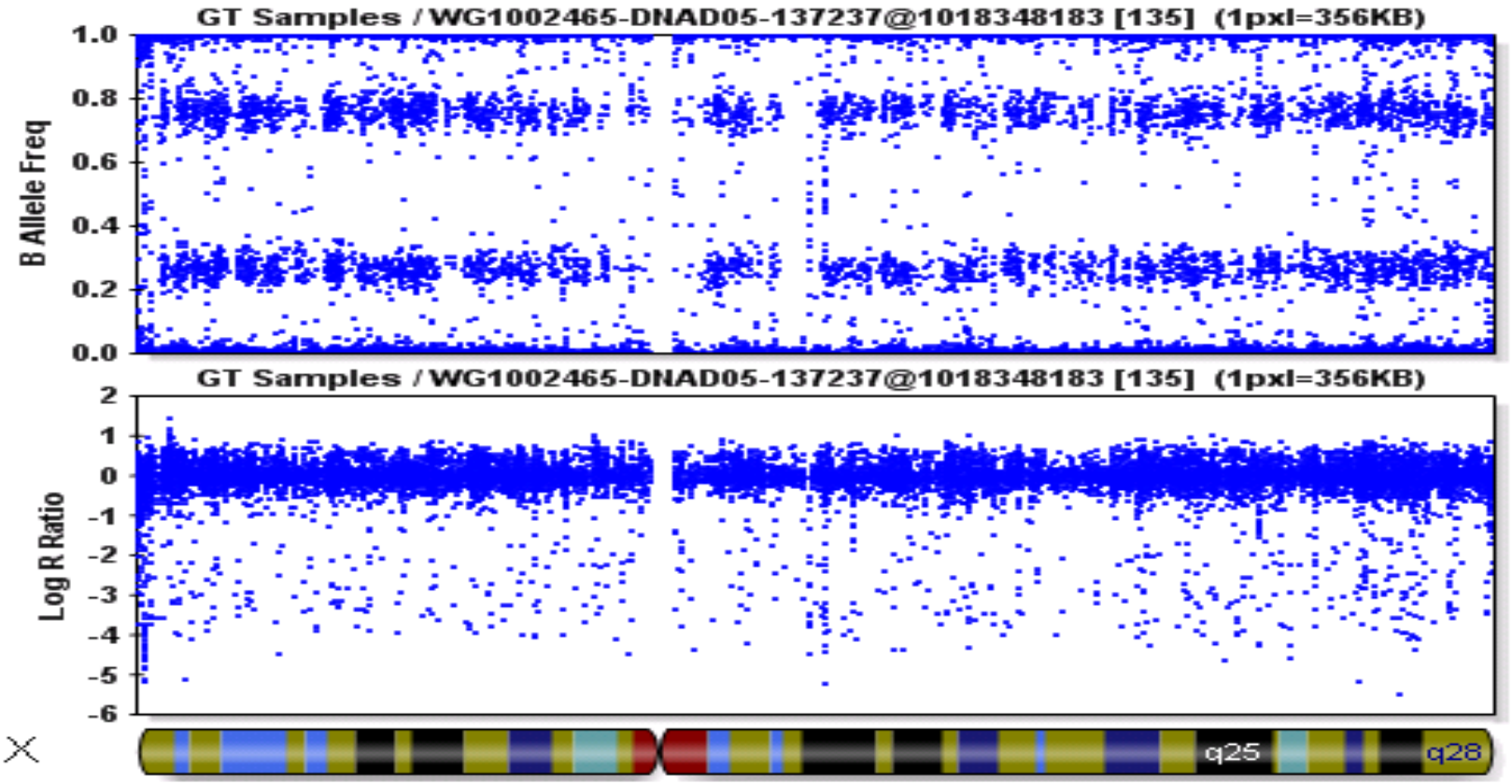
Sex Chromosome Anomalies



PENNSTATE

XXY/XY mosaic

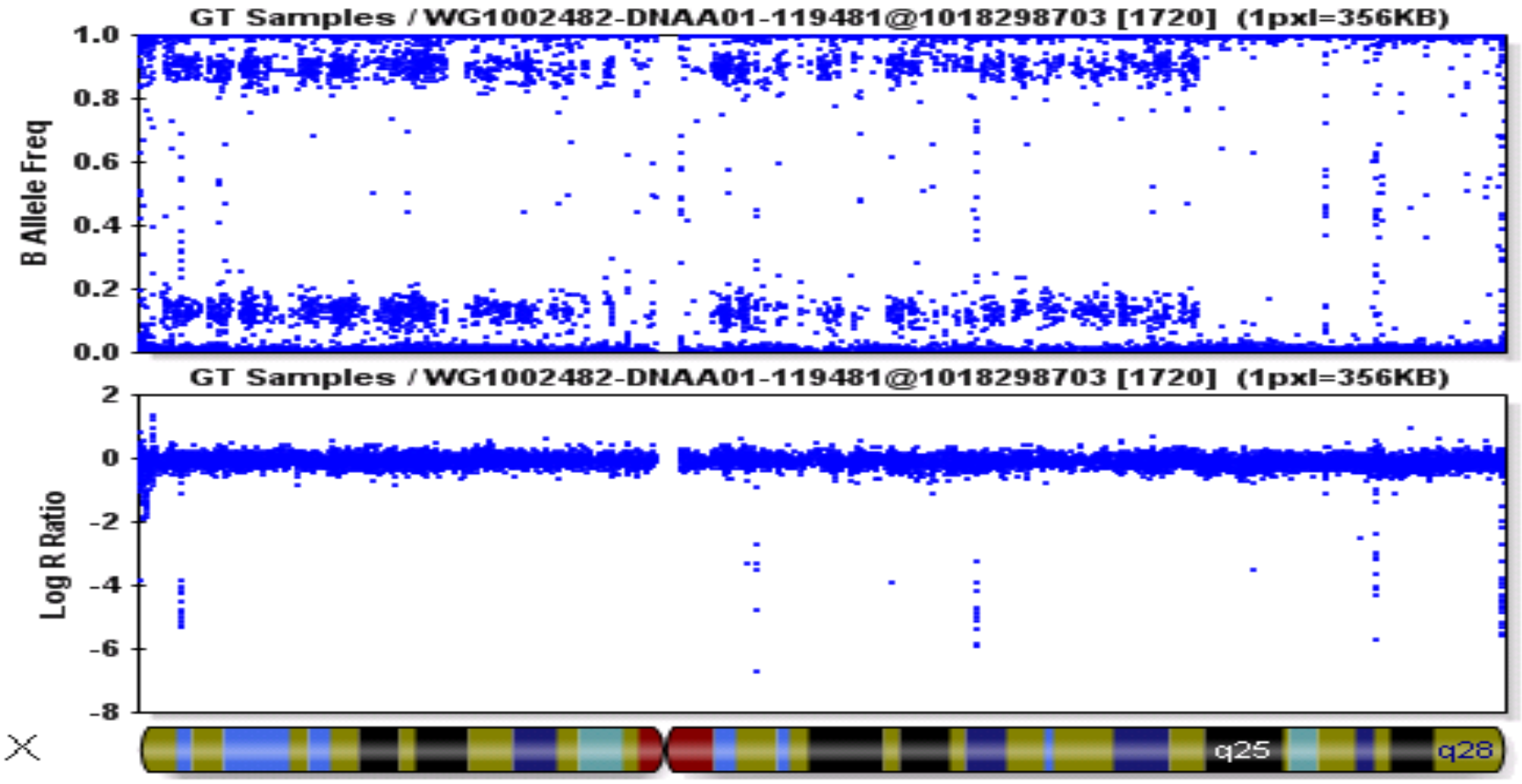
Sex Chromosome Anomalies



XXY

PENNSTATE
1855

Sex Chromosome Anomalies

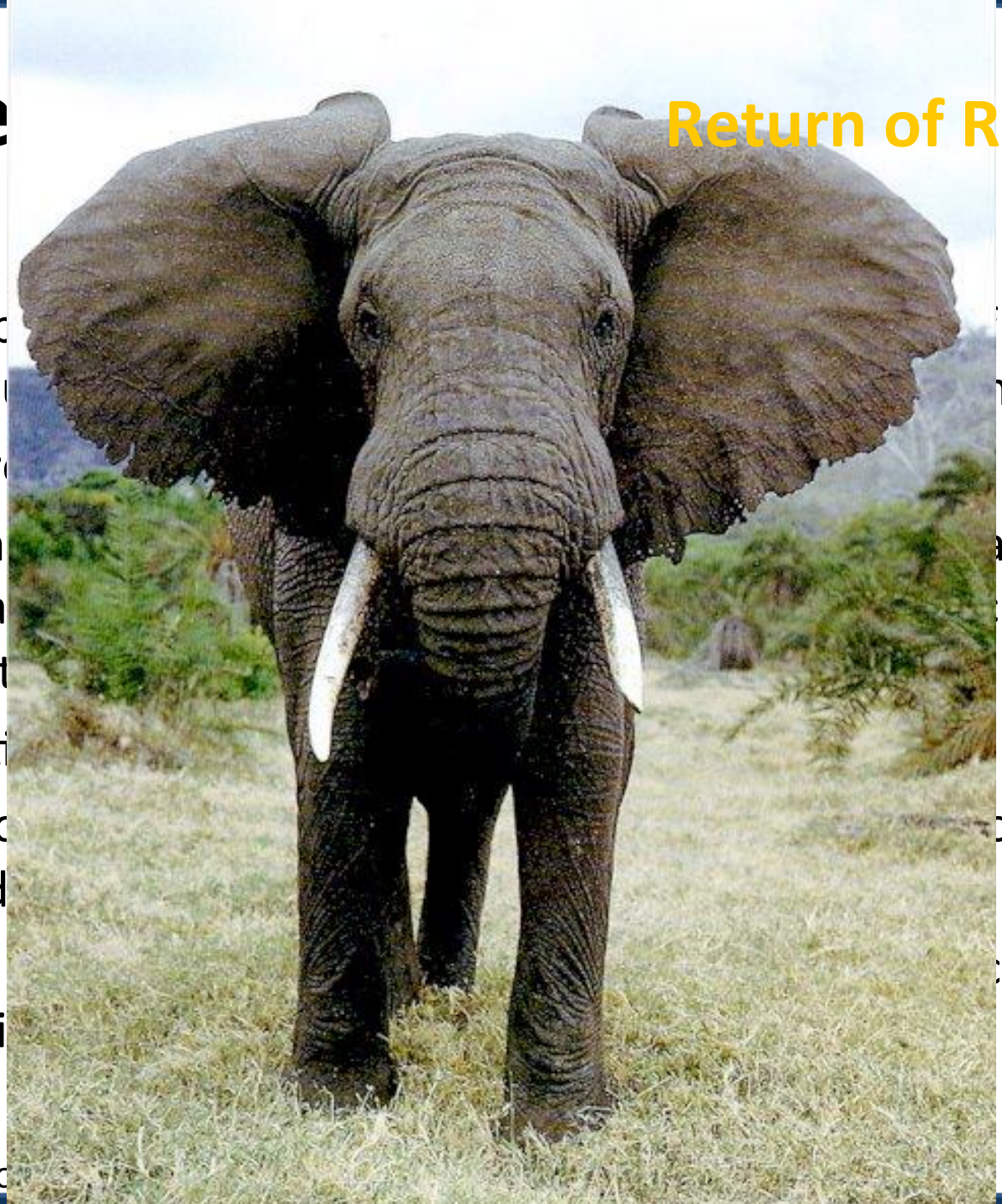


XX/XO mosaic

PENNSTATE

Incide

Return of Results



