

Physiological Functions of Imprinted Genes

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Epigenetics Cell Memory



Rainbow Cat

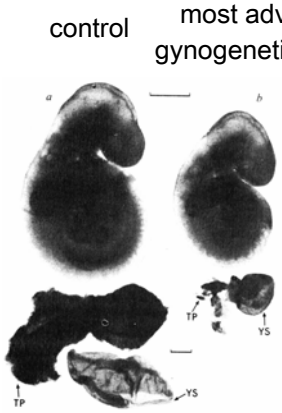


Copy Cat

Genomic Imprinting

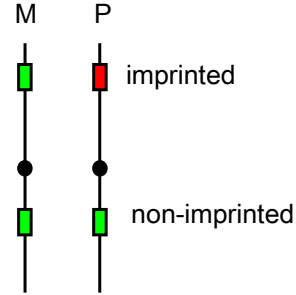
"Development of reconstituted mouse eggs suggests imprinting of the genome during gametogenesis"

Surani, Barton & Norris, Nature 308, 548-550 (1984)

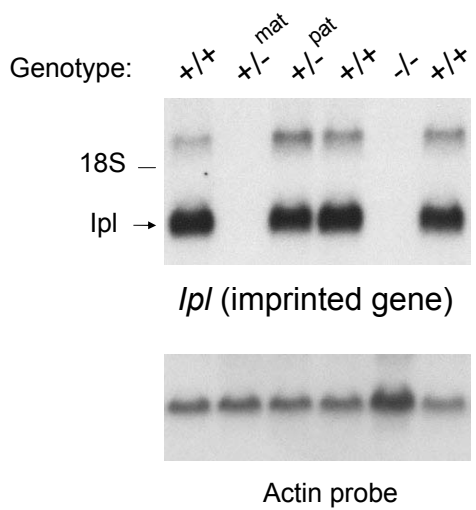


"Our model implies that the paternal and/or maternal genome (whole or in part) are somehow conditioned/alterd during gametogenesis and that this conditioning is completely reversible (as is the case for the X chromosome)."

McGrath & Solter, Cell 37, 179-183 (1984)



Genomic Imprinting: Gene Dosage



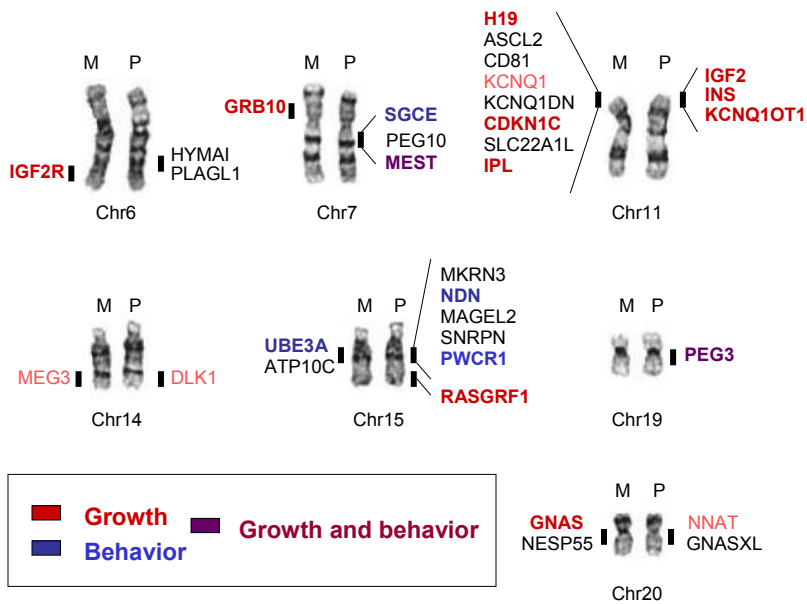
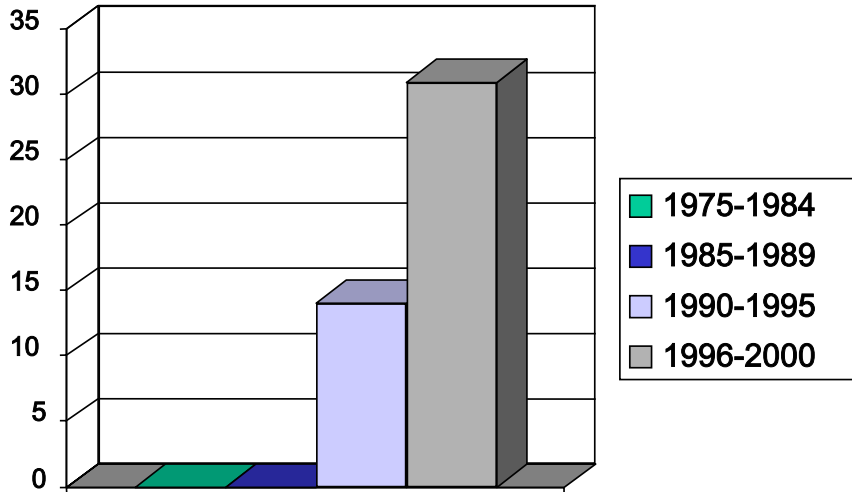
Theories of Imprinting

