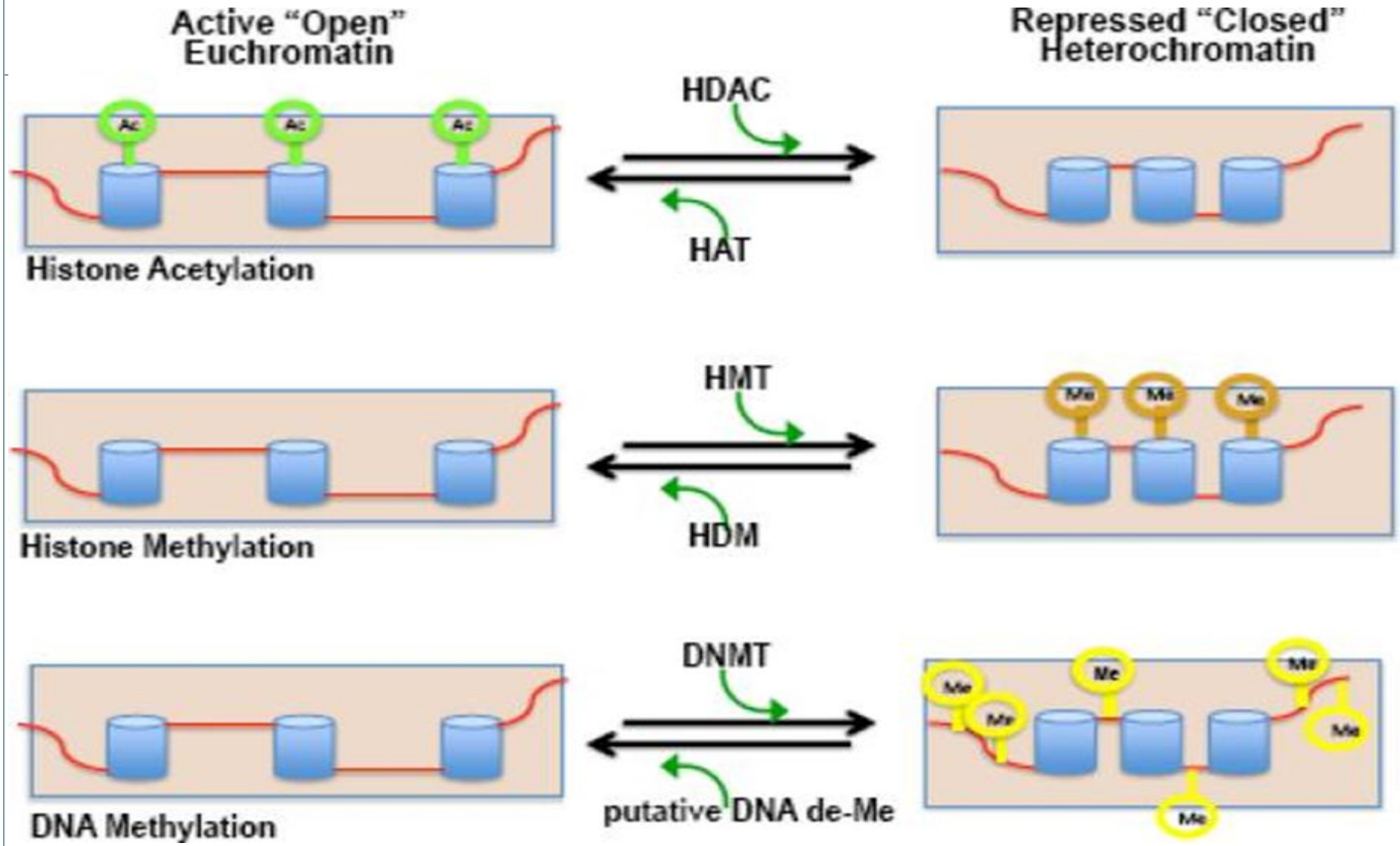
Epigenetics and Inheritance

AN EMERGING BASIC FIELD OF SCIENCE AT THE EPICENTER OF MODERN MEDICINE

PART 3

DNA and Histone Modification



www.ncbi.nlm.nih.gov/pmc/articles/PMC2842459/figure/F1/

Post-Transcriptional Gene Silencing by RNA Interference (RNAi)

DNA

From the mRNA precursors transcribed from the DNA, introns are spliced out and exons are spliced together.

↓

mRNA (messenger RNA)

↓

Proteins are made using non-coding rRNA (ribosomal RNA) and tRNA (transfer RNA), which were also transcribed from DNA, to translate the mRNA.

Non-coding RNAs transcribed from DNA and involved in gene silencing are called RNAi. They include miRNA (microRNA) , siRNA (small interfering RNA), and piRNA (PIWI-interacting RNA).

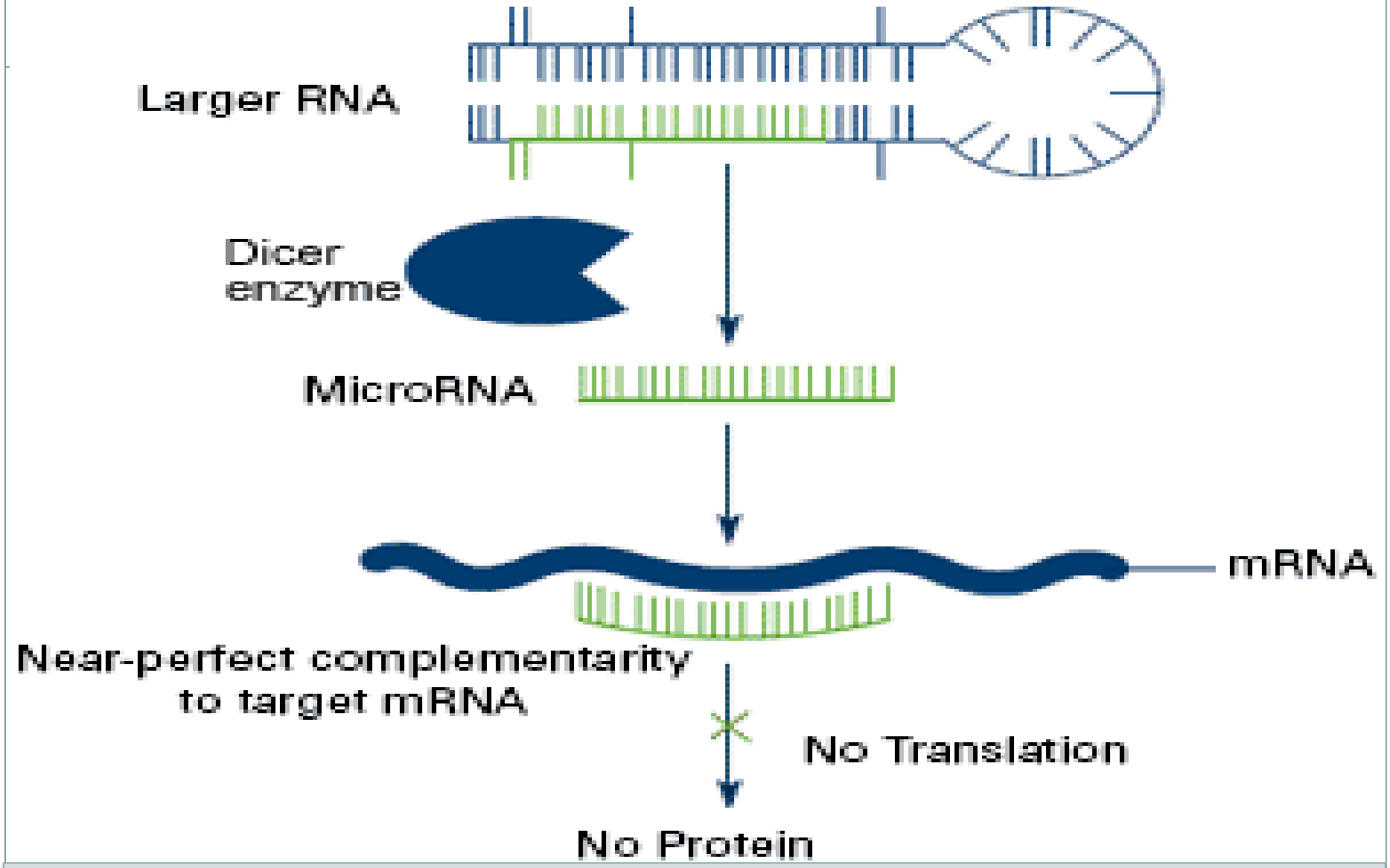
↓

RNAi modification- editing, splicing

↓

Modified RNAi cleave the mRNA into pieces so it cannot be translated into protein.

