

The NIH Roadmap Epigenomics Program: Sequencing Human Epigenomes from Head to Toe

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Funded by
NIH Common Fund

NIH Roadmap Epigenomics Program

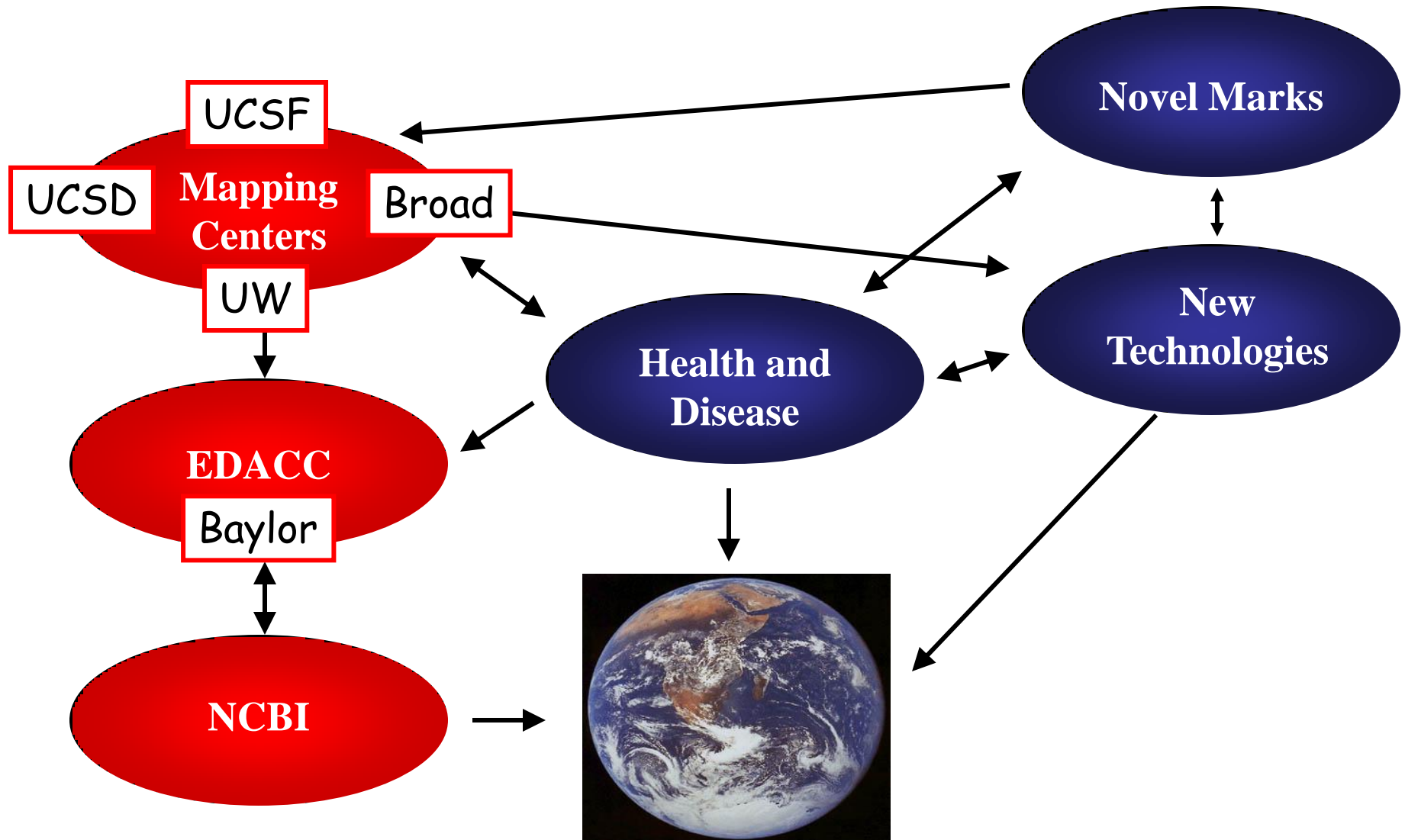
Program Goal:

Understand how epigenetic mechanisms contribute to disease

NIEHS: Lisa Chadwick, Fred Tyson

NIDA: Joni Rutter, John Satterlee

NIH Roadmap Epigenomics Program



Reference Epigenome Mapping Centers

Goal:

