

The NIH Roadmap Epigenomics Program



Kim McAllister
mcallis2@niehs.nih.gov
Program Administrator
Genes and Environment Health Branch
National Institute of Environmental Health Sciences

Epigenomic Changes Implicated in Many Human Diseases

Normal processes

Development
Cell differentiation
Aging



GENOME

EPIGENOME

DISEASE

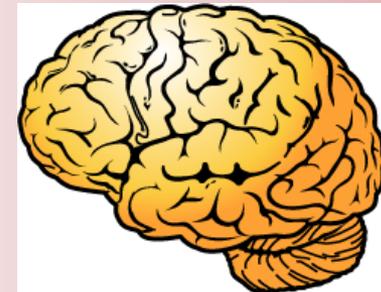


External influences

Environmental exposures
Nutrition
Chemical toxins
Metals
Mediators of stress
Infection (including HIV)
Drugs of abuse

Adverse health outcomes

Cancer
Cardiopulmonary disease
Autoimmune disease
Obesity
Diabetes
AIDS



Neurodevelopmental disorders
Schizophrenia
Depression
Alzheimer's Disease
Addiction

NIH Roadmap Epigenomics Program



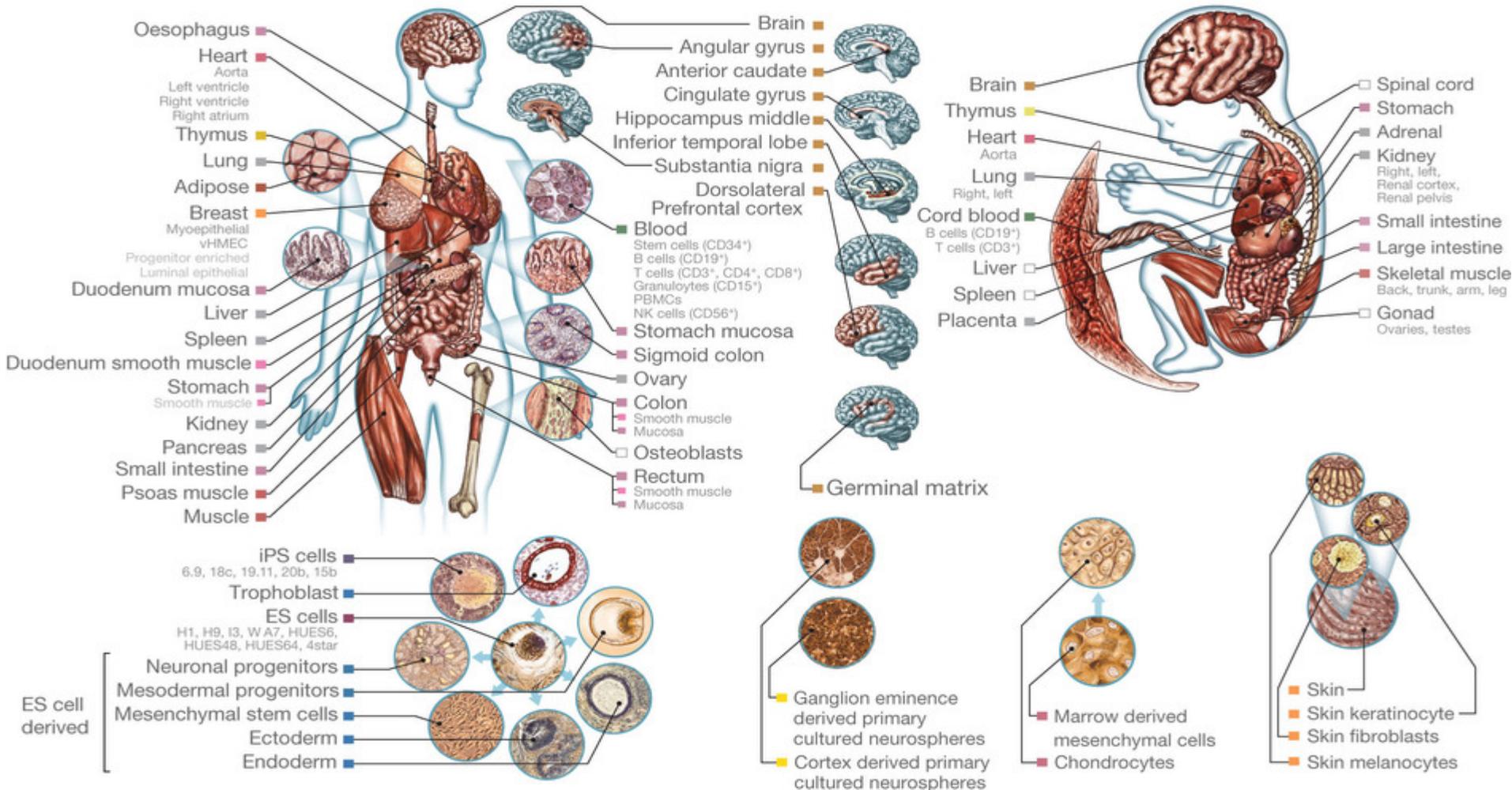
Roadmap Epigenomics Program

- Epigenomics of Human Health and Disease
- Technology Development in Epigenetics
- Discovery of Novel Epigenetic Marks
- Computational analyses of Reference Epigenomic data
- Functional Epigenomics (epigenomic manipulation)
- Technology Development - *in vivo* epigenetic imaging

The Reference Epigenome Mapping Consortium:

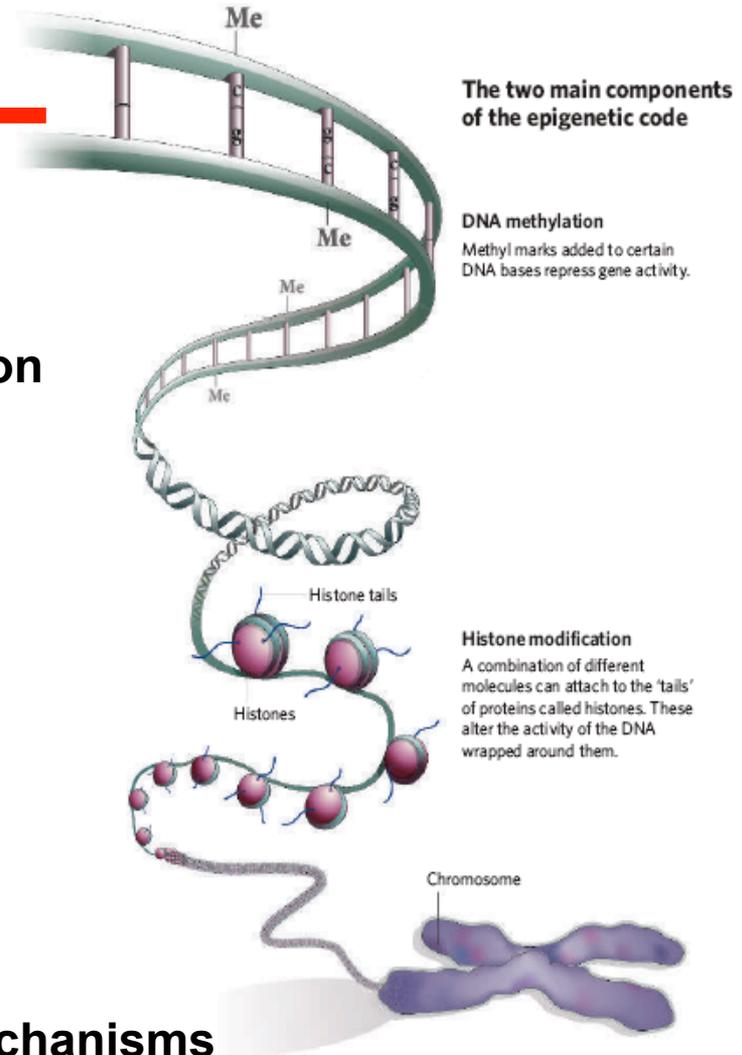
- Reference Epigenome Mapping Centers
 - Brad Bernstein & Alex Meissner* (Broad)
 - Joe Costello* (UCSF)
 - Bing Ren* (UCSD)
 - John Stamatoyannopoulos* (Washington)
- Epigenomics Data Analysis and Coordination Center
 - Aleks Milosavljevic* (Baylor)