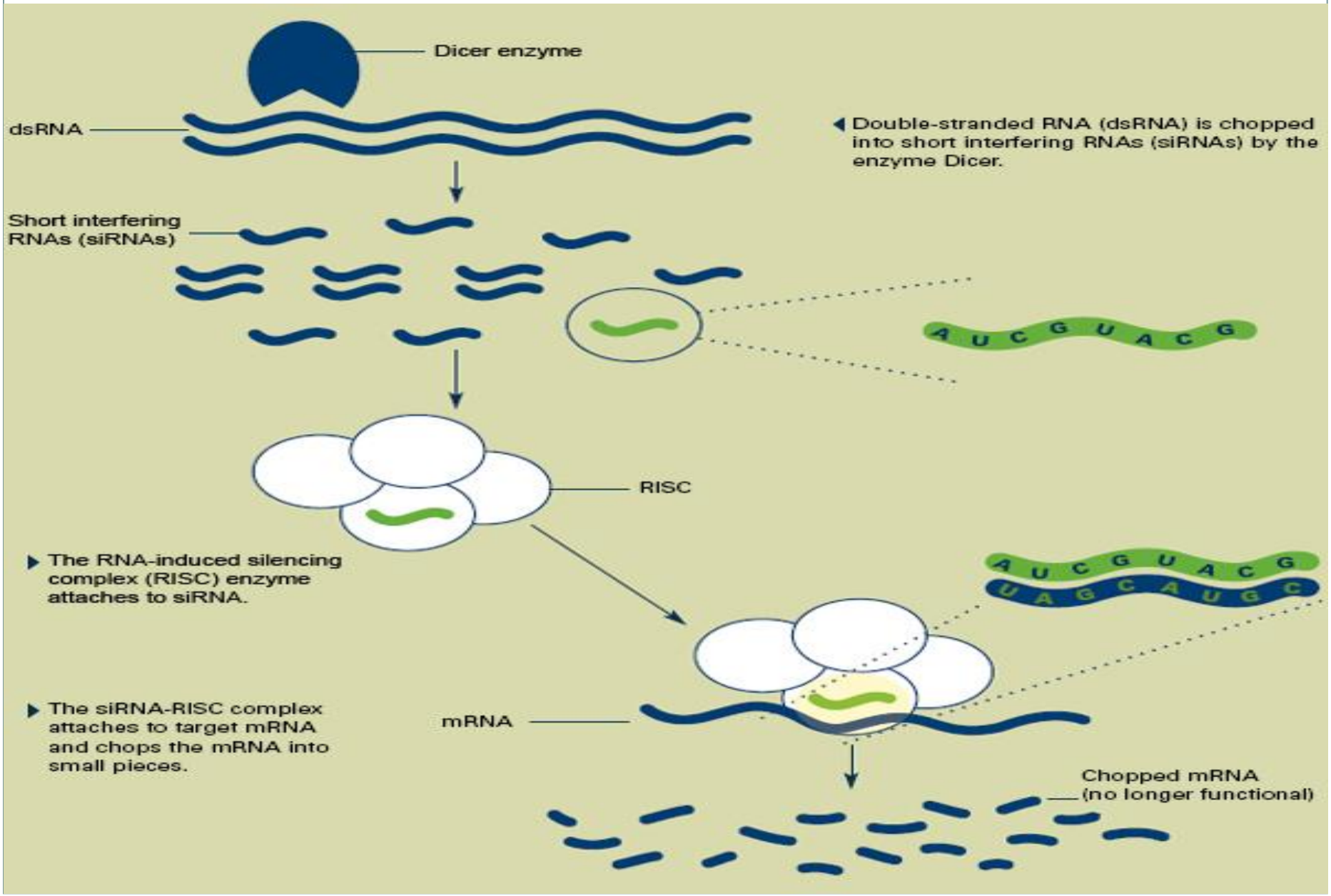
microRNA (miRNA)



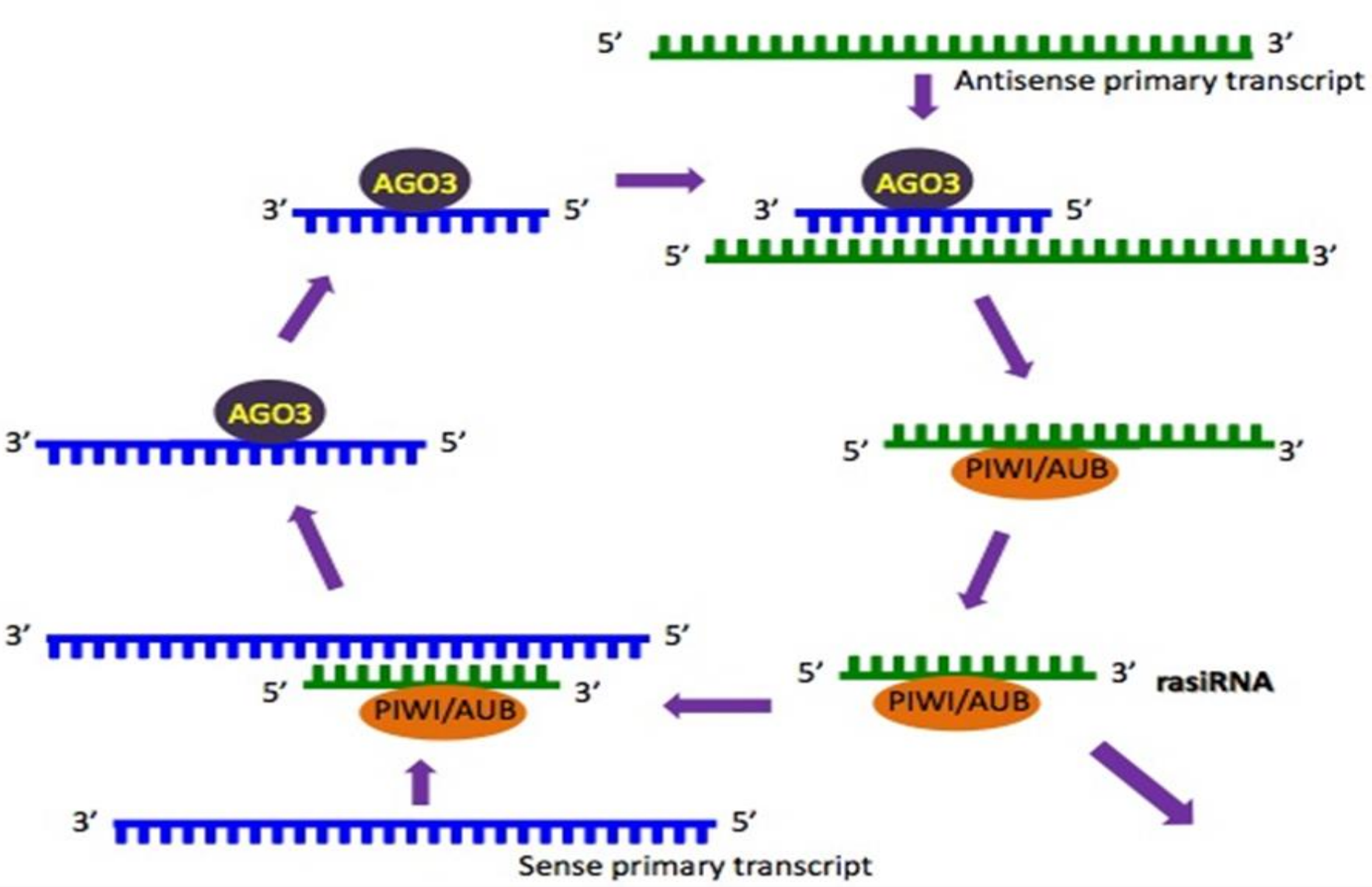
http://publications.nigms.nih.gov/thenewgenetics/chapter2.html

Short Interfering RNA (siRNA)

