

Purpose of Workshop Background Planning Process for Future Initiatives

From Genome Function to Biomedical Insight:
ENCODE and Beyond

March 10-11, 2015



National Human Genome
Research Institute

Purpose of Workshop

- Current phase of the ENCODE project ending in 2016
- Purpose of workshop is to obtain community input on future scientific areas NHGRI should support in the area of functional genomics that build on the success of the ENCODE project

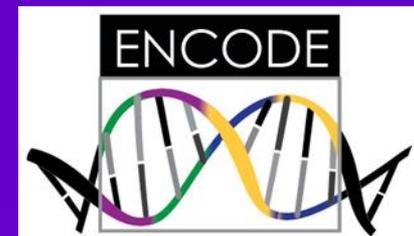
Functional Genomics Is Central To Realizing NHGRI's Goals

Non-coding DNA is important for disease and gene regulation

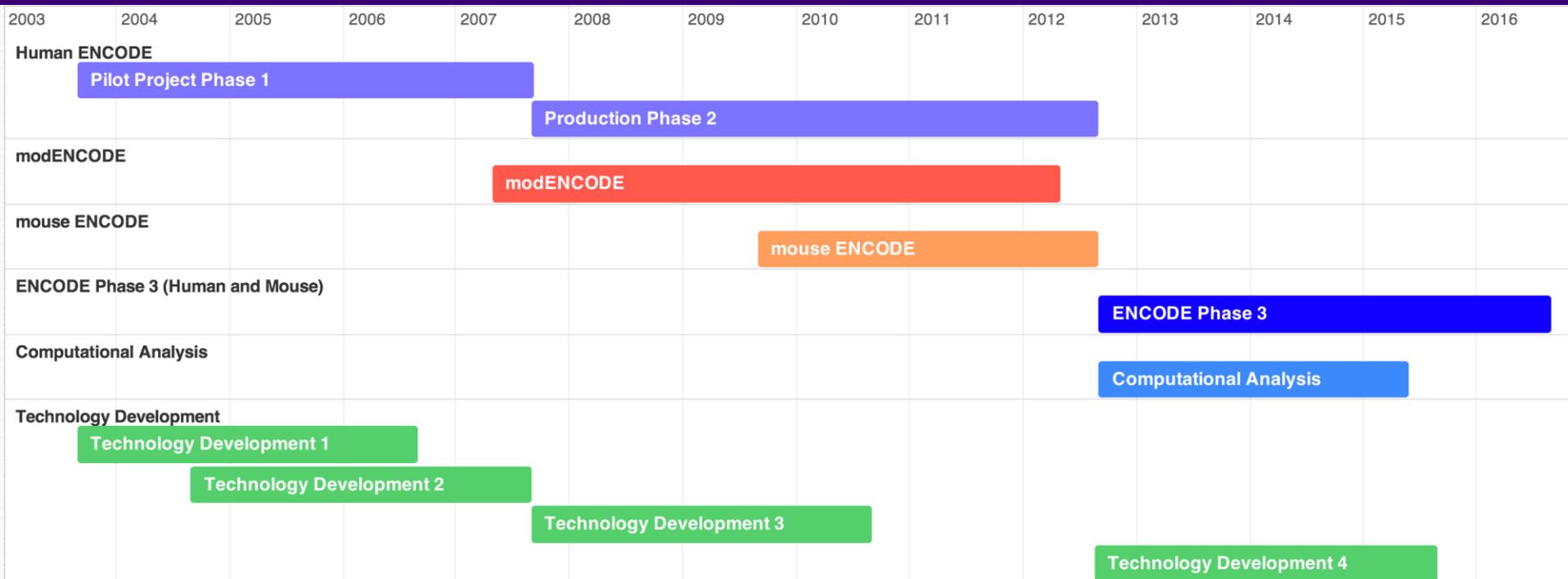
- About 90% of GWAS findings lie outside of protein-coding regions
 - Non-coding DNA variants are known to cause human diseases and alter human traits
 - About 80% of recent adaptation signatures lie outside of protein-coding regions
- **Comprehensive functional information about the human genome is needed for the interpretation of genomes, understanding genetic variation and applying genomics to the clinic.**

