Epigenetics, Imprinting and Human Health

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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

http://www.geneimprint.com
Fetal Origins of Adult Disease Susceptibility

Miracle: Epigenetic Modifications

• DUTCH FAMINE (1944-1945)
  • 16,000 people died

• CHINESE FAMINE (1959-1961)
  • 20 to 40 million people died

"I think you should be more explicit here in step two." 
from What's so Funny about Science? by Sidney Harris (1977)
Metastable Epialleles

The Agouti Sisters
Nature via Nurture
Viable yellow Agouti (A^vy) Locus

Food is Medicine!

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

Counteracting Forces
Artist: Collin Murphy

‘Let food be thy medicine, and medicine be thy food.’ Hippocrates

Dolinoy et al., PNAS 104: 13056-13061, 2007

http://www.geneimprint.com
You are What You Eat!

http://www.geneimprint.com
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."

Human 11p15.5

Mas
IGF2
H19
CTCF
MAS
IGF2
H19
ICR
Mat
Pat

http://www.geneimprint.com
“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

IGF2R & IGF2 Imprinting Evolved (150 M Years Ago)

* Nnat, Meg3, Dlk1

IGF2R Imprinting Lost (75 M Years Ago)

Primates
Scandentia
Dermoptera
Rodents
Ungulates
Marsupials
Monotremes
Birds

Artist: James Jirtle


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!

http://www.geneimprint.com
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.

*Luedi et al. Genome Res. 17: 1723–1730, 2007*
Lifestyle Also Affects Our Pets!