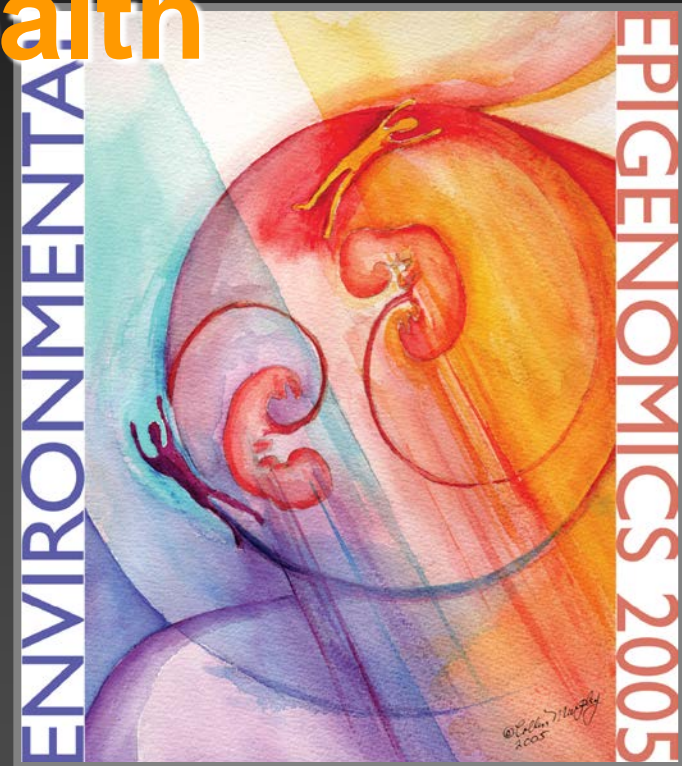


Epigenetics, Imprinting and Human Health

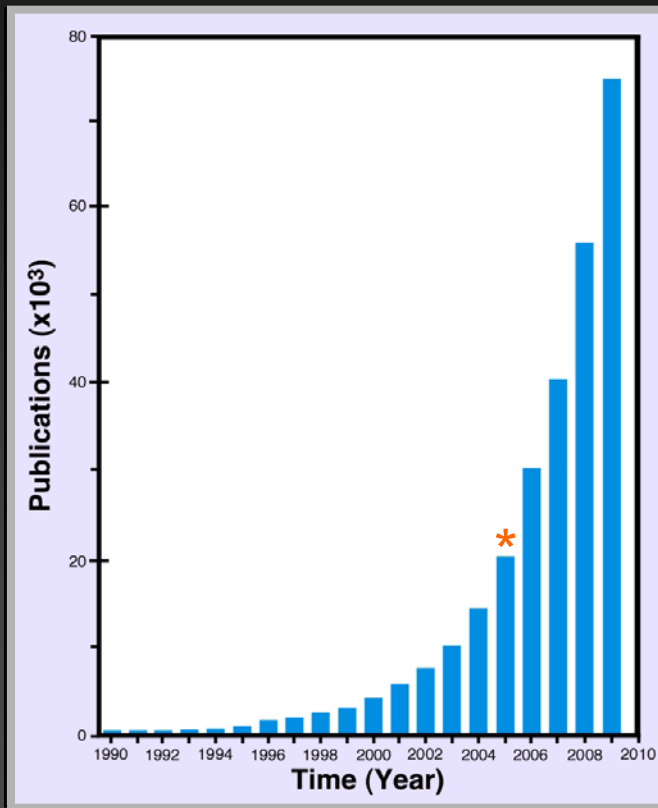
Randy L. Jirtle, Ph.D.
Department of Radiation
Oncology
Duke University Medical Center
Durham, NC 27710



Origins
Artist: Collin Murphy



History of Epigenetic Research



“Epigenetics is now the hottest thing in bioscience!”