http://publications.nigms.nih.gov/thenewgenetics/chapter2.html



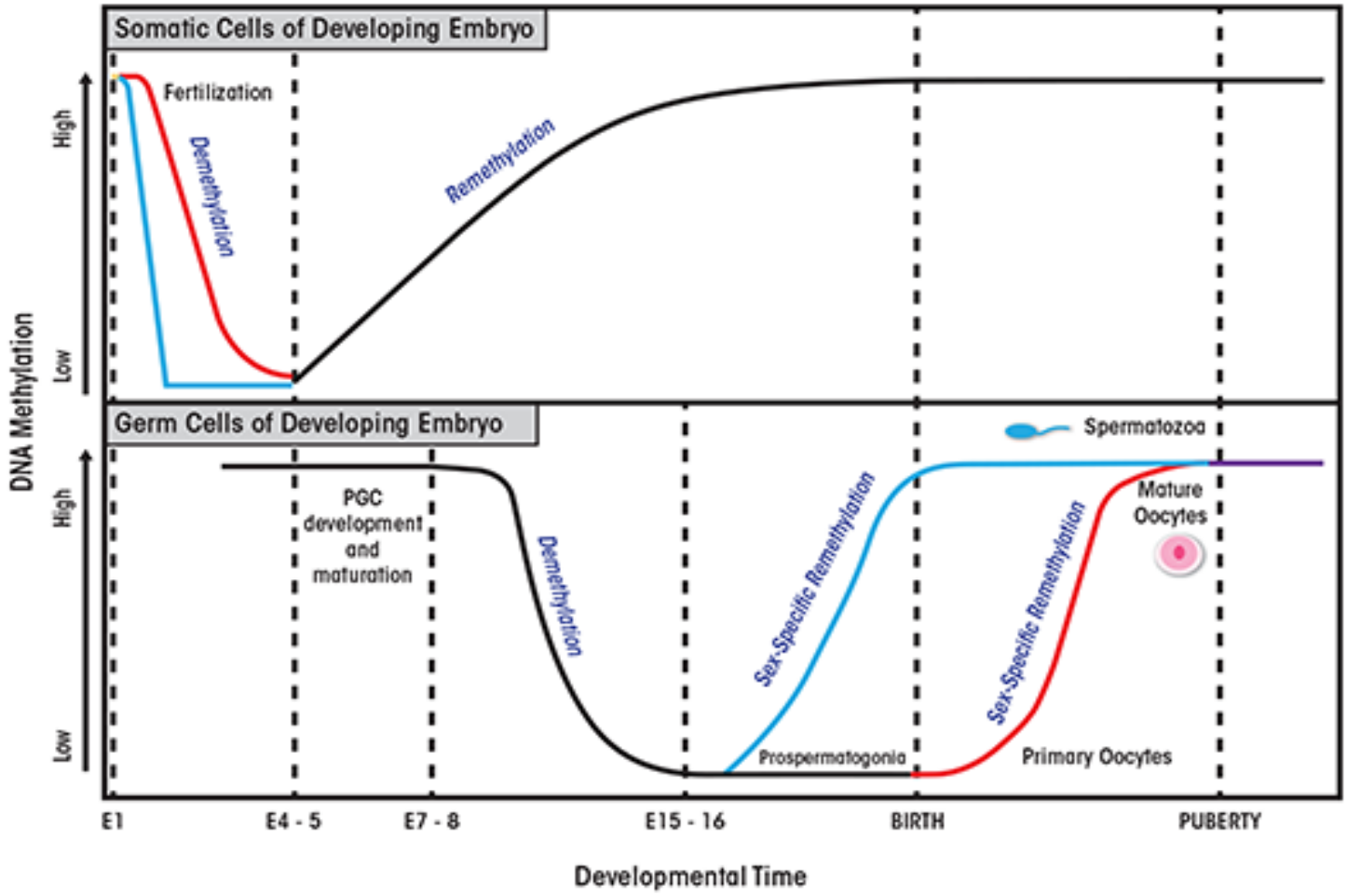
PIWI-interactingRNA (piRNA)



http://en.wikipedia.org/wiki/RasiRNA

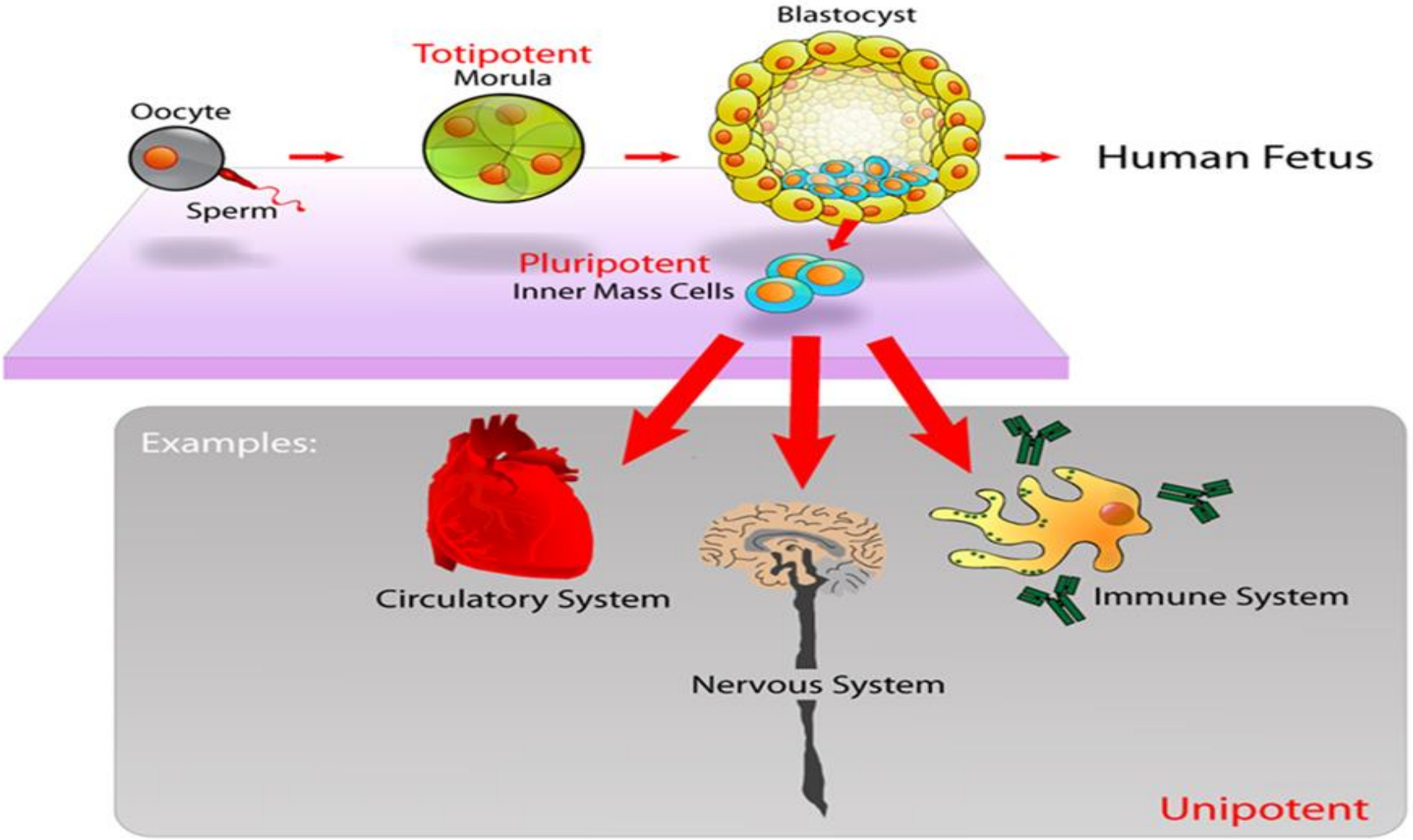
Epigenetic Reprogramming in Mice

http://pubs.niaaa.nih.gov/publications/arcr351/37-46.htm

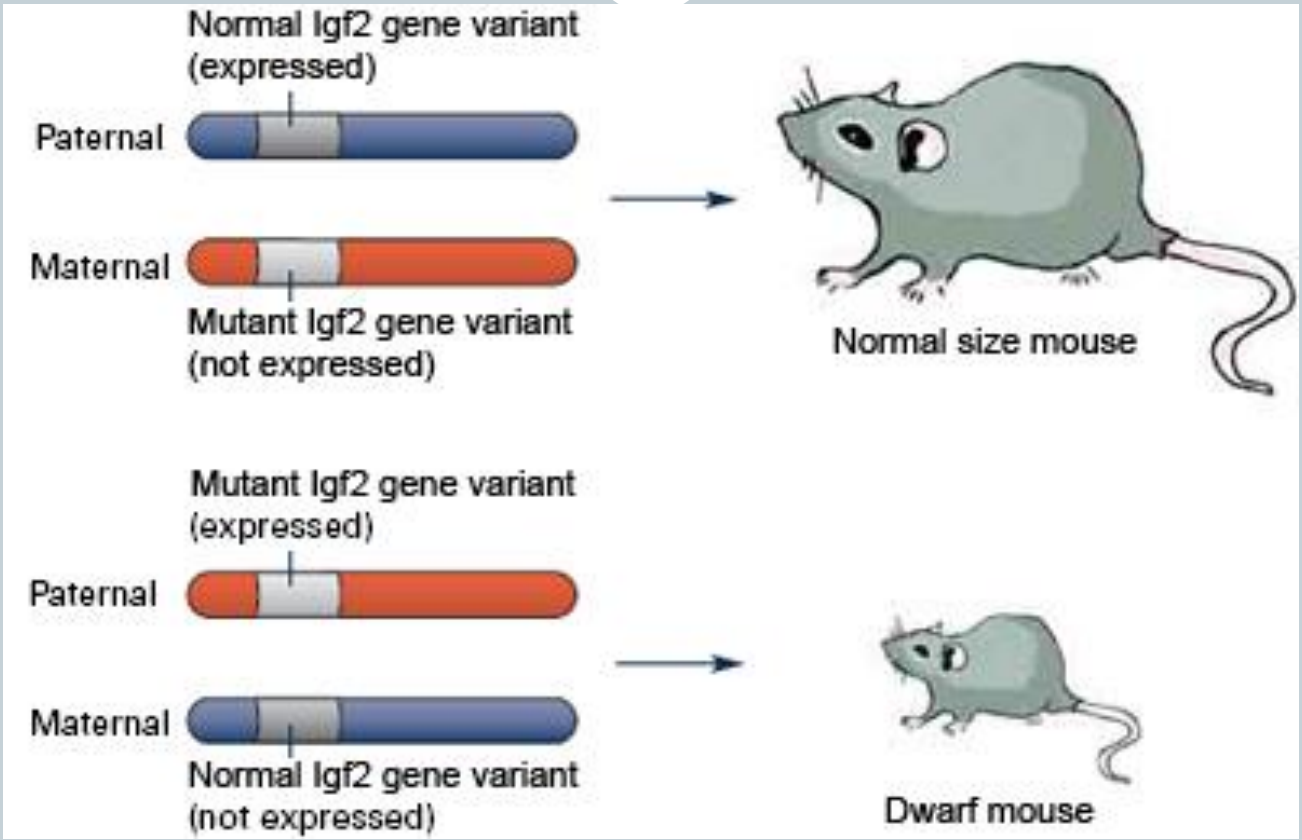


E1 = Embryonic Day 1; red line = maternal line, blue line = paternal line.
E4-5 = Embryonic Day 4-5; PGC = primordial germ cells.