Broad and deep mapping of epigenetic profiles in over 100 human primary cells and tissues



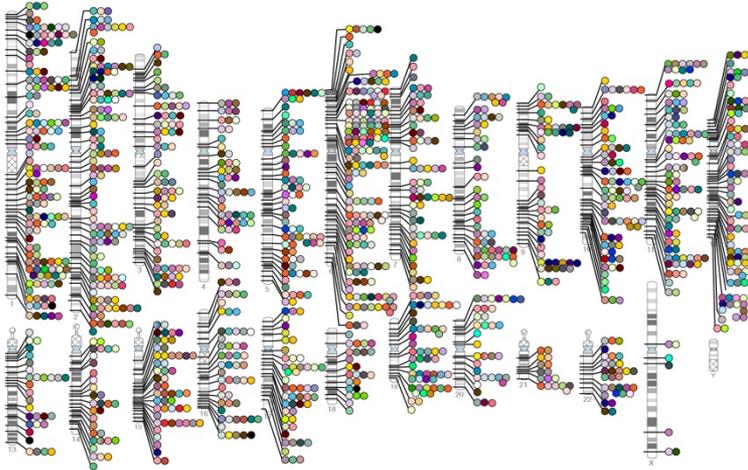
The Utility of Epigenomic Information

- **Marking of functional genomic elements** ←
- Environmental exposures
- Understanding development and differentiation
- Regenerative medicine (stem and iPS cells)
- Human disease
- **Interpreting GWAS** ←
- Biomarkers, diagnostics and therapies
- Exploring cross-talk between epigenomic mechanisms



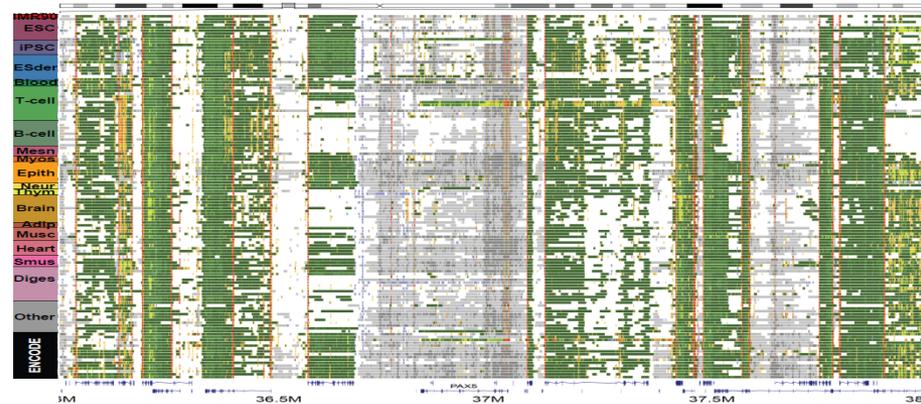
Using Epigenomic Data to Interpret GWAS Data