Create high quality epigenome maps of
human cells and tissues

Matching maps to diseases

Reference Map ←·····→ **Complex Disease**

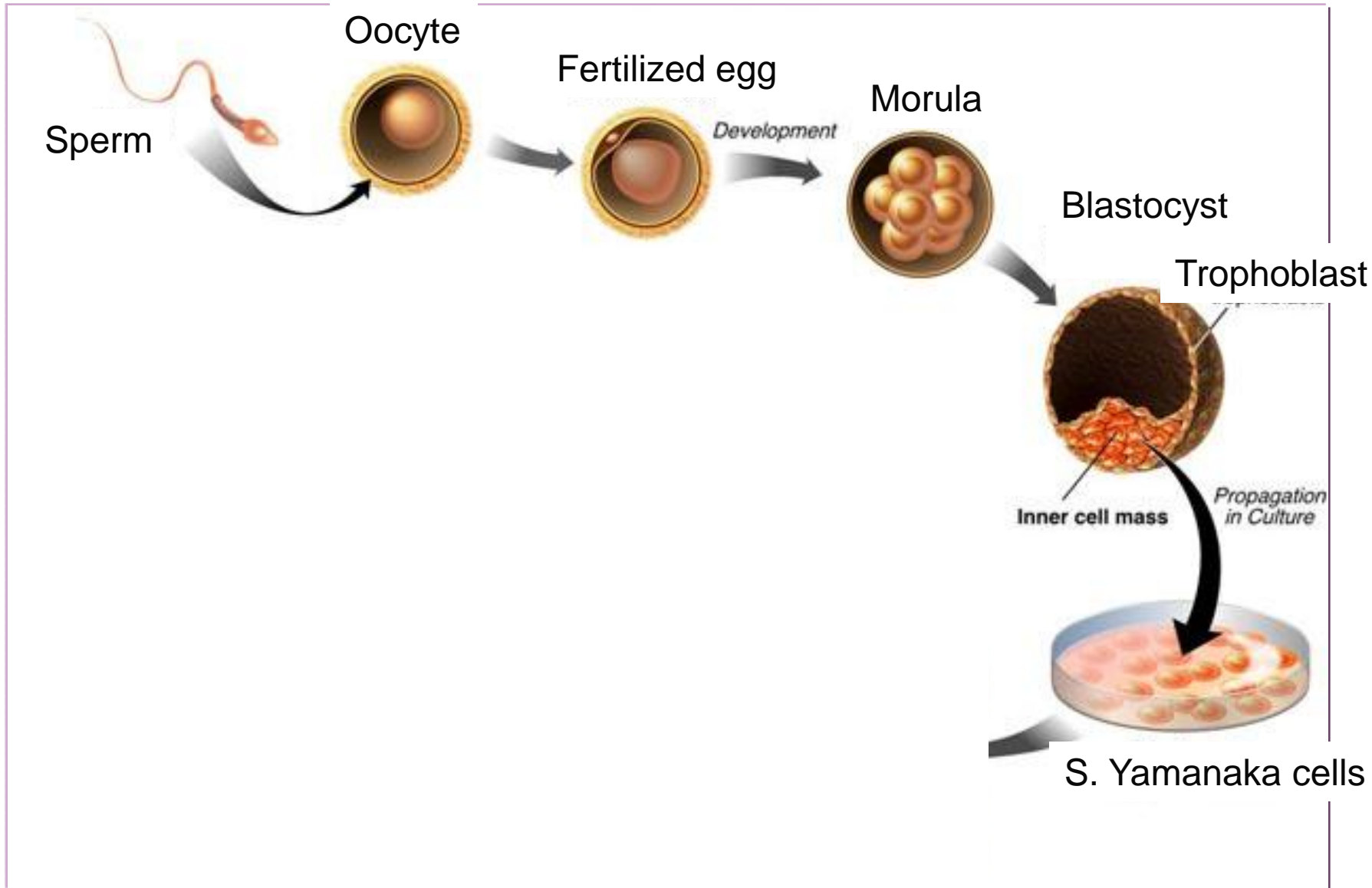
Immune system
Airway cells
Monocytes
Breast
Muscle, smooth, skeletal
Pancreatic islets, Adipocytes
Liver
Brain regions
Neural progenitors

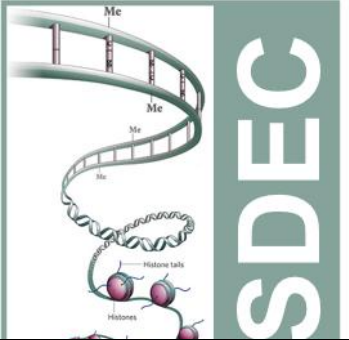
Asthma
Autoimmune disease
Atherosclerosis
Breast Cancer
Cardiopulmonary disease
Diabetes, Obesity
Schizophrenia
Autism
Dementia

Human Epigenome Assays

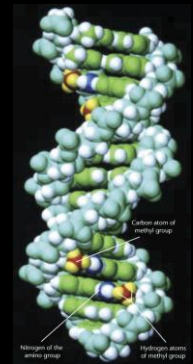
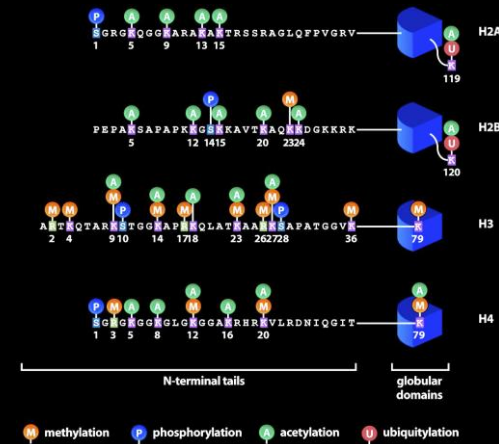
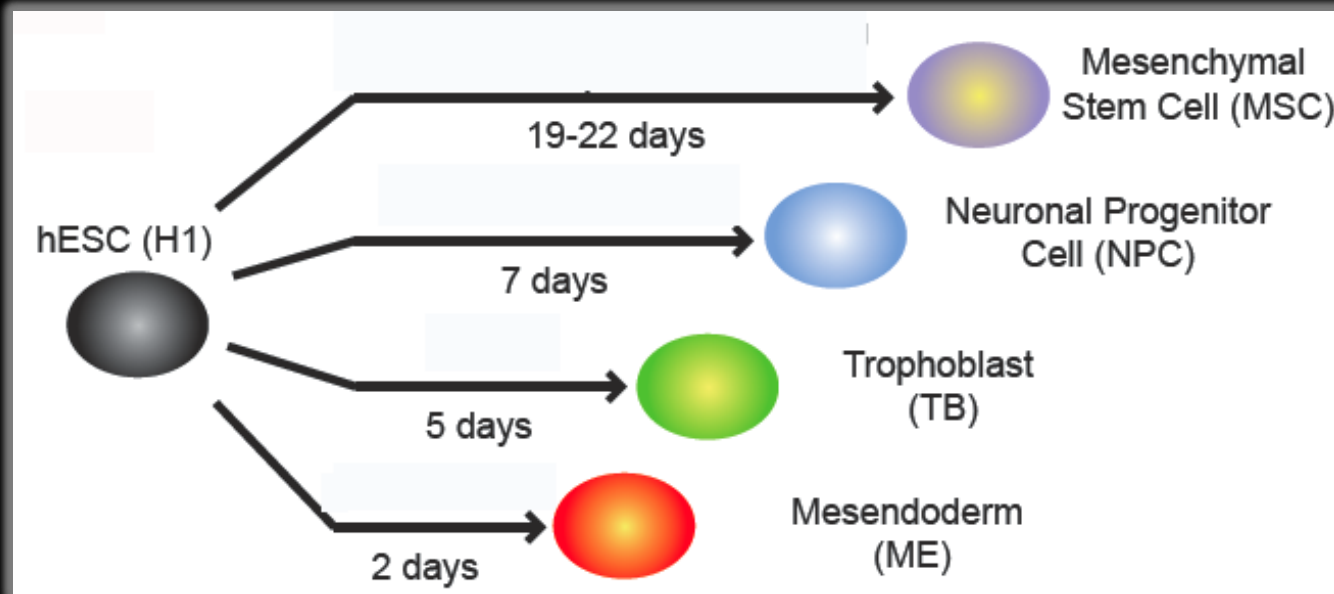
- DNA methylation (shotgun bisulfite, RRBS, MeDIP/MRE)
 - Histone modifications (H3K4me1, H3K4me3, H3K9me3, H3K27me3, H3K36me3, H3K27Ac*)
 - Chromatin accessibility (DNase-seq, ATAC-seq)
 - RNA by ssRNA-seq
 - miRNA by miRNA-seq
- Status on November 8, 2012:
334 Tissues/Cell types
2092 Epigenome/Transcriptome assays