Methylation As the Embryo Develops



Imprinting:
Imprinted Genes Bypass Epigenetic Reprogramming

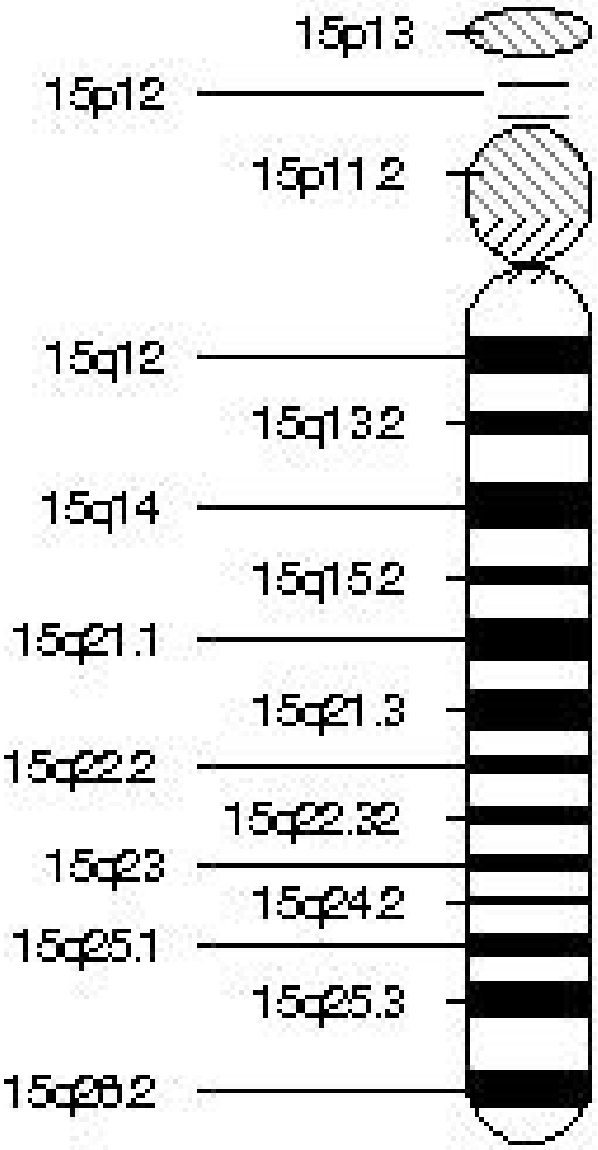


Igf2 is an imprinted gene. A single copy of the abnormal, or mutant, form of the Igf2 gene (red) causes growth defects. If the gene is imprinted (not expressed due to DNA methylation), then the offspring will grow according to the gene that is expressed.

http://publications.nigms.nih.gov/thenewgenetics/chapter2.html

Imprinting Syndromes PWS and AS

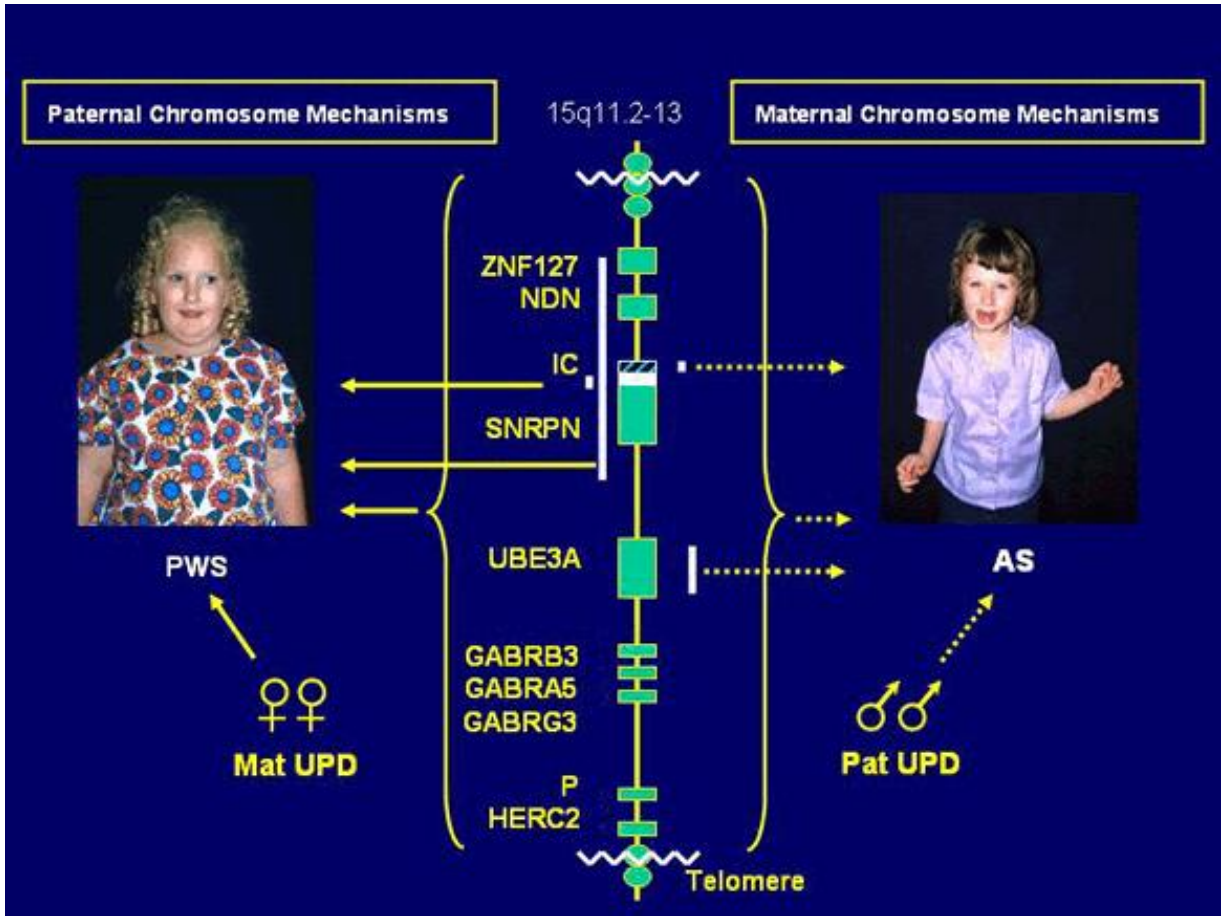
Prader-Willi Syndrome (PWS) and Angelman Syndrome (AS) are the result of the deletion of the 15q11.2-q13 portion of chromosome 15. However, each had very different symptoms depending on parent of origin of the deletion.



http://ghr.nlm.nih.gov/chromosome=15

Prader-Willi and Angelman Syndromes

https://www.peds.ufl.edu/divisions/genetics/teaching/syndrome_gene_maps.htm

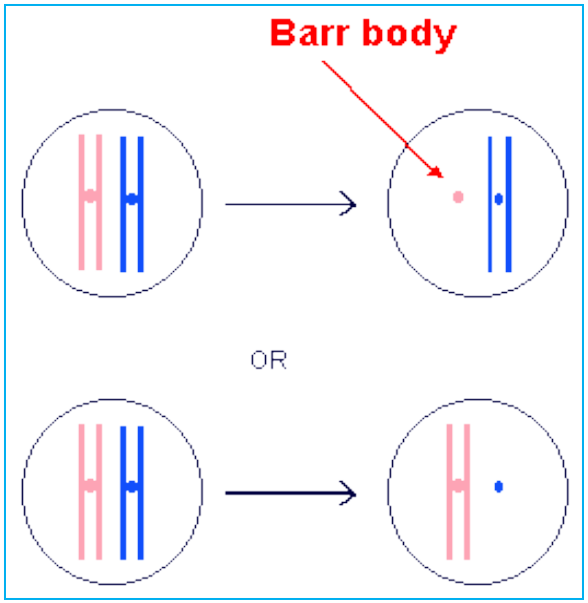


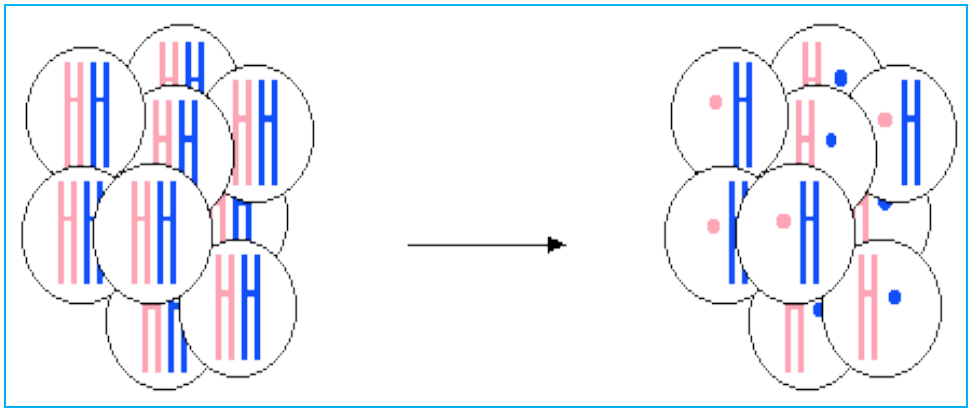
Large chromosome deletions in chromosome 15, imprinting mutations, and uniparental disomy (UPD) are the causes of these two syndromes.