- Usual p
  individ
  ngs
- This pr
  - gen
    alth-
    rela
    ial to
    part
- Potenti
  - who
    cidental
    find
  - use
    e of
    defi

PENNSTATE

http://www.phgfc

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

PENNSTATE

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?

PENNSTATE

Courtesy of Ellen Clayton

Direct-to-Consumer GWAS

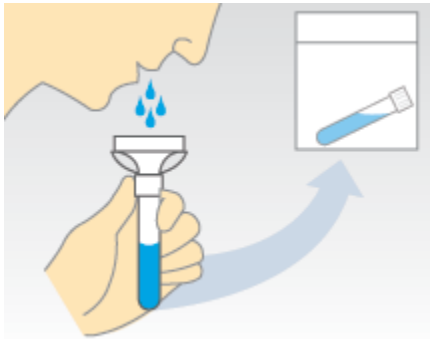
- Several companies are providing a GWAS service for interested customers
  - Affordable, easy

23andMe

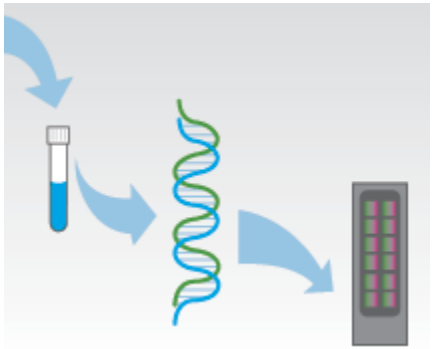
deCODEme

~~$985~~

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.

