Genomic Imprinting in Mammals

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Introduction

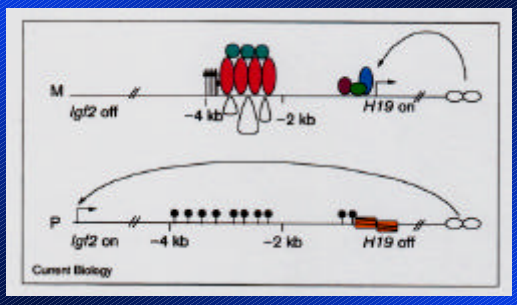
- Exception to the Mendelian inheritance
- An unusual yet important mechanism of gene regulation
- Only one of the parental copies of a gene is expressed
- The imprinted copies of the gene is considered to be the silent one
- Maternally expressed genes
- Paternally expressed genes

Evidence for Mammalian Genomic Imprinting

- Pronuclear transplantation
- Human triploids
- Uniparental chromosome disomies
- Chromosome deficiency in mice and humans
- Analysis of transgene expression
- Expression of specific genes in mice and humans

The Identification of Imprinted Genes

- In 1991, the first gene identified
  -IGF2: insulin-like growth factor 2
- As of April 1997, 19 imprinted genes had been identified in mammals
- To date, about 41 imprinted genes have been identified

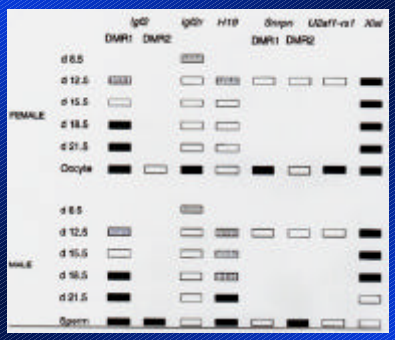


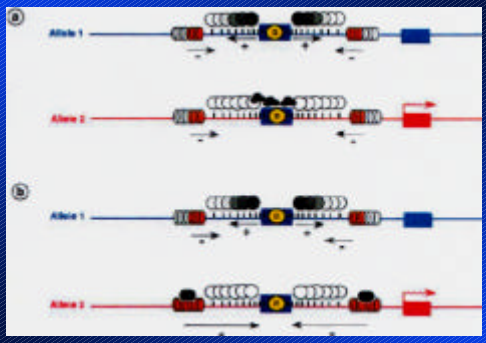
Imprinted Genes

Imprinted gene	Expressed allele	Mouse Chromosome	Human homologue
Igf2	Parental	7	Yes
Igf2R	Maternal	17	Yes
H19	Maternal	7	Yes
Xist	Paternal	X	NR
Grf1	Paternal	9	NR
U2afbp-rs	Paternal	11	No

Imprinting Mechanism (I)

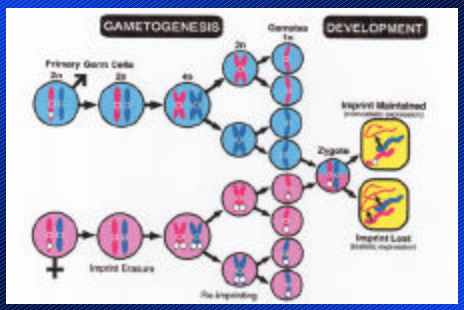
- DMR-allele-specific differential methylation region -Imprinting marker
- Direct repeat near CG-rich DMRs
- Imprinted genes tend to be clustered
- Regional organizations and spreading of the epigenotype during development

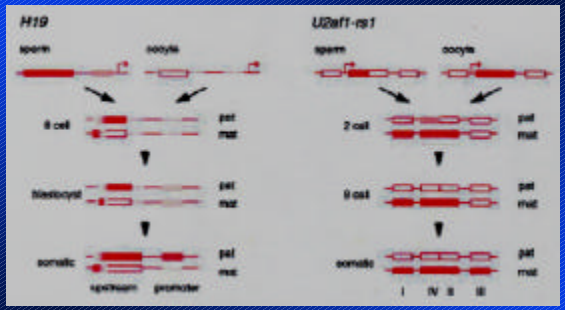




Imprinting Mechanism (II)

- Key stages of genomic imprinting during mammalian development
- Erasure
- Establishment
- Maintenance



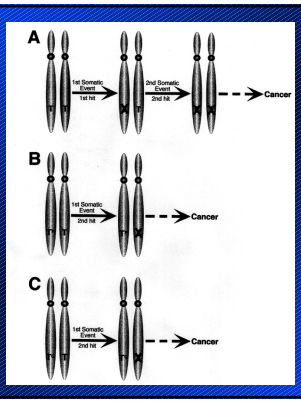


Genomic Imprinting and Genetic Disease

- Angelman syndrome, mapped to 15-11q-13q abnormal: loss of maternally expressed gene
- Prader-Willi syndrome, mapped to 15-11q-13q abnormal: loss of paternal expressed gene
- Bechwith-Wiedemann Syndrome

Genomic Imprinting and Cancer

- Wilms' tumors - preferential loss of maternal 11p15 in BWS population (Bechwith-Wiedemann Syndrome)
- Tumor suppressor gene inactivation by genomic imprinting for a two-hit model of carcinogenesis



A Tale of Two Brains

- Possibilities:
- Human mother's genes make the biggest contribution to the part of the brain that society value most-the cortex.
- Human father's genes contribute more to the primitive regions.