https://www.peds.ufl.edu/divisions/genetics/teaching/syndrome_gene_maps.htm

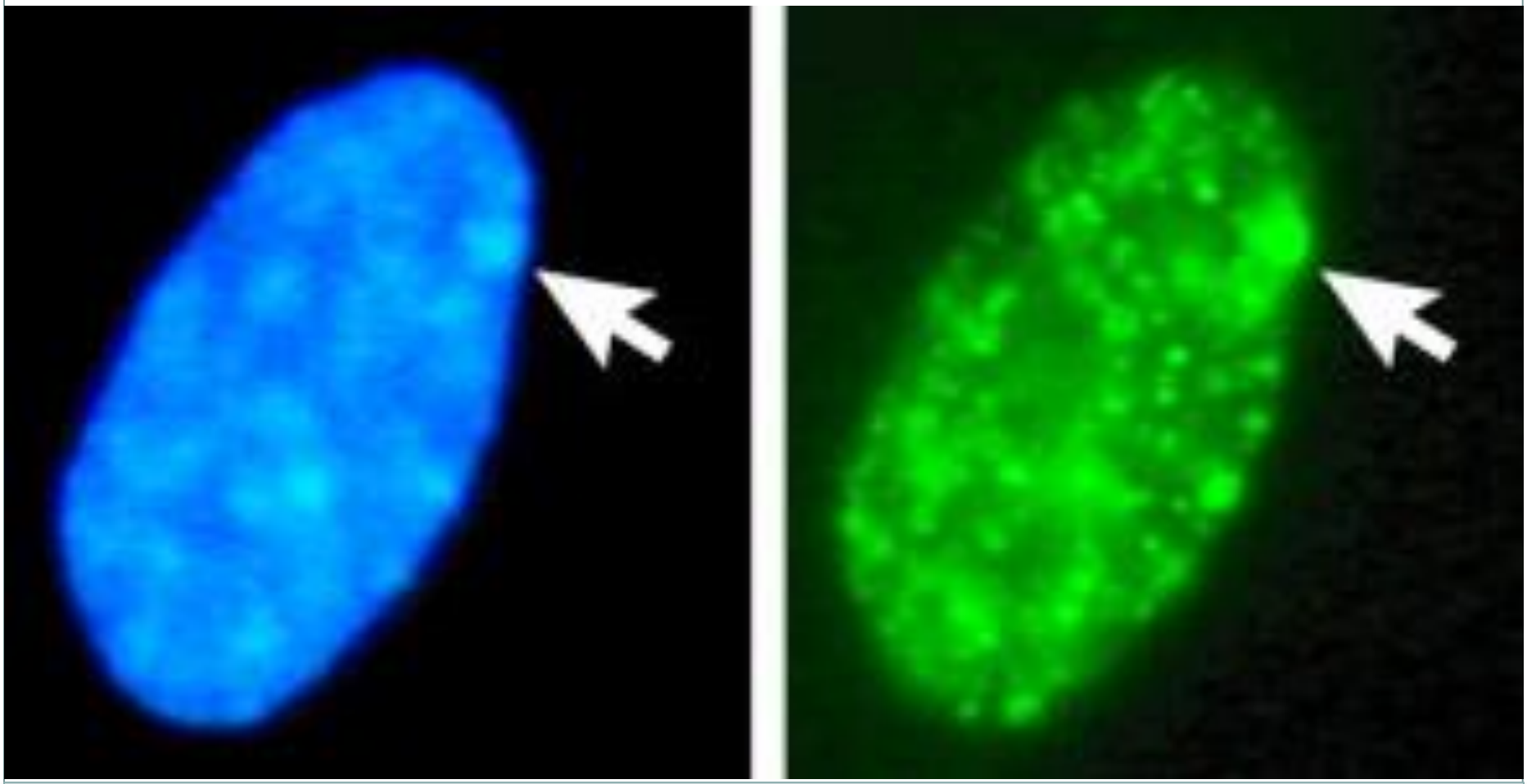
X-Inactivation: Barr Bodies Form Randomly in Cells

In the drawing at the top, 2 cells each with 2 X chromosomes are shown. In the upper drawing at the top, the pink chromosome has been inactivated. All future cells produced by this cell will have an inactivated pink chromosome. In the drawing below it, the blue chromosome has been inactivated. All future generations of this cell will have an inactivated blue chromosome. The drawing at the bottom shows the mosaic nature of Barr body formation.