ENCODE: Encyclopedia of DNA Elements

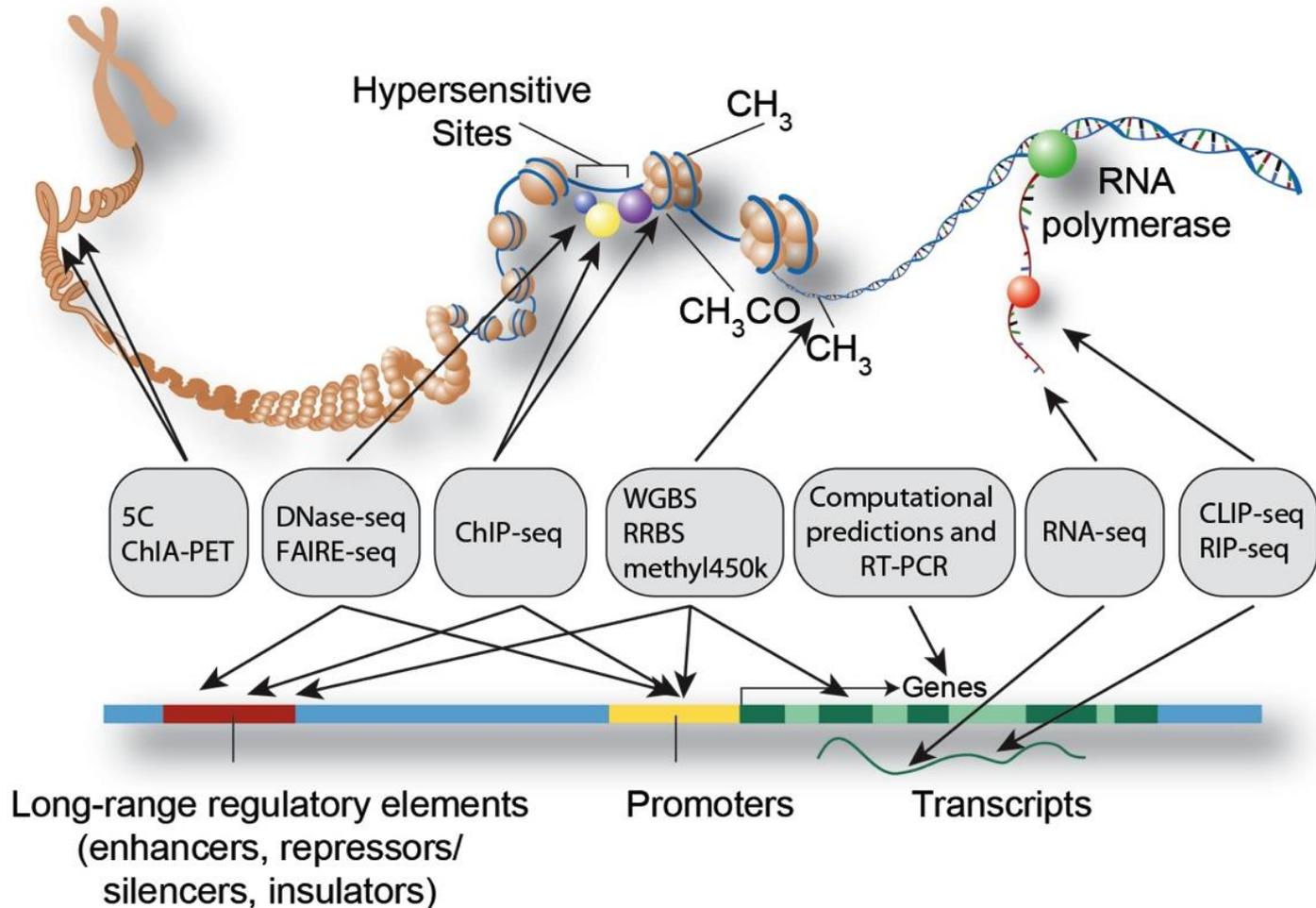
- Compile a comprehensive encyclopedia of all sequence features in the human genome and in the genomes of select model organisms
- Make resource freely available to community to enhance understanding of:
 - regulation of gene expression
 - genetic basis of disease