Sequencing Epigenomes from Head to Toe





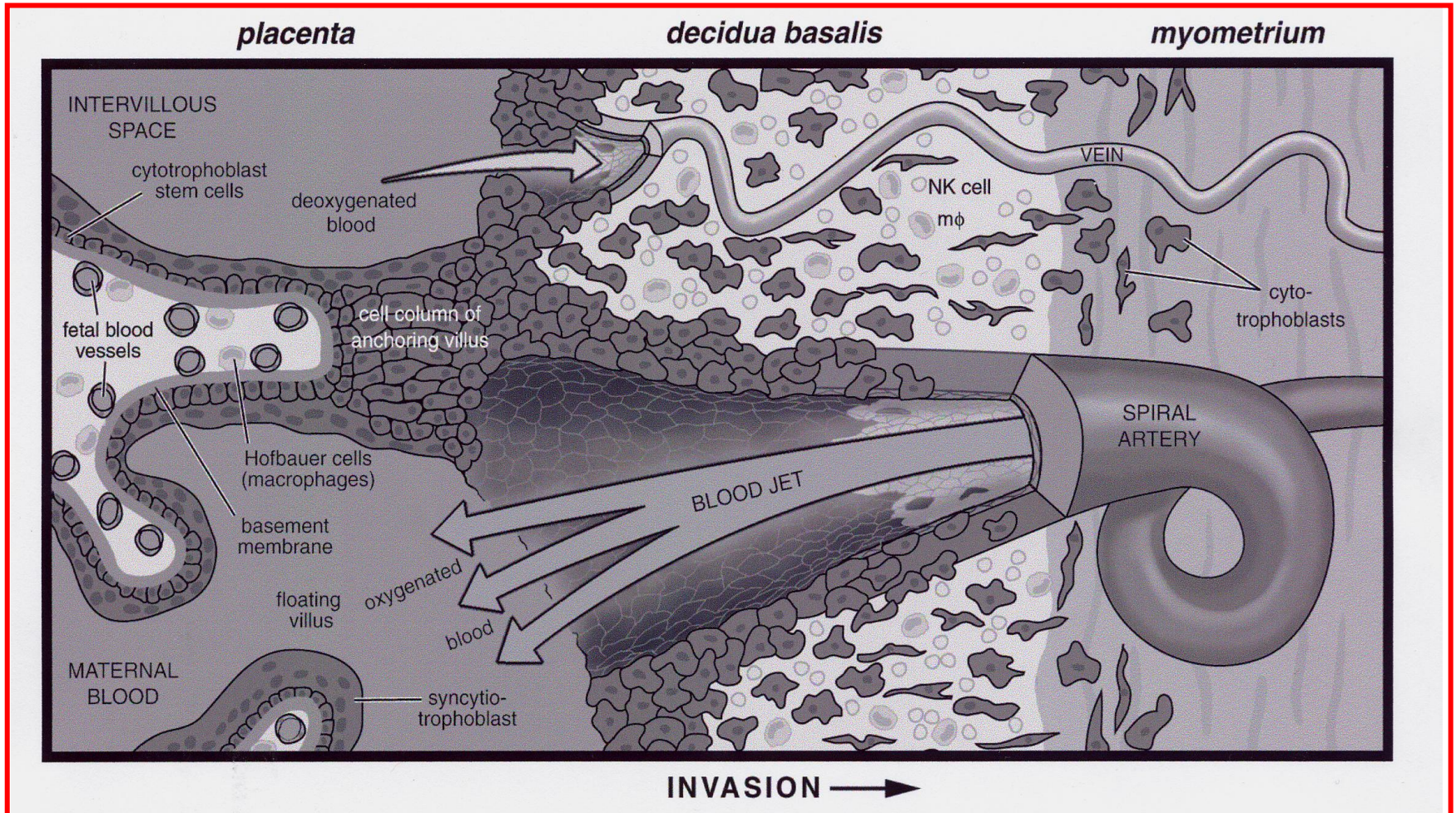
Epigenomic analysis of multi-lineage differentiation of hESCs