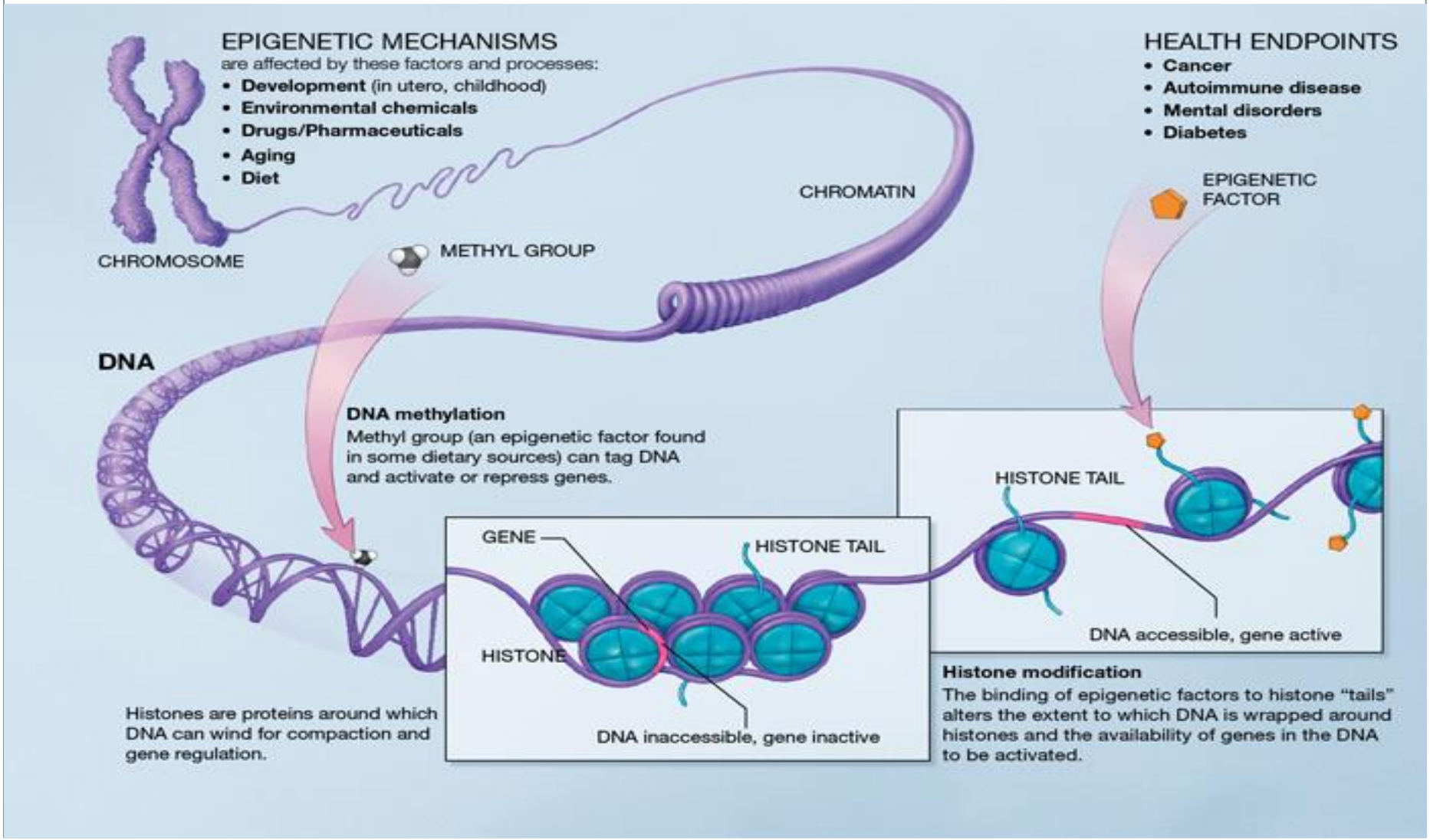


Barr Bodies



Inactive and Active Genes

http://upload.wikimedia.org/wikipedia/commons/d/dd/Epigenetic_mechanisms.jpg

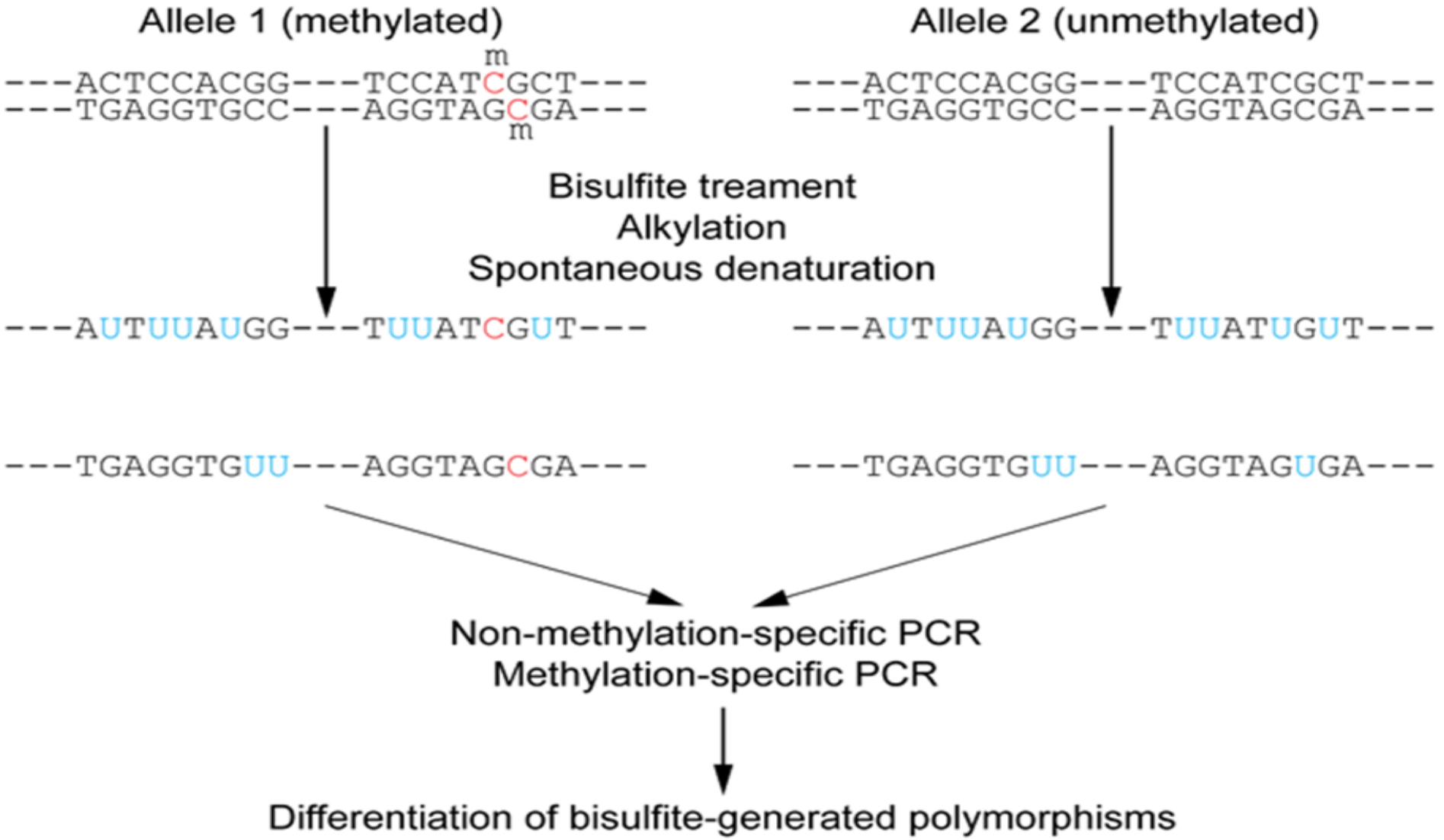


Monozygotic Twins

Although genetically identical, the 60 year twin on the left has developed cancer and the one on the right is healthy. When a study of their genome and epigenome was conducted, it was clear that one twin had more methylations in her epigenome than the other due to different environmental exposures she had during her life.

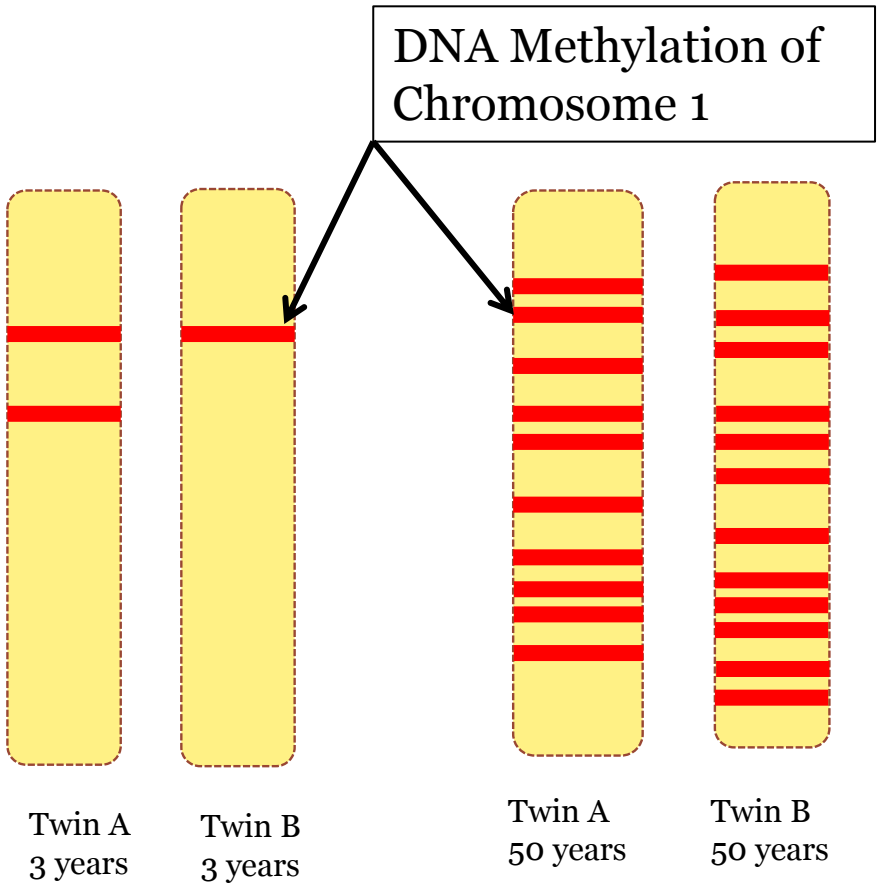
www.pbs.org/wgbh/nova/body/epigenetics.html-Aired July24,2007 on PBS