ENCODE Timeline

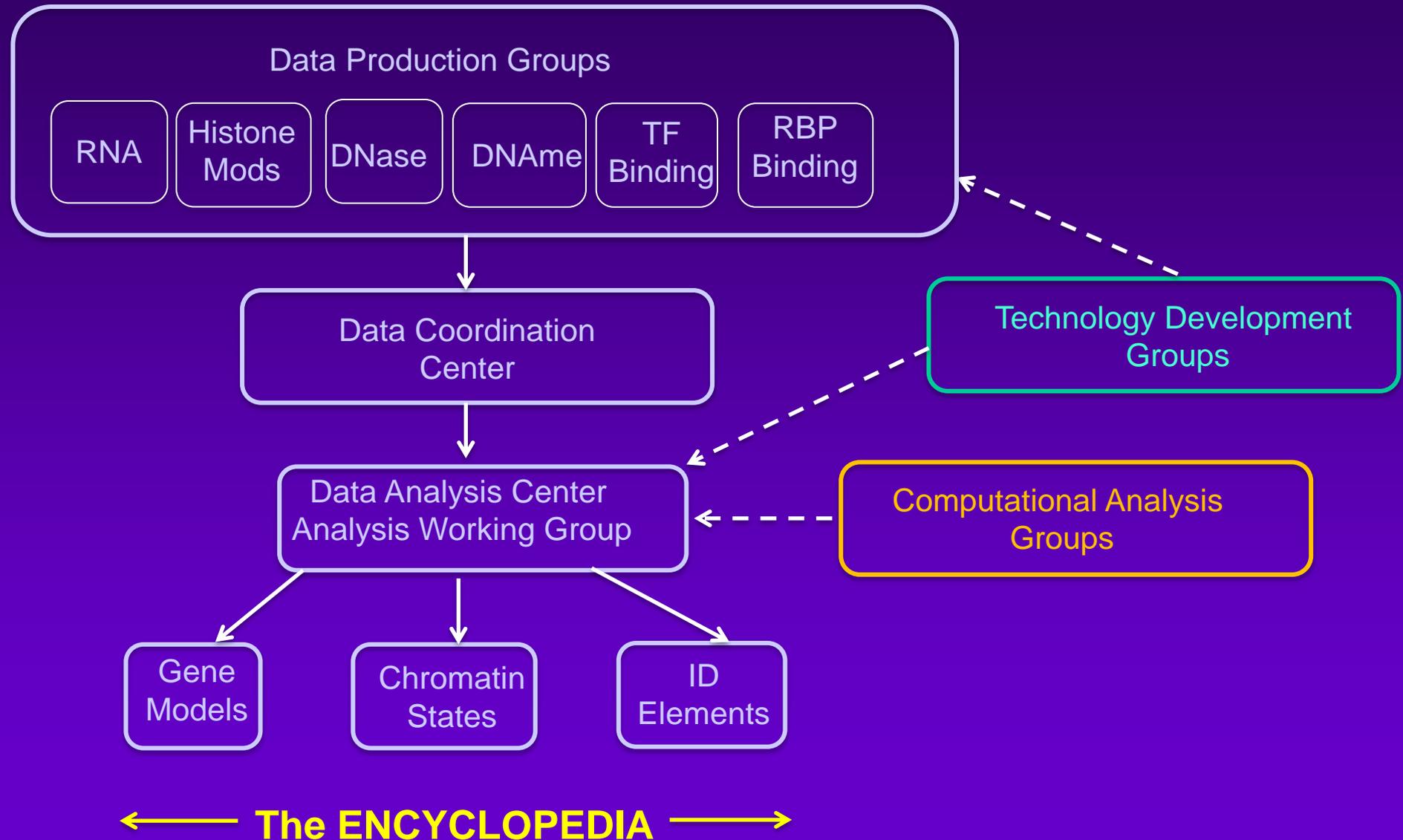


ENCODE Data Types



Modified from PLoS Biol 9:e1001046, 2011
Science 306:636, 2004

ENCODE 3 Structure



Consortium Features

- Highly collaborative and synergistic effort
- Mix of investigator-initiated and “top-down” directed projects
- Focused management and coordination
- Quantitative milestones for data production
- Generation of high quality data
- Use cost-effective, high-throughput methods that takes advantage of economies of scale
- Focus on resource generation for community
- Develops data standards and common data formats, and uses common cell types
 - Facilitates data integration and analysis
 - Provides transparency about data, experiments, data quality