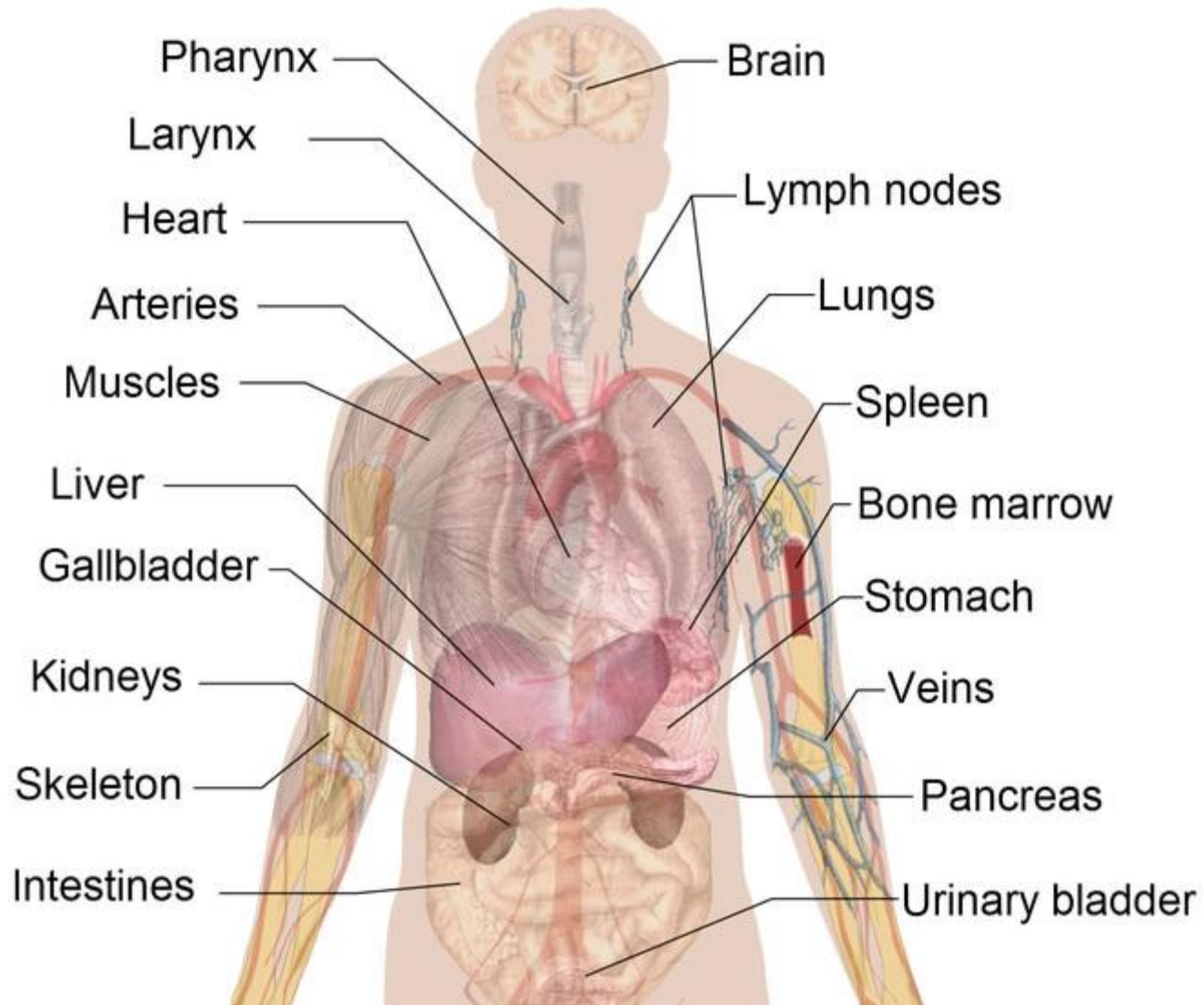
Mapping of DNA methylation and ~24 histone modifications in human ES cells and ES cell derived cell lineages. ES cells grown and differentiated by James Thomson lab, ChIP-Seq performed by Ren lab and Methylation analysis performed by Joe Ecker lab. All data released at SRA - SRP000941.

Placenta

Maps of two developmental time points, 3 tissue regions, 3 tissue regions, one purified cell type