Methyl Mapping



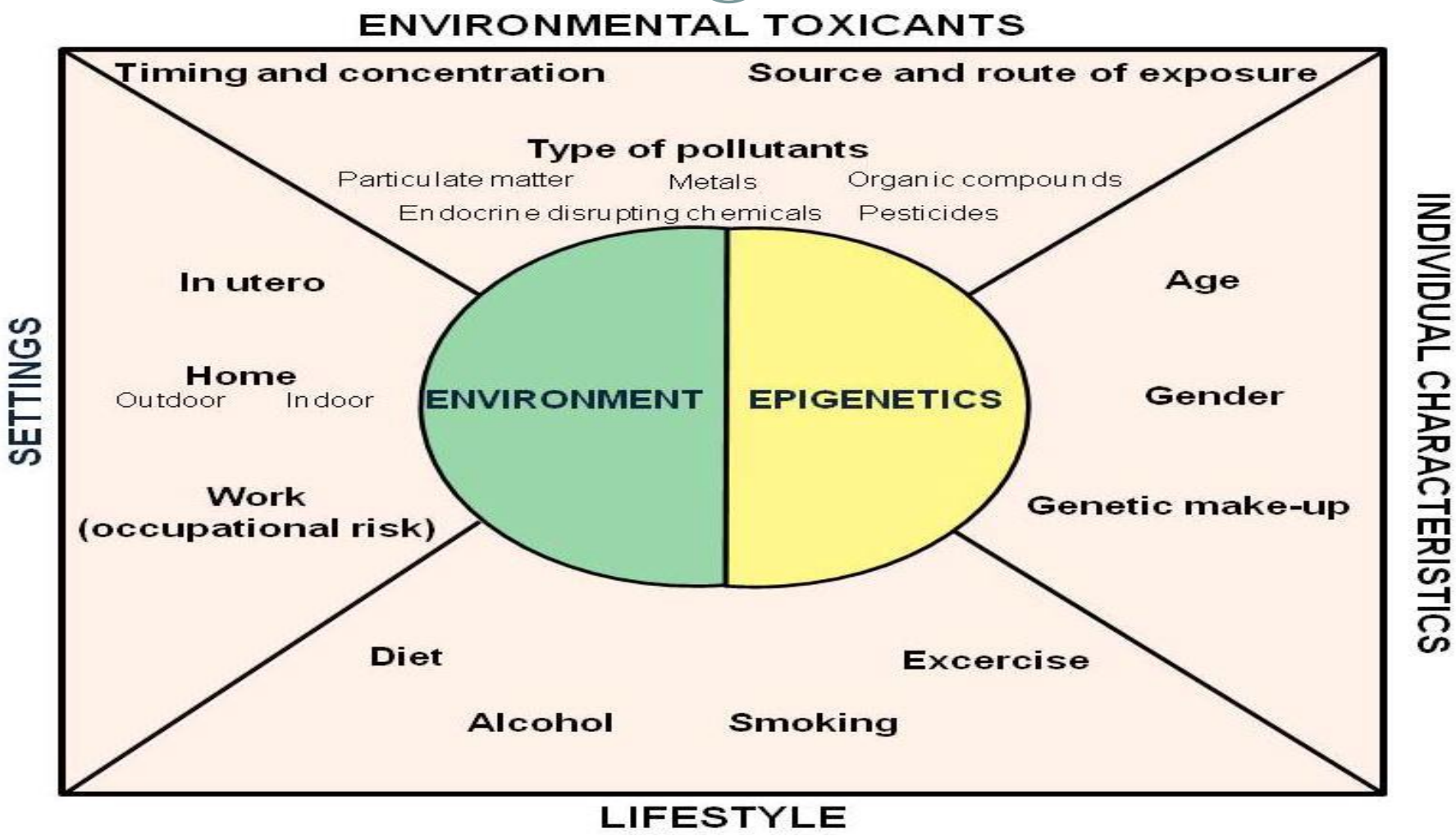
Methylation in Identical Twins

Shown are methylation patterns for three-year-old twins and 50-year-old twins with the differences highlighted in red. In addition, twins who had spent the most time apart and had more divergent medical histories exhibited the greatest epigenetic differences.



Drawing: Lynda Jones, MS, ONPRC

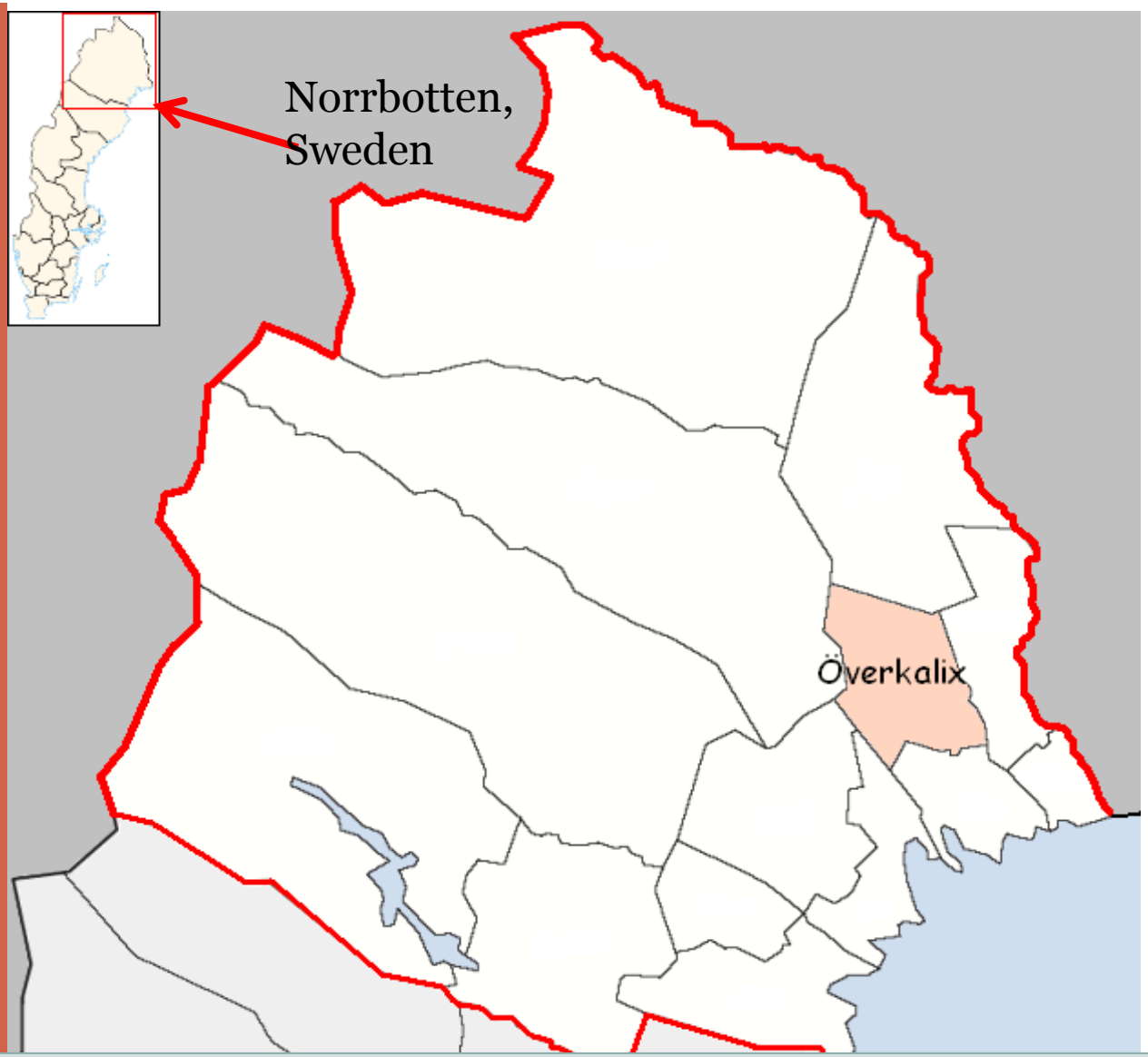
Environmental Factors That Affect Epigenetic Expression



http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3752894/figure/F1/

Epigenetics & Inheritance

In the 1980's, Dr. Lars Olov Bygren at the Karolinska Institute in Stockholm studied 19th century feast and famine data in the isolated Överkalix region of Norrbotten, Sweden.



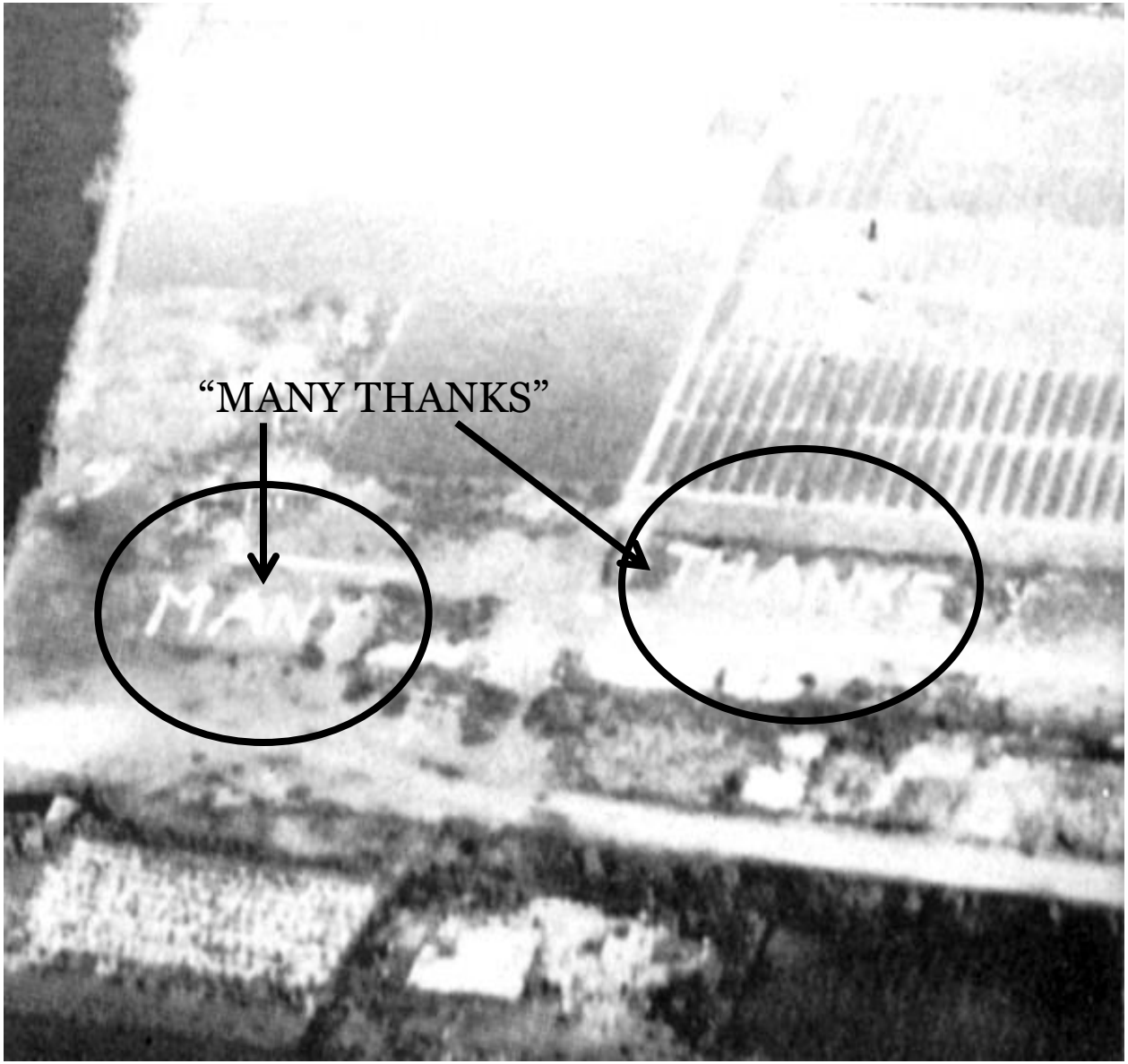
Agouti Mice

Despite their appearance, the two mice are genetically identical but epigenetically different.