ENCODE Accomplishments

- Rapid, pre-publication release of thousands of experiments
 - Well-documented, high quality
 - Uniformly processed data; processing pipelines available on cloud
- Development and dissemination of analysis tools
- Data Interoperability
- Updated informed consent language for open access to genomic data
- Consortium publications
- Data used by research community in over 750 publications, including disease studies to help identify causal variants

Functional Genomics Projects

- NHGRI
 - ENCODE
 - Genomics of Gene Regulation (GGR)
 - FunVar
- NIH Common Fund
 - Epigenomics
 - Genotype-Tissue Expression (GTEx)
 - Knock-out mouse project (KOMP)
- International Projects
 - International Human Epigenomics Consortium

Workshop Objectives

1. Discuss the scientific questions and opportunities for better understanding genome function and applying that knowledge to basic biological questions and disease studies through large-scale genomics efforts.
2. Consider options for future NHGRI projects that would address these questions and opportunities.

Discussion Considerations

- Main areas for discussion:
 - Continued data generation
 - Enabling basic biology and disease studies
 - Technology development
- Bold new ideas that NHGRI can catalyze
- Seeking general guidance, not too specific so as to not create conflicts for participants with potential funding opportunities
- Projects appropriate for NHGRI vs. other NIH Institutes, other U.S. and international funding agencies
 - Opportunities for collaboration

NHGRI-focused efforts

- Resource generation and dissemination
- Technology development
- Implementation of new genomics technologies and approaches
- Research consortia when high level of coordination and staff involvement appropriate
 - Multiple models of varying degree of coordination and management
- Investigator-initiated research

Agenda

- Introductory talks to set the stage:
 - From Genome Function to Biomedical Insight: Defining the Scientific Challenges
 - Genome Function Circa 2016: Updates from Related Projects
 - Proposals for Future Directions
 - ENCODE PI Vision for Functional Genomics
 - Recommendations for “Integrating Genomic Variant Discovery with Genome Function” from NHGRI Planning Workshop on the Future of Sequencing

Agenda

- Topic #1: Identifying and characterizing functional elements
- Topic #2: Using genomic assays of function to interpret the role of genetic variants in disease
- Topic #3: Using genomic assays of function to study basic biological questions

Topics 1-3 Discussion Questions

1. What types of projects should NHGRI consider funding and what gap in knowledge will they address?
2. What systems would be appropriate for study?
3. How many projects (and at what scale) would be needed in order to obtain a sense of the generalizability of the approach(es)?
4. What is the utility of generating new data using methods employed in ENCODE) vs. exploiting newer/different methods.
 - a. What would be required to make the new findings interoperable with previous ENCODE findings? How important is this consideration for this topic?

Topics 1-3 Discussion Questions (con't)

5. What are the infrastructure needs, e.g., databases/data portals, experimental standards, computational tools?
6. What organizational structure(s) may best support the proposed efforts?
7. What opportunities exist for synergies/coordination with other programs, partnership with other entities, e.g., other ICs – for both biology and disease studies?
8. What is an appropriate scale and estimated budget required to accomplish goals?

Overall discussion

- Cross-cutting ideas
- Priorities
- Balance of activities

Next steps

- Current phase of ENCODE ends in 2016
- Planning process in 2015
 - Planning Workshop
 - Concept Clearance(s) reviewed at May 2015 National Advisory Council for Human Genome Research Meeting
 - Potential FOA(s) to be released Summer 2015
- Review and Funding 2016

Many Thanks!

Organizing Committee:

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Carol Bult

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Capital Consulting Corporation:

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The ENCODE 3 Consortium



<http://www.genome.gov/26525220>

ENCODE

External Consultants Panel



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NHGRI Staff

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Hannah Naughton

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Division Director

Jeff Schloss



Housekeeping Items

- Webcasting workshop: please use mics!
- Googledoc for meeting notes
- Capital Consulting Corporation (CCC) staff on site
- Boxed dinners delivered late this afternoon
- If not ordered, can purchase snacks at café upstairs during coffee break
- Shuttles to hotel:
 - Tonight at 9 p.m.
 - Tomorrow at 7 a.m. to get through security
- Transportation to airport
 - Recommend arranging through hotel -OR-
 - See CCC staff before lunchtime tomorrow to sign up
- Send reimbursement vouchers to CCC by end of March

ENCODE Publications