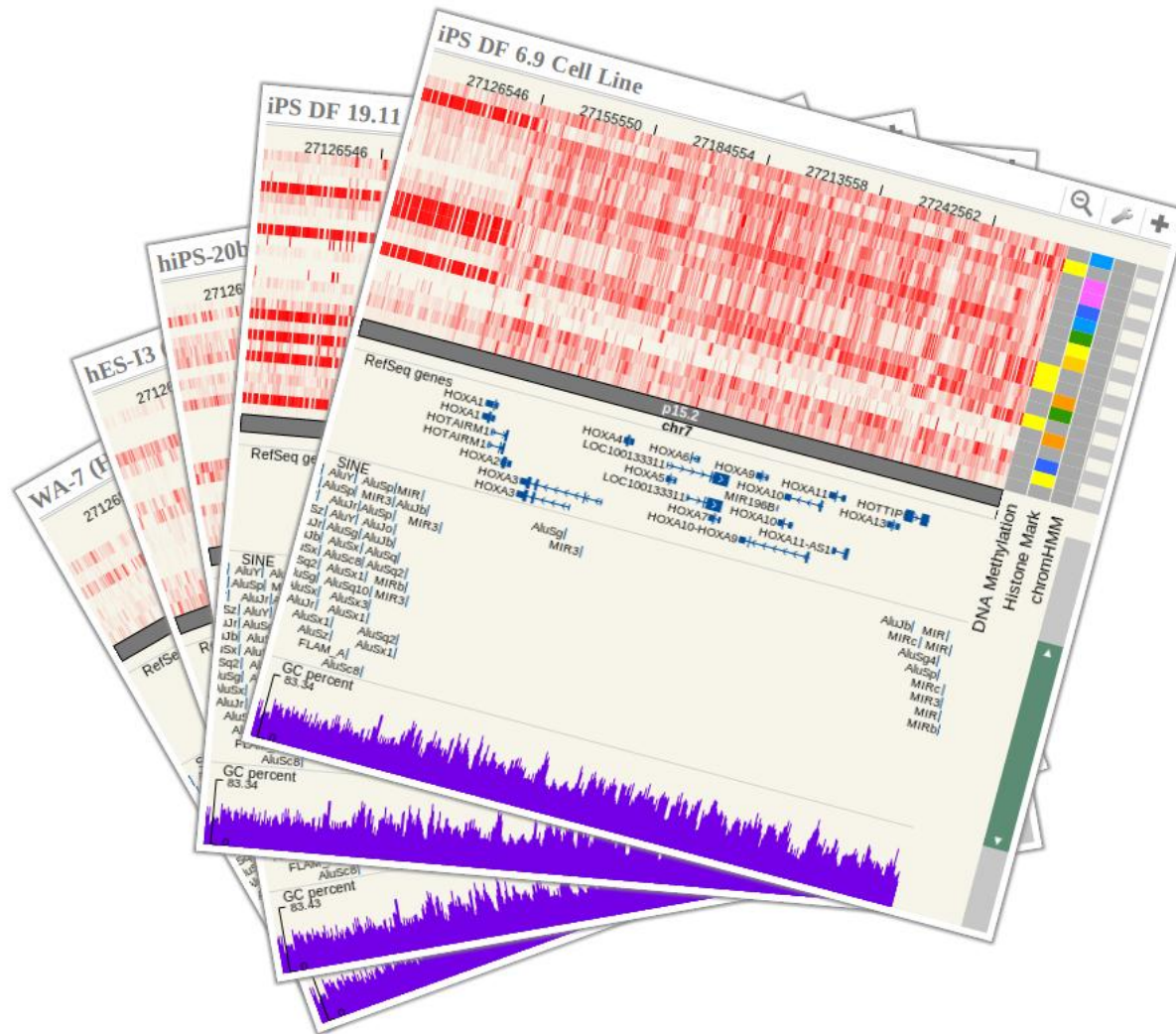


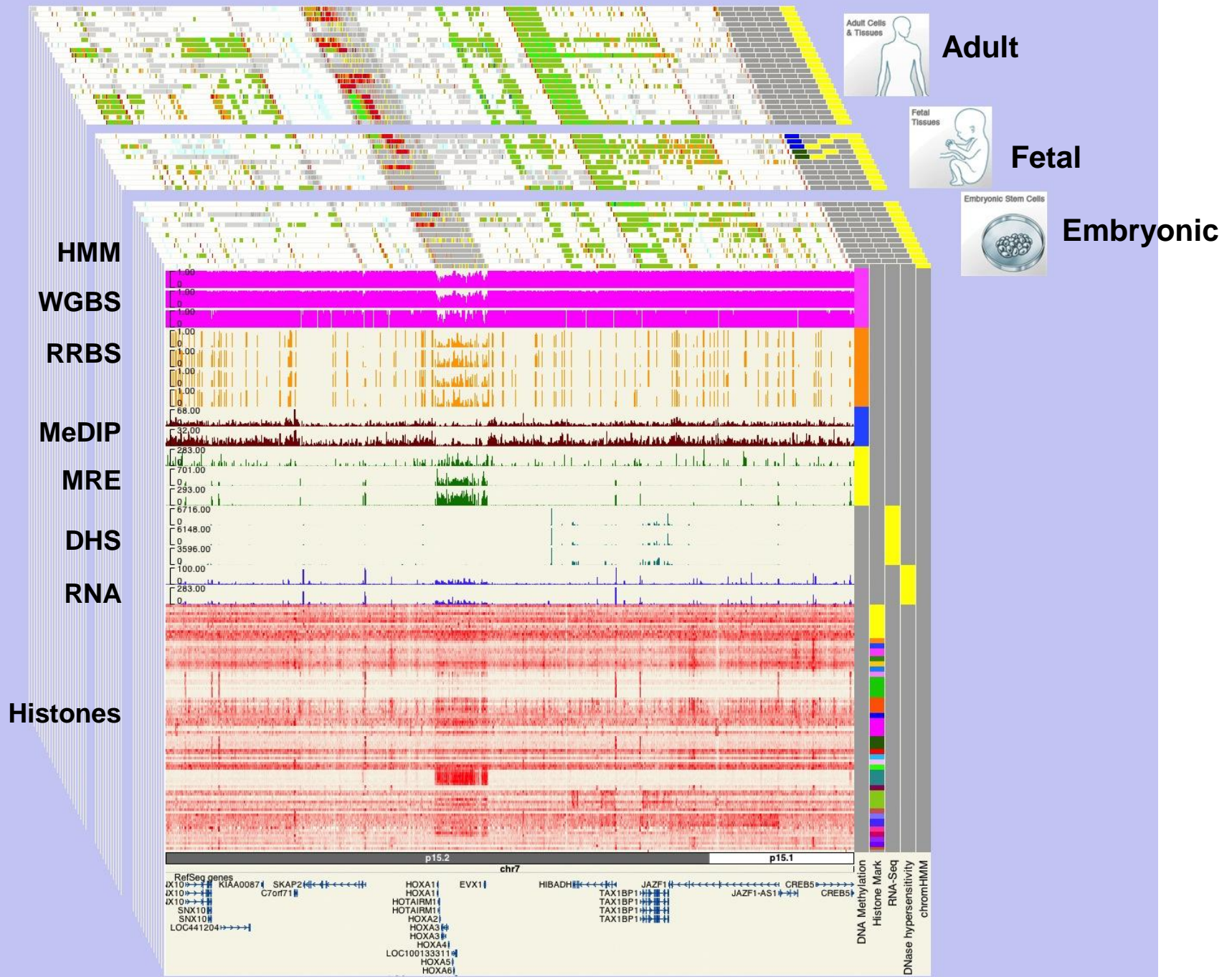
One Genome, Many Epigenomes



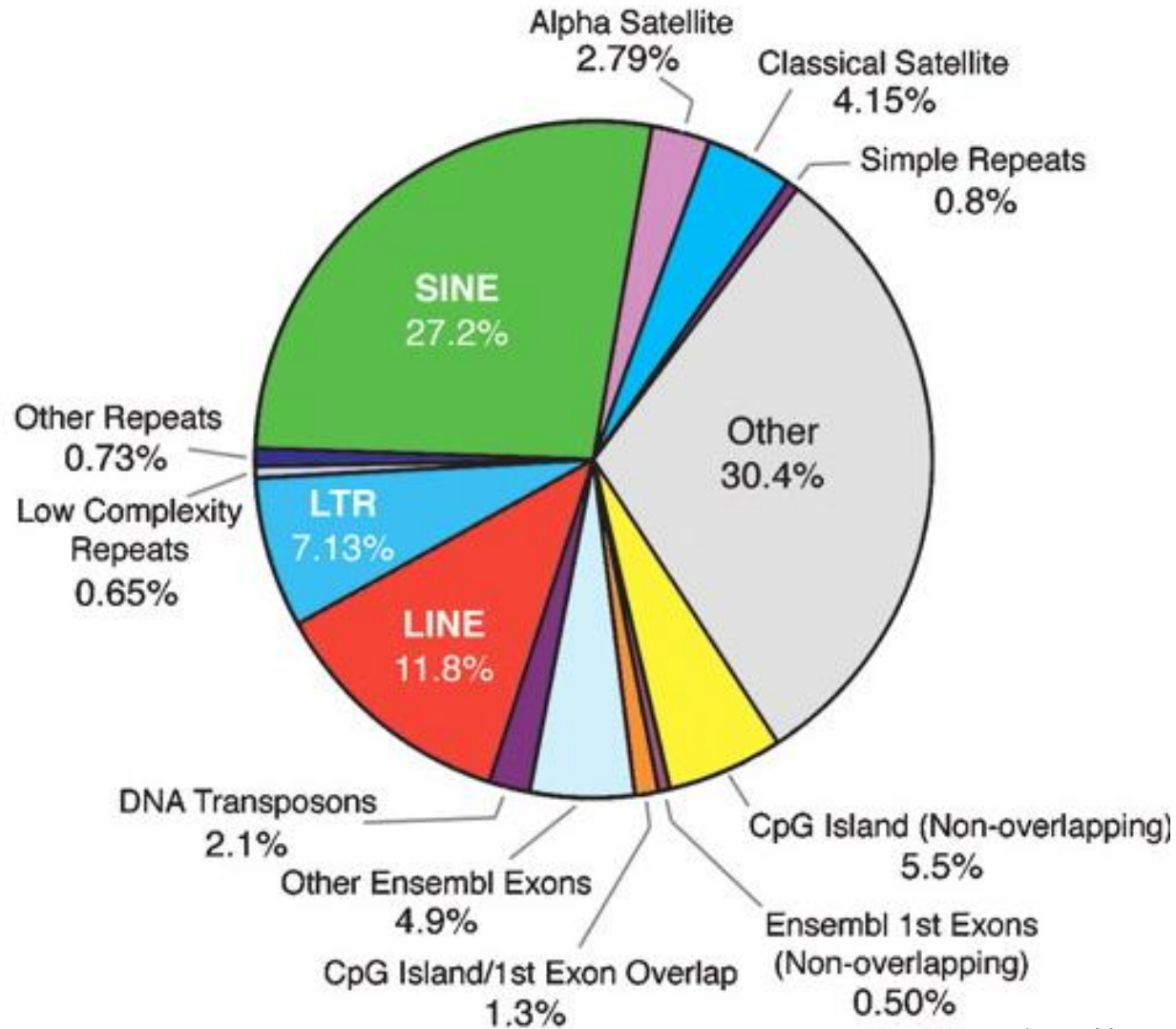
Navigating Complete Epigenomes