Unfortunately, however, many scientists and administrators still

Just

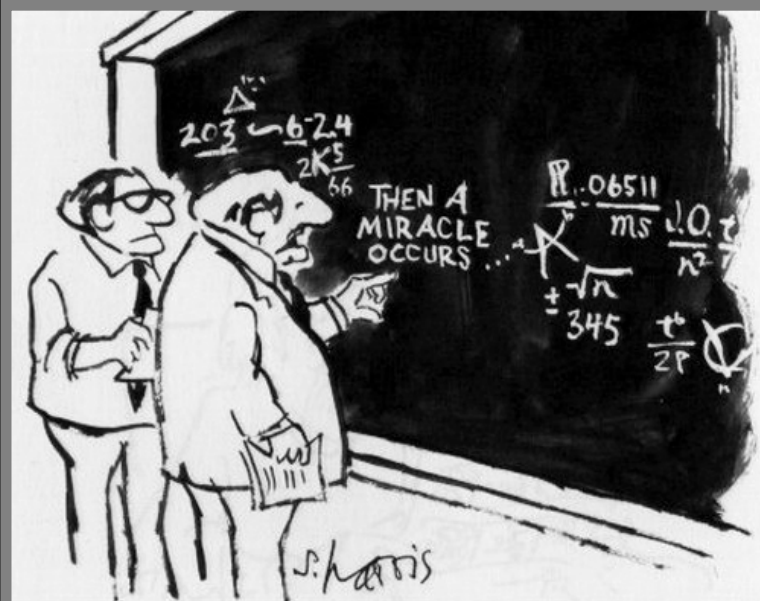
Don't

Get

It!

- **Scientific Community:** *Doubling of epigenetic papers every two years*

Fetal Origins of Adult Disease Susceptibility

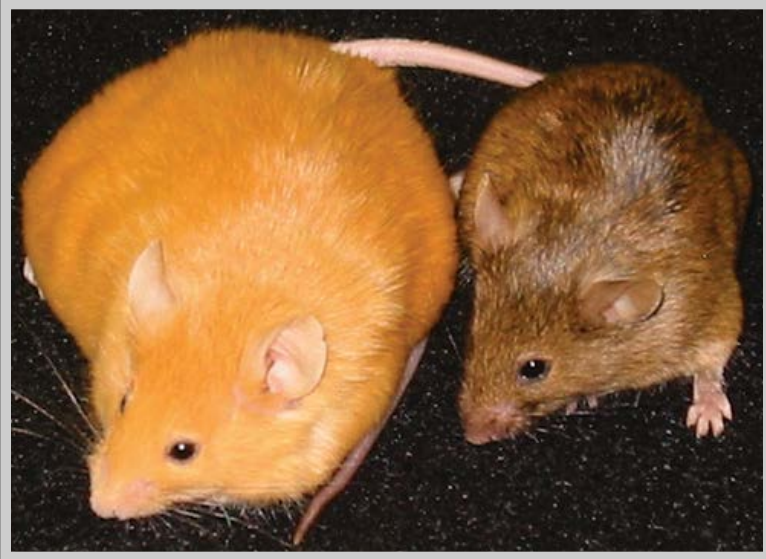


"I think you should be more explicit here in step two."

from *What's so Funny about Science?* by Sidney Harris (1977)

- **DUTCH FAMINE (1944-1945)**
 - 16,000 people died
- **CHINESE FAMINE (1959-1961)**
 - 20 to 40 million people died