- Mechanism: locations of imprinted domains dictated by DNA methylation and regional chromatin structure in gametogenesis
 - multiple imprinted genes clustered in megabase-scale regions*
 - imprinting determined by allele-specific DNA methylation at critical sites*

Theories of Imprinting

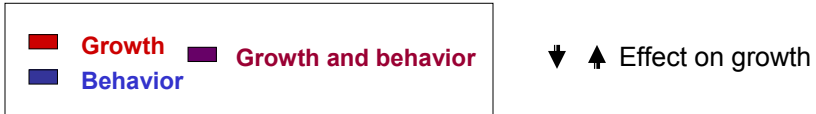
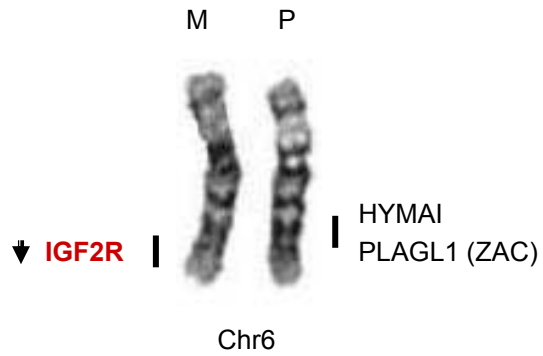
- Mechanism: locations of imprinted domains dictated by DNA methylation and regional chromatin structure in gametogenesis
 - multiple imprinted genes clustered in megabase-scale regions*
 - imprinting determined by allele-specific DNA methylation at critical sites*
- Biological Function: conflict between maternal and paternal “drives” for reproductive success.
 - paternally silenced genes retard growth of the conceptus; maternally silenced genes promote growth and increase nutritional demands on the mother*

Imprinted Genes

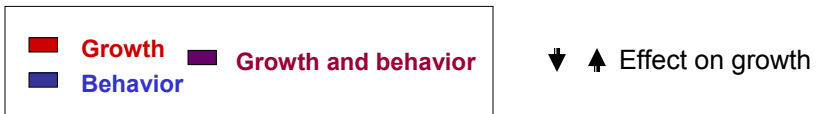
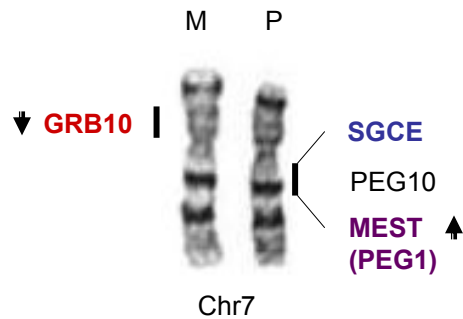