<http://epigenomegateway.wustl.edu/browser/roadmap/>



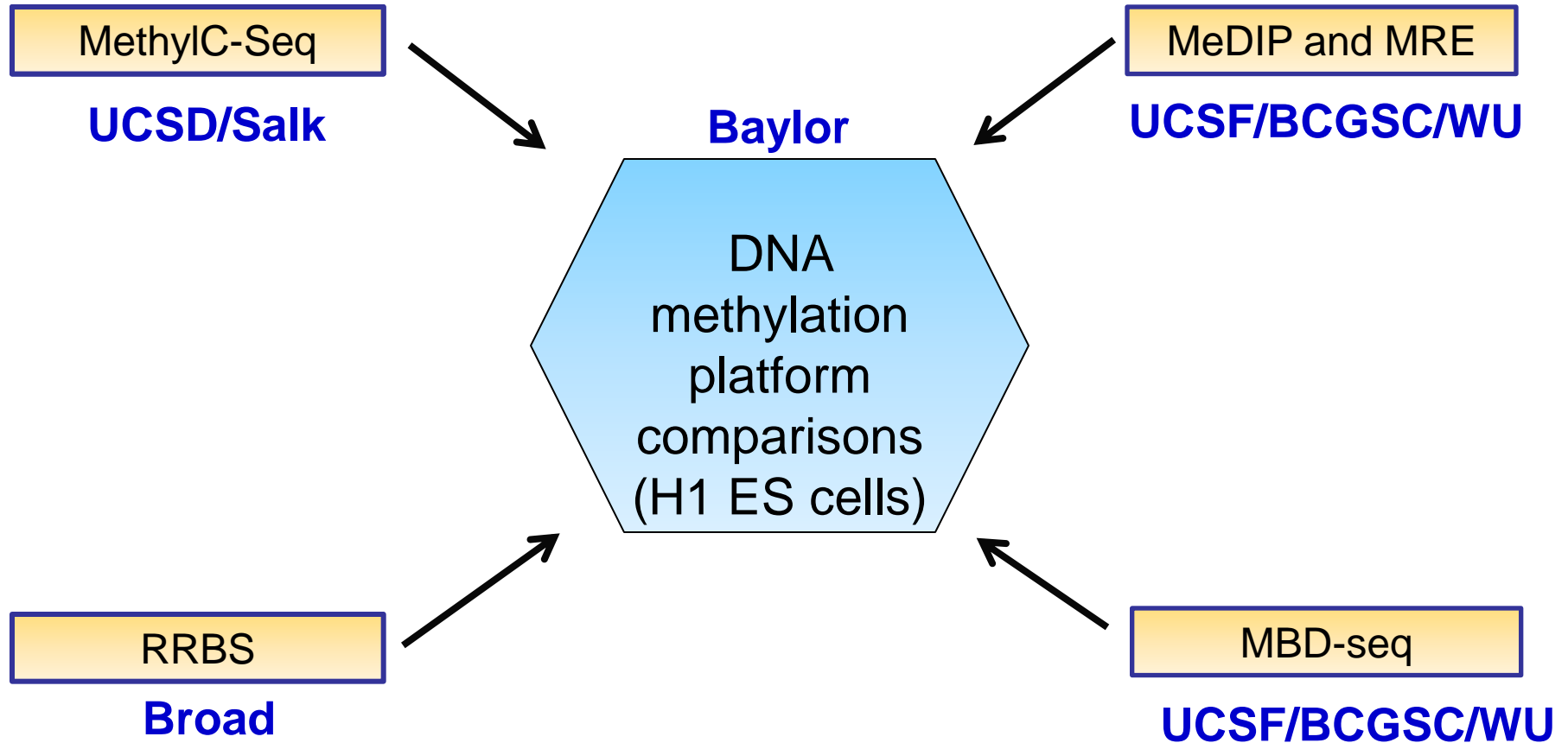


The DNA Methylome: 28,848,753 CpG sites

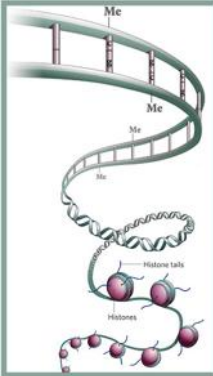


(Rollins et al, 2006)