Miracle: *Epigenetic Modifications*



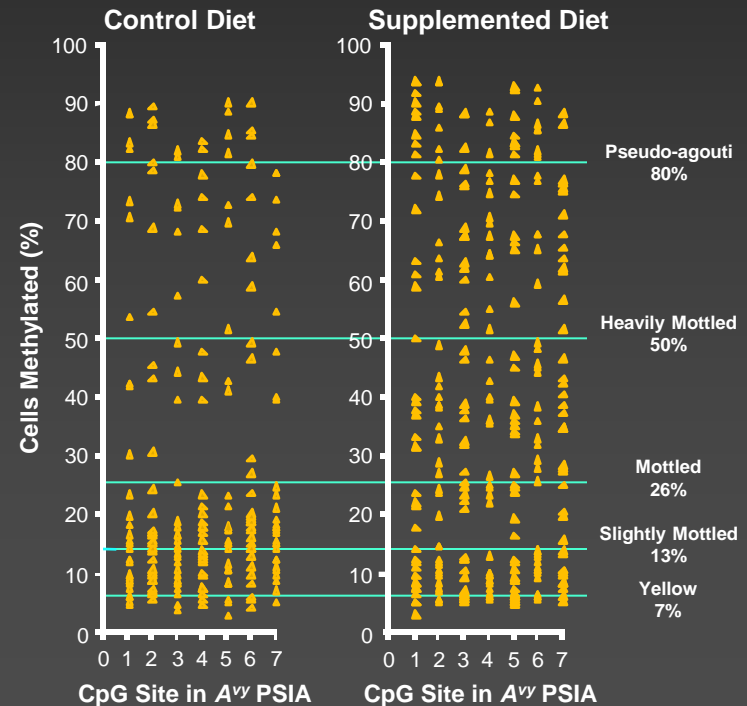
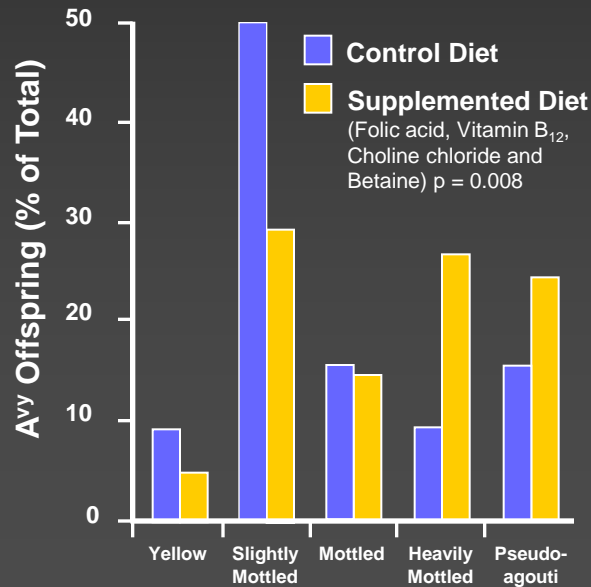
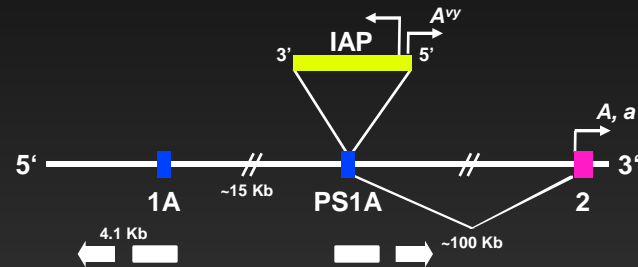
The Agouti Sisters

Metastable

Epialleles

Nature via Nurture

Viable yellow Agouti (A^{vy}) Locus



Food is Medicine!



Counteracting Forces

Artist: *Collin Murphy*

'Let food be thy medicine, and medicine be thy food.' *Hippocrates*

Agouti Coat Color Distribution



Control Diet



**Dietary Supplementation
Methyl Donors or Genistein**



**Endocrine Disruptor Exposure
Bisphenol A (BPA)**



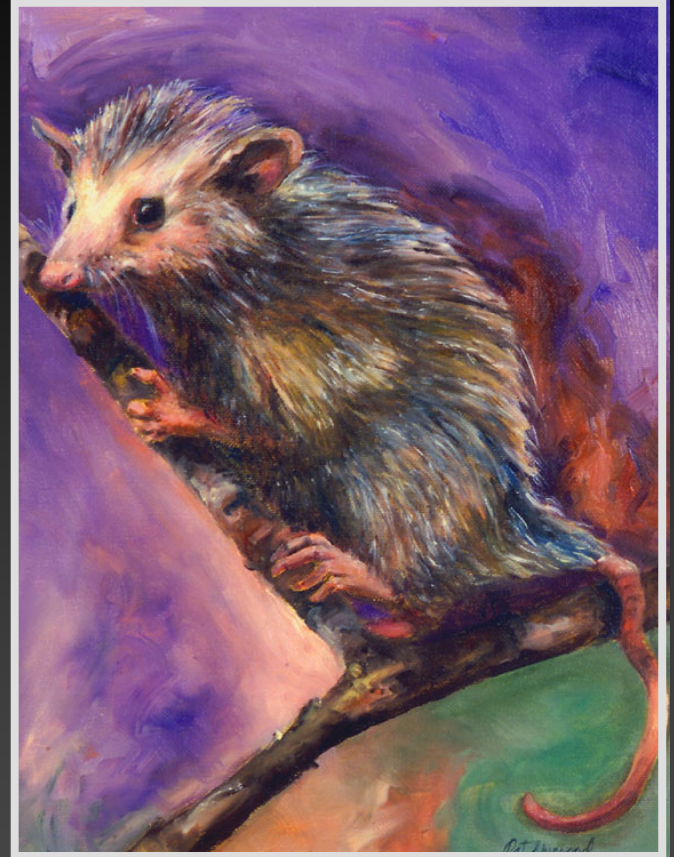
**BPA Exposure plus
Methyl Donor or Genistein
Supplementation**

You are What You Eat!