Tycko and Morrison, J Cell Physiol, 2002

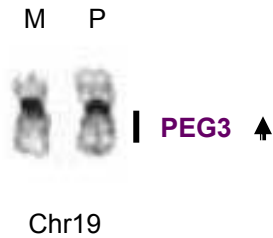
Imprinted genes on Mm17/Hs6



Imprinted genes on Mm11/Hs7

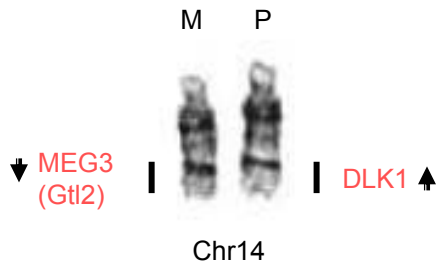


Imprinted Genes on Hs19q/Mm7



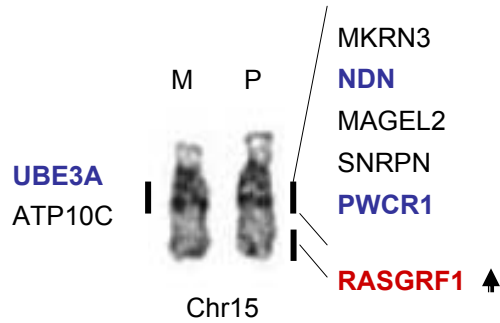
■ Growth	■ Growth and behavior	▼ ↑ Effect on growth
■ Behavior		

Imprinted Genes on Hs14q32/Mm12



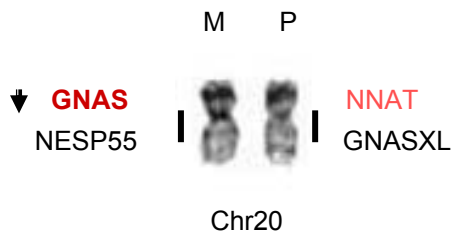
■ Growth	■ Growth and behavior	▼ ↑ Effect on growth
■ Behavior		

Imprinted Genes on Hs15q/Mm7



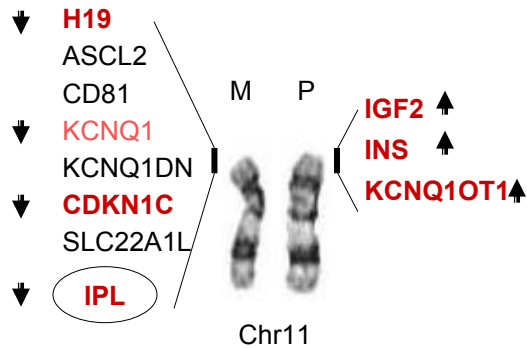
■ Growth	■ Growth and behavior	↓ ↑ Effect on growth
■ Behavior		