Comparison of Sequencing-based DNA Methylation Methods



Harris et al, NIH Roadmap Epigenome Consortium,
Nature Biotechnology, Oct 2010; Bock et al, 2010

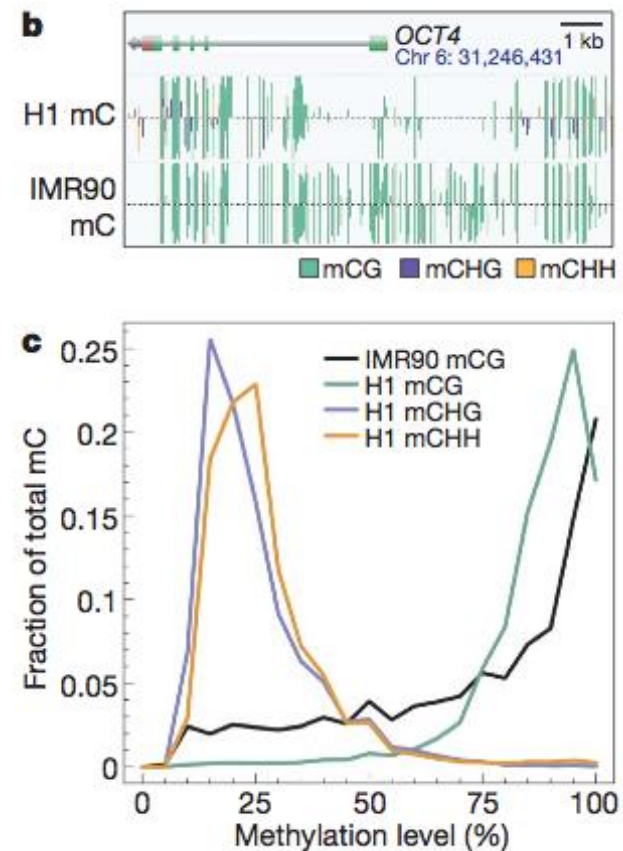


SDEC

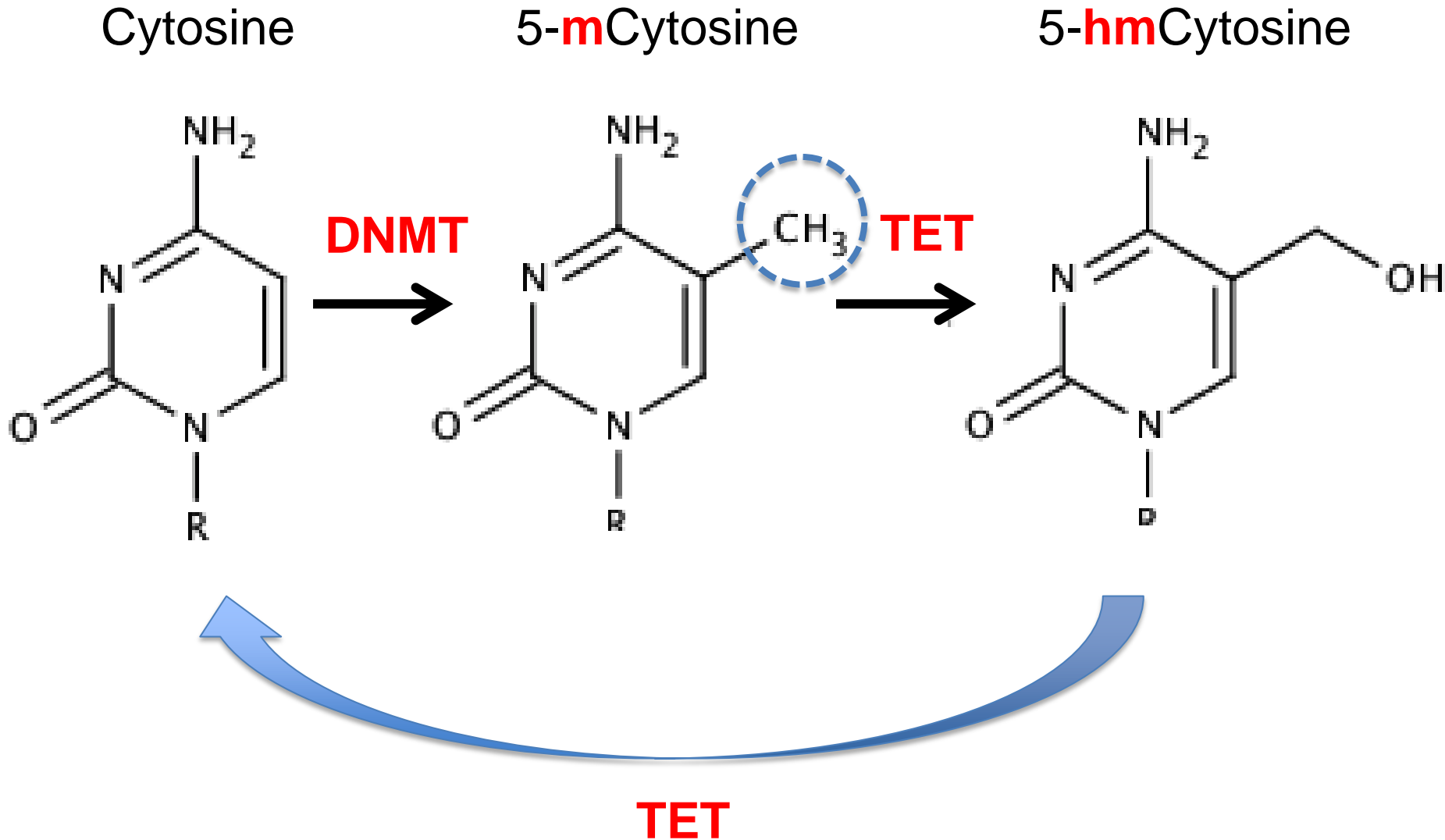
Overview of DNA methylome in mammalian cells