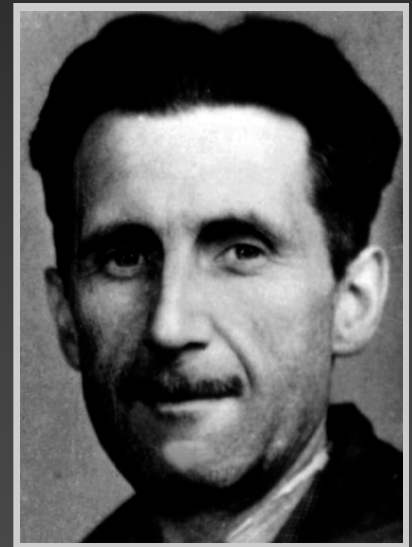


Genomic Imprinting Evolution



Artist: Pat Sherwood

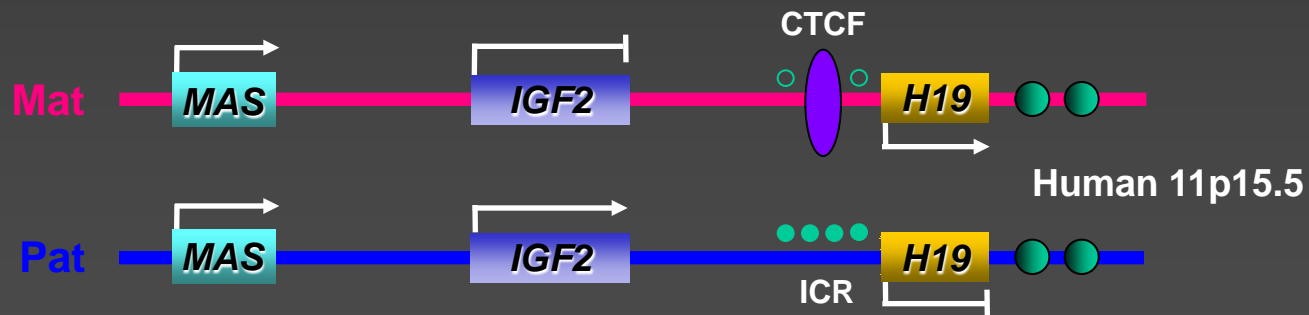
“All animals are equal, But some animals are more equal than others.” *George Orwell*



Imprinted Genes

Autosomal Genes with a Sex

“Imprinting results in parent-of-origin dependent monoallelic expression.”



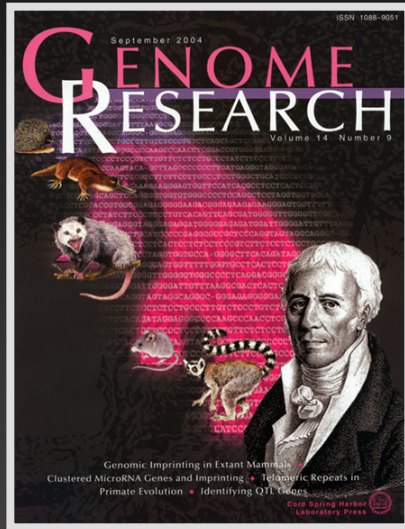
“Nothing in biology makes sense except
in the light of evolution.” *Theodosius Dobzhansky*



Theodosius Dobzhansky
(1900 -1975)

Imprinting Evolution

Species, Tissue, Time, and Sex Dependent
Gene Expression



Artist: James Jirtle

IGF2R & IGF2
Imprinting Evolved
(150 M Years Ago)

IGF2R
Imprinting Lost
(75 M Years Ago)

* *Nnat*, *Meg3*, *Dlk1*

Primates

Scandentia

Dermoptera

Eutherians

Rodents

Ungulates

Marsupials

Monotremes

Birds

Killian *et al.* Mol. Cell 5: 707-716, 2000

Killian *et al.* Hum. Mol. Genet. 10: 1721-1728, 2001

Evans *et al.* Mol. Biol. Evol. 22: 1740-1748, 2005

<http://www.geneimprint.com>



Consequence of Divergent Evolution of Imprinting

- Biological responses due to imprinting dysregulation will be difficult to extrapolate between species.
- Mice are not humans!

Neo-Rosetta Stone



Artist: James Jirtle

Future Objectives

- Identify human imprinted genes and their epigenetically-controlled regulatory elements - *The Imprintome*.
- Determine the role of imprinting in human diseases and neurological disorders.

Lifestyle Also Affects Our Pets!