Imprinted Genes on Hs20q/Mm2



■ Growth	■ Growth and behavior	↓ ↑ Effect on growth
■ Behavior		

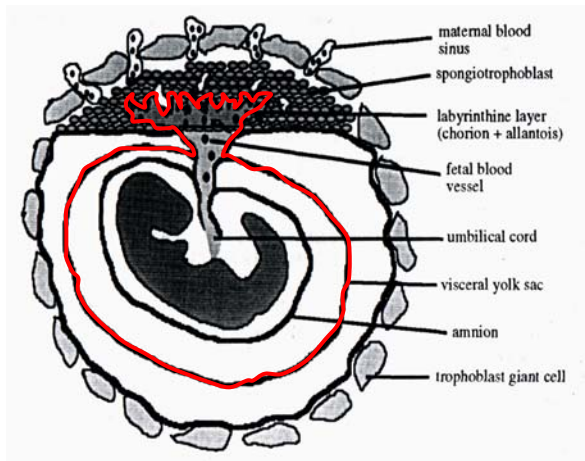
Imprinted Genes on Hs11p15/Mm7



█ Growth	█ Growth and behavior
█ Behavior	

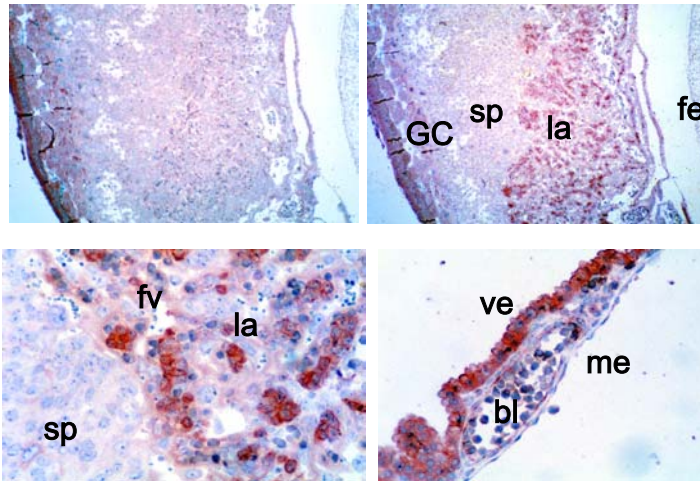
↓ ↑ Effect on growth

Feto-Maternal Interaction: Extraembryonic Tissues

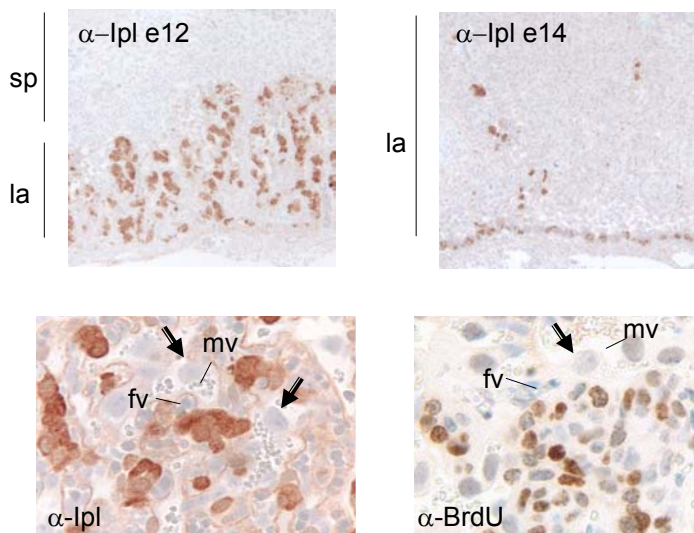


[Cross, J.C., Annals NY Acad Sci]

Expression of *Ipl* in Extraembryonic Tissues

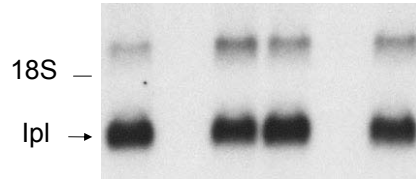


Ipl-positive cells disappear at mid→late gestation

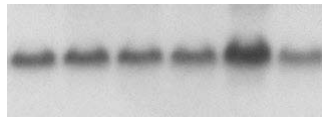


Ipl KO mice

Genotype: +/+ mat +/− +/− pat +/+ −/− +/+

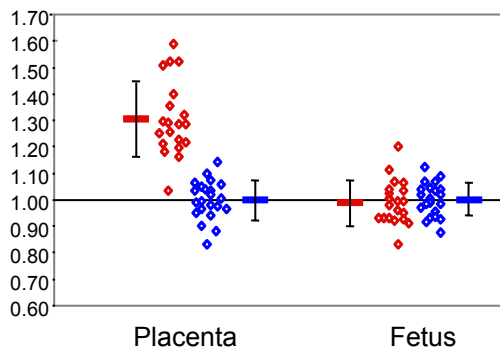


Ipl (imprinted gene): cDNA probe



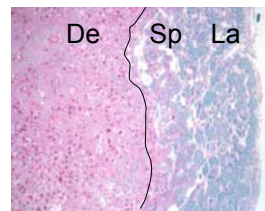
Actin probe

Placental Overgrowth in *Ipl* KO Mice

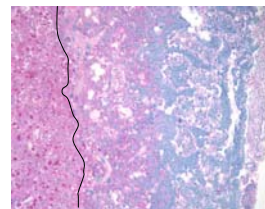


◇ Ipl-negative

◇ Ipl-positive

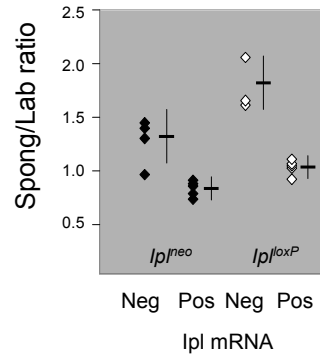
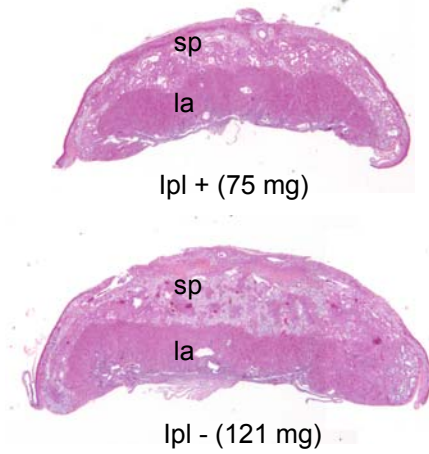