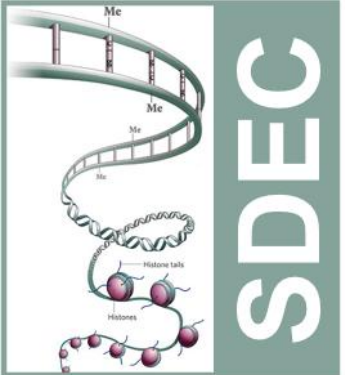
- ✓ DNA methylation is widespread in the mammalian genome, affecting >90% CpG sequences.
- ✓ Methylation is depleted from active cis-elements such as promoters and enhancers
- ✓ Abundant non-CpG methylation was observed in embryonic stem cells but not in fibroblasts

#2 Scientific Discovery of 2009,
TIME magazine



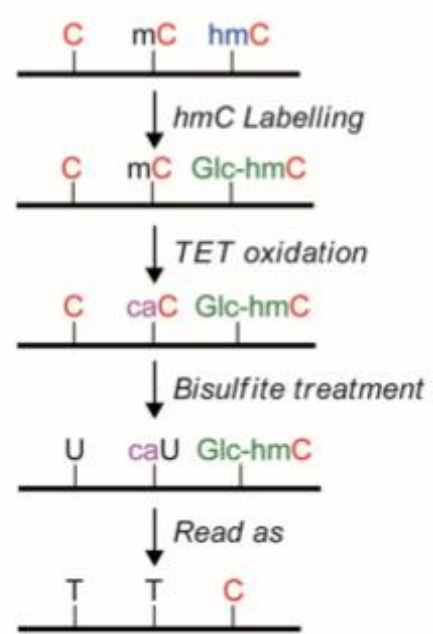
DNA methylation and Hydroxymethylation



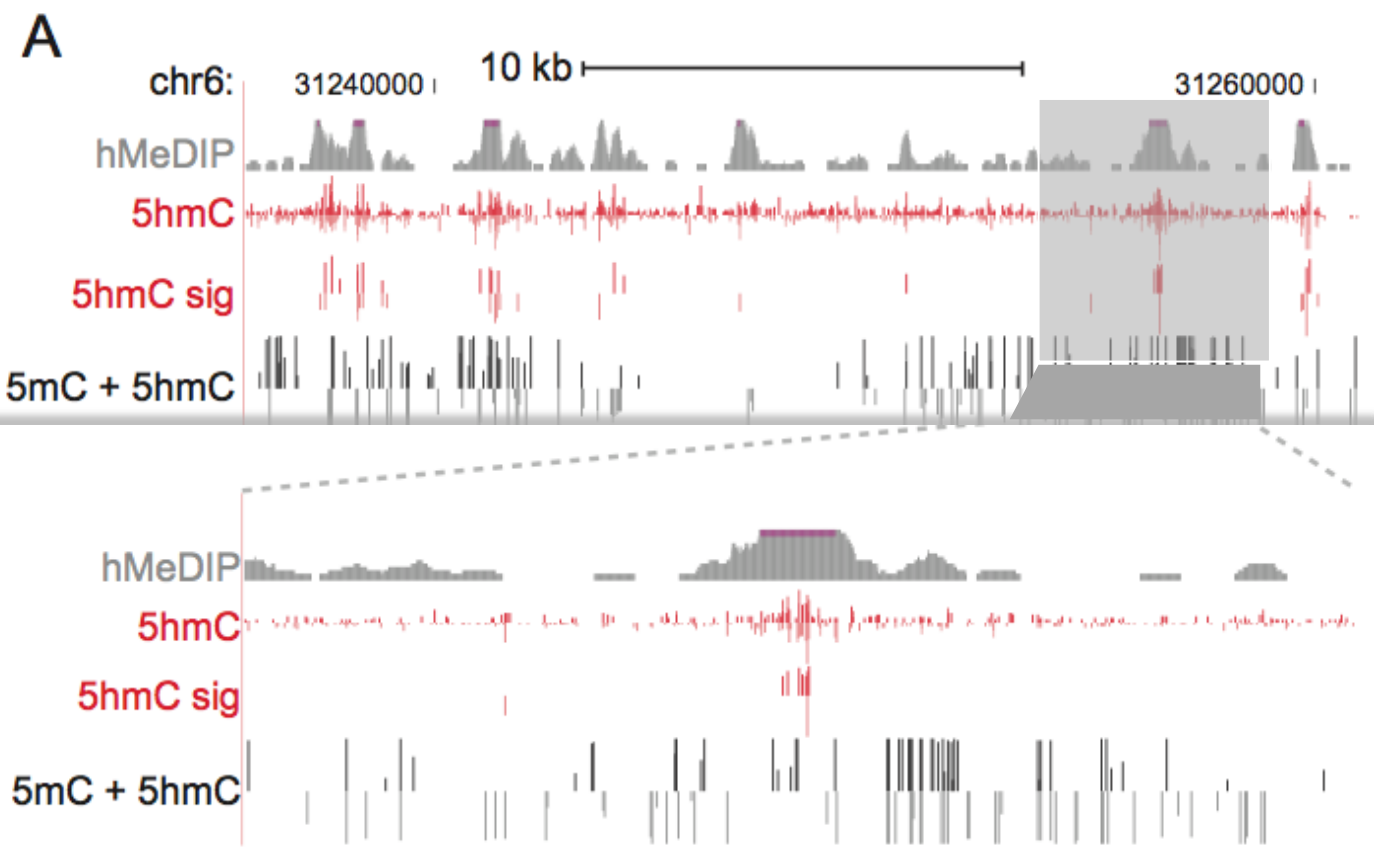


TAB-Seq reveals genome-wide distribution of 5hmC at base resolution

TET-Assisted Bisulfite Sequencing (TAB-Seq)



Distinguishes 5hmC from 5mC when combined with methylC-Seq



Yu et al., Cell, 2012, 149(6):1368-80

5hmC occurs almost exclusively in CpG context
5hmC is enriched at distal cis-elements

Four Roadmap Epigenome Mapping Centers

Broad Institute (Brad Bernstein, Alex Meissner)

UCSD (Bing Ren, Joe Ecker)

UCSF (Joe Costello, Martin Hirst)

UW (John Stamatoyannopoulos)

Data Coordination and Display

Baylor (EDACC, Aleks Milosavljevic)

NCBI (Greg Schuler, Tanya Barrett)

Washington University (Ting Wang)

UCSC (David Haussler, Jim Kent)

Data Analysis (ARRA funding)

MIT (Manolis Kellis)