PENNSTATE
1855

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

PENNSTATE

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

PENNSTATE

DTC Whole Exome/Genome Sequencing Services Are Now Available

illumina

Life Sciences | Personal Sequencing | Diagnostics

everygenome

ABOUT US | GENOMES 101 | TEST PROCESS | GENOME RESOURCES | HEALTH PROFESSIONALS

Every genome tells a story. What's yours?

Access the bigger picture for your patients

Through comprehensive genetic sequence information.

- Individual genome sequencing: $19,500 per genome
- Medically indicated cases approved through the Illumina subsidy program: $9,500 per genome
- Groups of five individuals ordered through the same physician: $14,500 per genome

Reduced price for medically indicated cases is subsidized by Illumina. Eligibility is determined through submission of an Illumina Medical Review form and subsequent approval by the Illumina Medical Advisory Board.

Latest News | Events

- Next generation sequencing in a family with autosomal recessive Kahrizi syndrome (OMIM 612713) reveals a homozygous frameshift mutation in SRD5A3
- Wash U Study Highlights Power of Sequencing Patient Tumors in Breast Cancer Clinical Trial
- Faces of America: A look at identity and ancestry through genome sequencing - a New PBS Series film
- My Genomic Self - Steven Pinker published in The New York Times Magazine
- Will You Get Cancer? - Matthew Herper and Robert Langreth in Forbes
- A conversation about Personalized Medicine with Steven Pinker, Anne Wojcicki, George Church, and Linda Avey

Quick Links

- What is a genome and what kinds of information does it contain?
- How does Individual Genome Sequencing read your genetic story?
- How does the Individual Genome Sequencing process work?
- How can changes in your DNA impact your health?
- What are genetic diseases and how are they passed from one generation to the next?

Personal Genome Registry

- Have you already been sequenced? Register your genome here.

Contact Us

First Name: *

Last Name: *

Country: *

Email: *

Phone:

Reason for Inquiry: *

Where did you hear about our service? *

Comments:

SUBMIT

Media | Privacy Policy | Legal Notices | Visit Corporate Site | Site Map

Illumina ようこそイルミナ株式会社へ 中文网站

Please note:
Individual Genome Sequencing will be performed in Illumina's CLIA (Clinical Laboratory Improvements Amendment)-certified and CAP (College of American Pathologists)-accredited Clinical Services Laboratory's, under a valid and unexpired California Clinical Laboratory License. The Individual Genome Sequence information is generated by licensed personnel using an analytically validated process. Consistent with Lab Developed Tests, it has not been cleared or approved by the U.S. Food and Drug Administration.

This genome sequence information can be analyzed to potentially aid your doctor in the evaluation of a broad range of health conditions or physiological traits. You will not receive medical results, or a diagnosis, or a recommendation for treatment from Illumina. Any results arising from the analysis of your genome sequence information that might be deemed medically actionable should be confirmed using alternative testing. If you have any questions or concerns about what you learn through your genome sequence information, you should contact your doctor or a genetic counselor.

Currently Illumina does not accept orders for individual genome sequencing services from the following states: Florida, New York, and Rhode Island.

http://www.everygenome.com/

Knome

Sequencing services

For researchers that do not already have sequence data ready for interpretation, we also offer turn-key sequencing and interpretation services. Through our network of sequencing partners, we have the ability to meet a wide variety of turnaround time, coverage, regulatory, and budgetary requirements. Moreover, because sequencing and reference data come in many complicated and potentially confusing formats, our experience in managing raw sequencing output from disparate sources can prove crucial to the success of your project.

Sample preparation and/or collection. We are experienced in coordinating sample preparation, DNA extraction, and validation from blood, tumors, and other tissues.

Whole-genome and exome sequencing. We can arrange the most appropriate scale (whole genome or exome) and mean depth of sequencing for your project. For exome projects, we offer advanced solid or liquid exome capture methods to deliver reliable data—even from challenging DNA sources such as formalin-fixed, paraffin-embedded tissue.

All coverage depths. Depending on project requirements and budgets, we provide mean coverage depth of between 5x to 100x or more via any of the leading short-read methods. All sequencing conforms to standard human subjects ethical protocols. In addition, CLIA-certified sequencing is available.

http://www.knome.com/

Questions???

PENNSTATE
1855