Ipl-positive

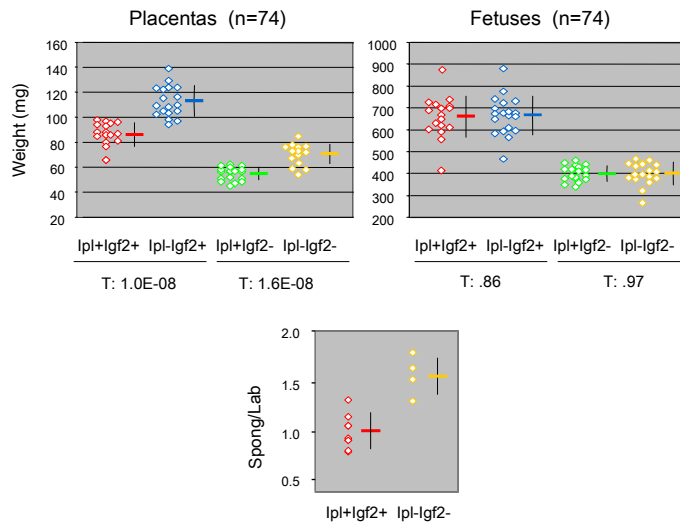


Ipl-negative

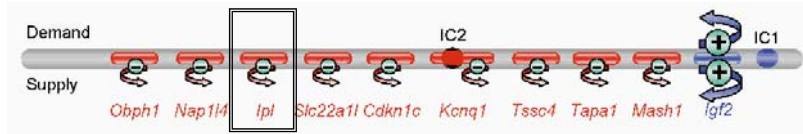
Expansion of Spongiotrophoblast in *Ipl*-null Placentas



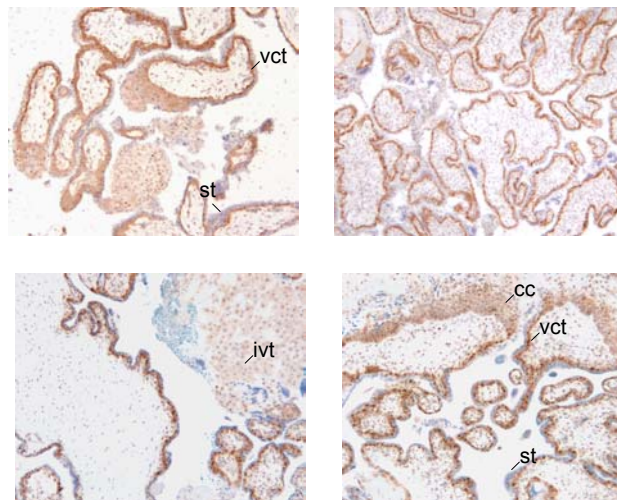
Ipl controls placental size independently of *Igf2*



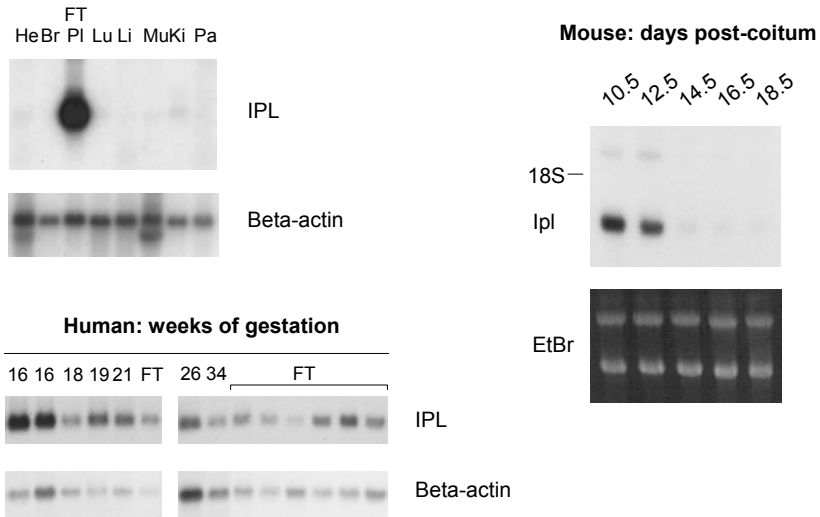
Ipl: maternal expression/paternal repression
of a gene that restrains placental growth