Dutch Winter of Hunger 1944-1945

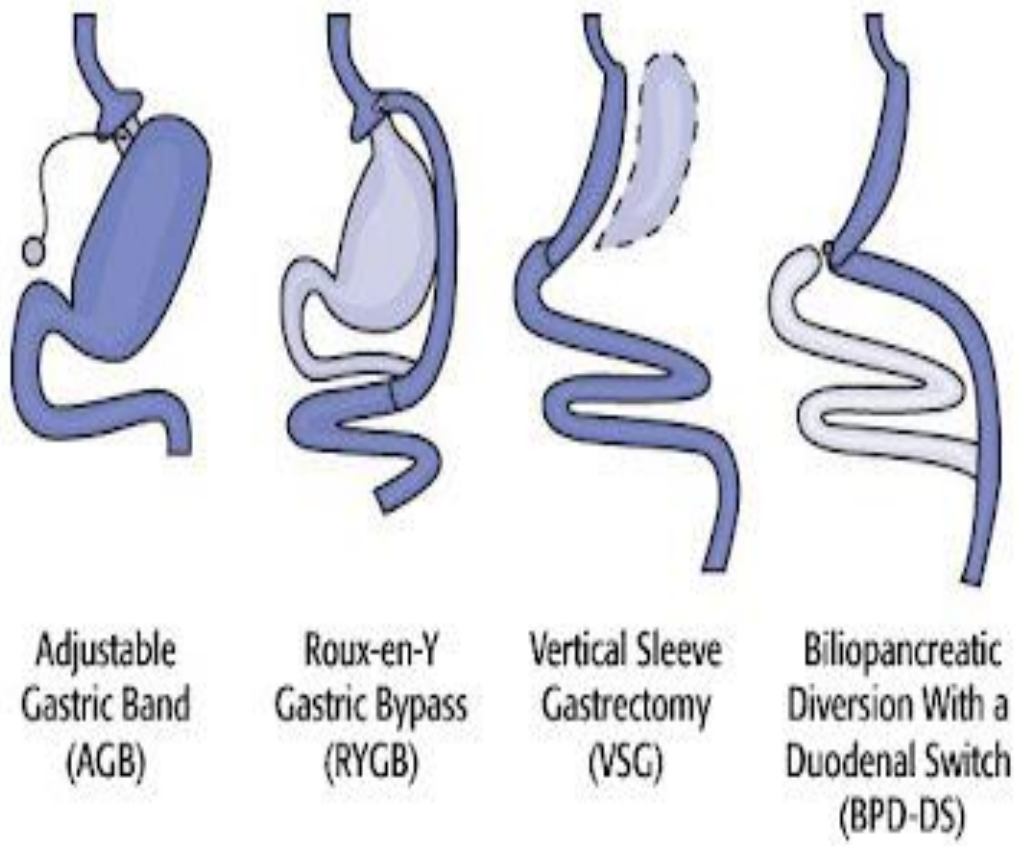
Beginning in November,1944 until April,1945 when the they were liberated by the Allies, the Dutch had little to eat except tulip bulbs - thousands starved to death.

In May, 1945, the Dutch spelled out "MANY THANKS" in tulips to the Allied planes as they flew over distributing food.



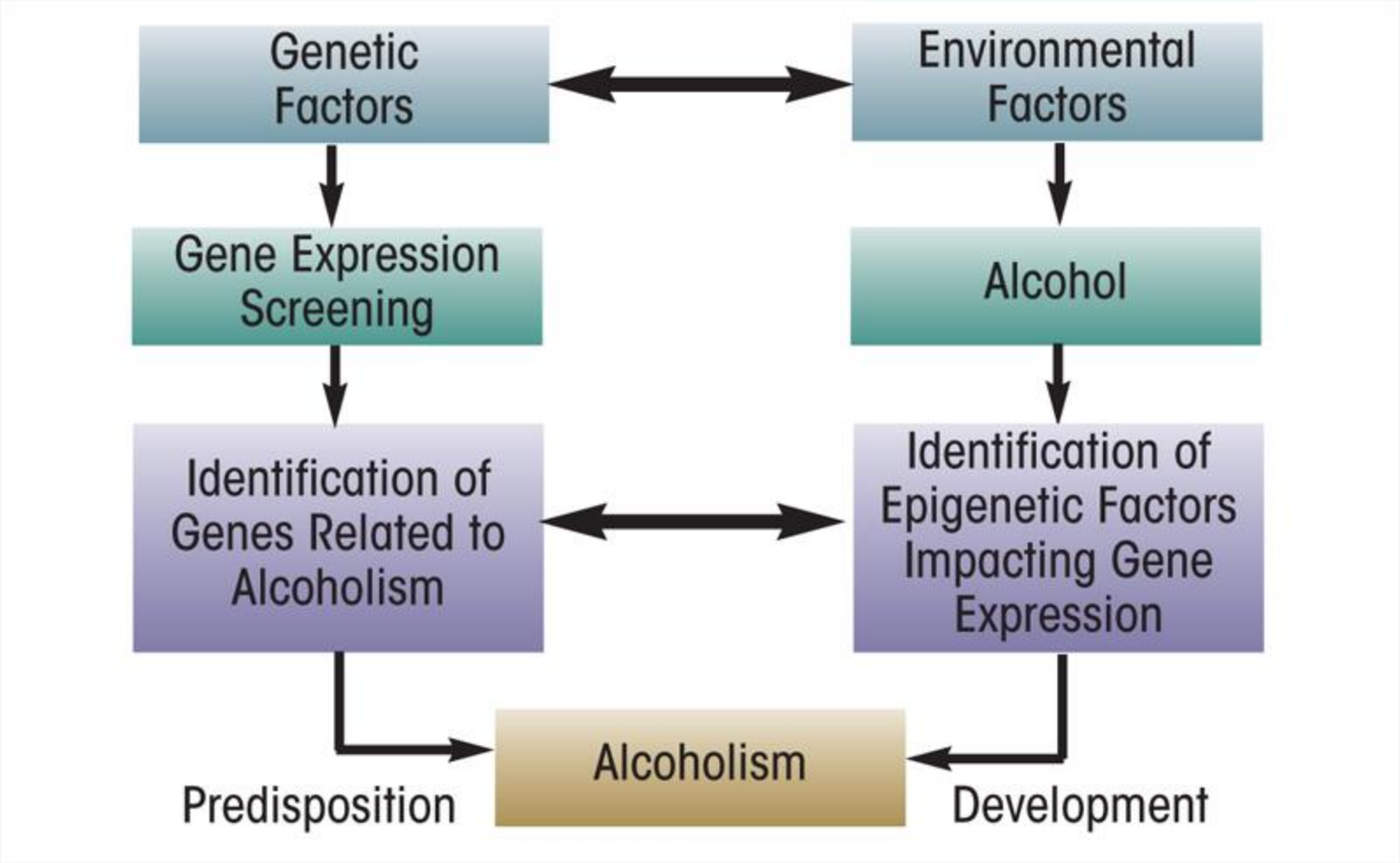
Epigenetic Inheritance and Obesity

There are 4 common types of the Bariatric Surgery: AGB, Roux-en-Y gastric bypass (RYGB), biliopancreatic diversion with a duodenal switch (BPD-DS), and vertical sleeve gastrectomy (VSG).



http://www.win.niddk.nih.gov/publications/gastric.htm Image credit: Walter Pories, M.D. FACS

Hypothetical Model of Interactions Between Genetic Factors and Environmental Factors Resulting in Alcoholism



http://pubs.niaaa.nih.gov/publications/arcr343/293-305.htm

Epigenetic Inheritance and Smoking

A 2012 study published *in Human Molecular Genetics* found strong evidence that tobacco use can chemically modify and affect the activity of genes through hypomethylations which are known to increase the risk of developing cancer.

This was the first study to establish a close link between epigenetic modifications on a cancer gene and the risk of developing the disease.

Photo: http://www.pbs.org/newshour/rundown/cdc-lung-cancer-rates-drop-dramatically/

Smoking Affects Both Mother and Child

Another study published in 2012 in *Environmental Health Perspective* identified a set of genes including *AHRR* and *CYP1A1* with methylation changes present at birth in children whose mothers smoked during pregnancy.

Photo: chp.niehs.nih.gov/120-a402a/