Gene variants in human disease



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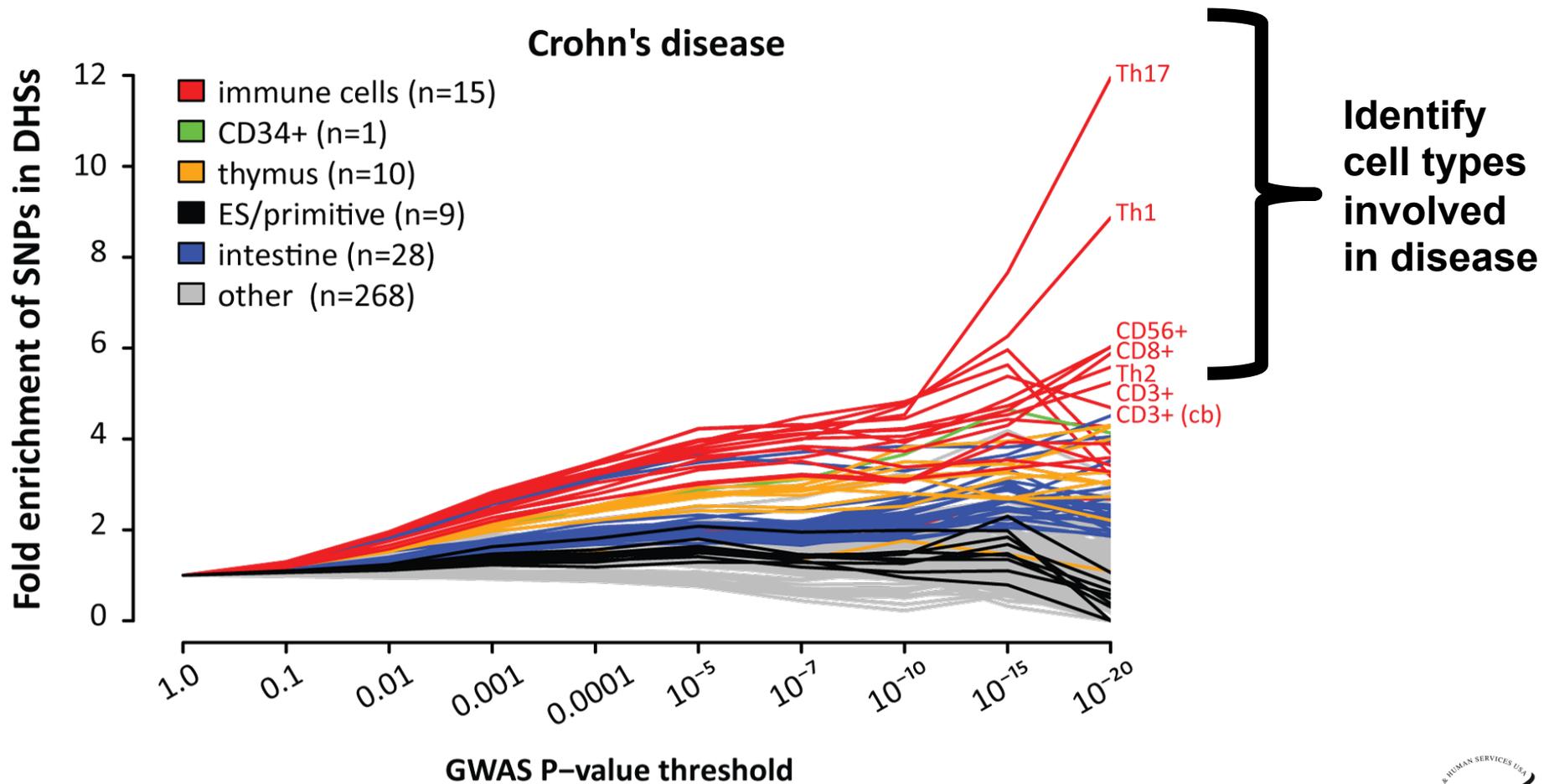
Epigenomic data for many normal human cell/tissue types



- 77% of disease variants are in/near enhancer elements or promoters*
- Variants are in regulatory regions NOT protein coding regions
- Generate hypotheses about function

*DNase I hypersensitive sites

Use Epigenomic Information for “Normal” Cells/Tissues to Identify Pathogenic Cell Types



Recent Roadmap Epigenomics Program Publications



Feb 19, 2015

8 publications in Nature

- Integrative analysis 111 reference epigenomes
- Haplotypes
- 3D structure
- Autoimmune disease
- Neuronal differentiation
- Cancer cells of origin

15 additional publications, Nature-associated journals

- Alzheimer's disease
- Epigenomic imputation
- Colon cancer
- Sexual dimorphism and fetal growth
- Stem cells
- Age-related epigenomic variation
- Breast cell epigenomes
- Roadmap Epigenome Browser
- Asthma susceptibility