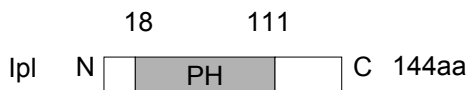
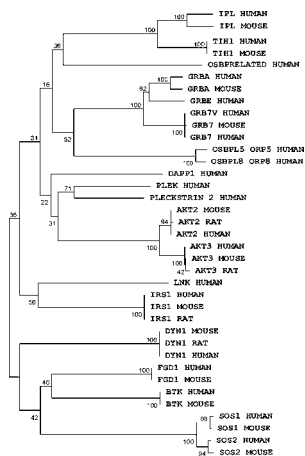
Human IPL marks villous cytotrophoblast



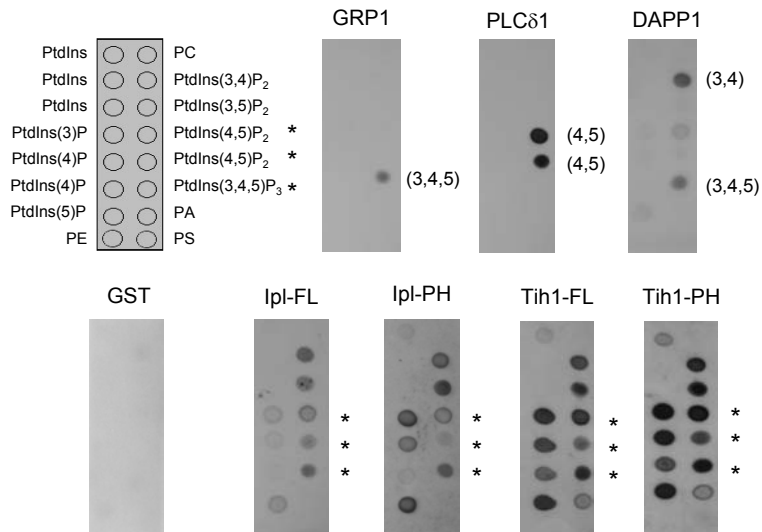
Human *IPL* is expressed in the placenta throughout gestation



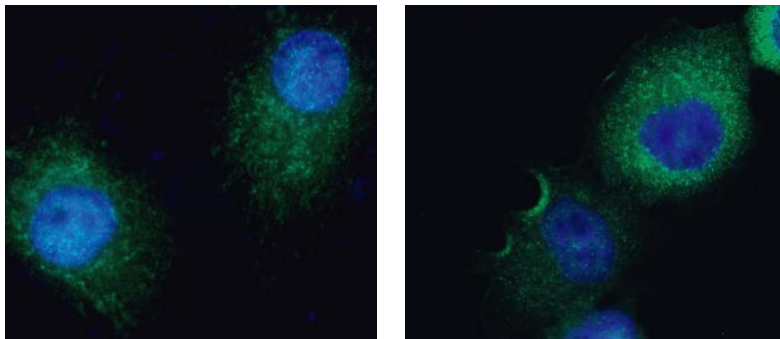
How does IPL inhibit placental growth?



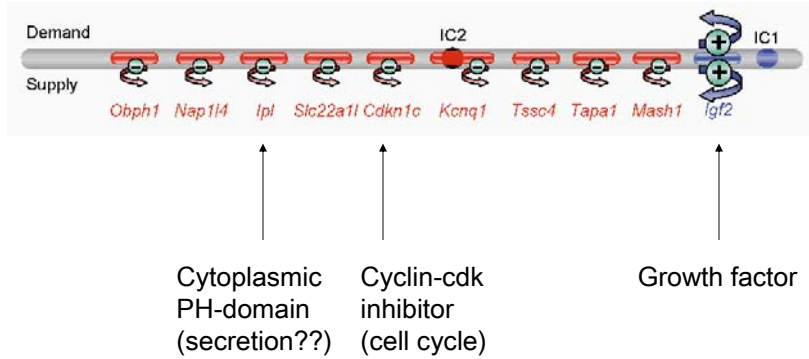
IPL is a bona fide PH-domain protein



Punctate (vesicular?) cytoplasmic distribution of IPL protein



Diverse biochemical pathways control supply and demand for maternal nutrients via imprinting



Q: Imprinting and IUGR?

