



Mini Med School VIII

Demystifying the research, engaging the public

Epigenetics!

Glossary

Fall 2007

Epigenetics: It's all around you!

Research Education

Training ♦ Support ♦ Opportunities



Welcome to the Mini Med School at the Child and Family Research Institute

On behalf of the Faculty and Staff at the Child and Family Research Institute (CFRI), we would like to welcome you to CFRI's 8th annual Mini Med School. We are looking forward to offering you an engaging program of activities and insights on cutting edge health research.

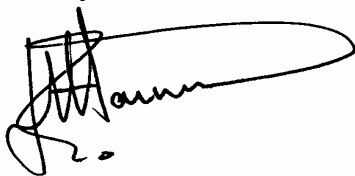
This semester, you will be studying topics in **Epigenetics** with some of the leading researchers and clinicians in the field. The curriculum of six sessions was designed by this term's Mini Med School Co-Deans, **Drs. Angela Devlin, Michael Kobor, and Wendy Robinson**, along with members of the Mini Med School faculty. The Research Institute is pleased to support Drs. Devlin, Kobor, and Robinson, along with all of the investigators who are donating their time and expertise over the next six weeks.

We are again pleased to welcome many local high school students into our program this term, and sincerely hope that Mini Med School might inspire these young and curious minds towards a future in health research. In fact, we invite high school students with good attendance records at the Mini Med School to apply for a summer studentship through the program. The studentship is an opportunity to gain research experience during the summer break. Details on this competition will be announced during the series.

As health researchers and clinicians, we know that the public is keenly interested in our work and its impact on the social wellbeing of children and families. It is not always easy to find the time and the best ways to convey this information. We hope that the Mini Med School series will be a step in this direction.

Enjoy your studies with us!

Sincerely,



Dr. Geoff Hammond
Scientific Director,
Child and Family Research Institute

A

Acetylation

Enzymatic addition of an acetyl group(s) to a molecule. Acetylation/ deacetylation of histone groups regulates gene activity by affecting which genes are switched off/on.

ACTH

Adrenocorticotrophic hormones (ACTH) are produced by the pituitary gland in the brain and stimulate the production of hormones in the adrenal cortex.

Adenine

One of five nucleotide bases present in nucleic acids. Adenine pairs with thymine (DNA) or uracil (RNA).

Agouti gene

In mice, the agouti (A) gene controls the deposition of yellow pigment in developing hairs. There are several alleles (DNA sequence variants), some of which are dominant e.g. lethal yellow (Ay), which results in embryonic lethality if mice inherit 2 copies. Methylation of the agouti gene reduces its expression, lowering the quantity of yellow pigment produced without altering the sequence of the gene.

Allele

One of the alternative versions of a gene. Each allele is the result of variation in DNA sequence.

Amino Acid

The building blocks of protein, for which DNA carries the genetic code.

B

Vitamin B12 or Cobalamin

An essential water soluble vitamin found at high levels in meat, fish and dairy products. It is required for the synthesis of DNA, for maintenance of the nervous system and red blood cells, and for methylation reactions. Vitamin B12 deficiency can present clinically as megaloblastic anemia and poor status is associated with hyperhomocysteinemia and disrupted methyl group metabolism. Intestinal absorption of vitamin B12 requires a protein called intrinsic factor, which is produced by the stomach. Absence of intrinsic factor results in poor absorption of vitamin B12 and a condition known as pernicious anemia.

Base (organic)

There are two classes of nucleotide bases (purines and pyrimidines) found in DNA and RNA. Adenine and guanine are purines; cytosine, thymine and uracil are pyrimidines.

Betaine or Trimethylglycine

A nutritional component found at high levels in sugar beets (beet root), whole wheat, and shellfish. Our bodies can also synthesize betaine from choline. Similar to MTHF, betaine can serve as a methyl group donor during the recycling of homocysteine to methionine.

Blood alcohol level

The level of alcohol that can be measured in the blood.

Biological embedding of early experience

Biological embedding occurs when: experience alters human development; systematic differences in experience (e.g. different social environments) lead to different developmental states; and the differences are stable, long-term, and influence health, well-being, learning, and/or behaviour over the life course.



Cell

Cells are the membrane-bound units of which biological material is composed. First visualised by Robert Hooke in the 1600s as the small compartments that comprise a piece of cork.

Chaperone

Cellular machinery that facilitates correct assembly of complex molecules.

Choline

Choline is an essential nutrient found at high levels in eggs, soy and liver. It has three important biological functions: (i) required for the synthesis of phosphatidylcholine, a phospholipid and important component of cell membranes; (ii) required for the synthesis of the neurotransmitter, acetylcholine; and (iii) serves as a precursor in the synthesis of betaine and is therefore important in methylation reaction. Choline deficiency can cause liver damage.

Chromatin

The complex of DNA and protein in the nucleus of a cell.

Chromosome

The DNA of a cell is packaged into discrete units called chromosomes.

Cloning

Term coined by JBS Haldane in the 1960s to describe the process whereby humans can mimic the natural process of identical twinning. Therapeutic cloning is that undertaken to harvest special cells for therapeutic use (embryos are not developed to term), whereas reproductive cloning describes that undertaken to clone whole organisms.

Codon

A triplet of three consecutive bases in a DNA or RNA molecule, specifying a single amino acid.

Corticosterone

A hormone produced by the adrenal cortex (outer layer of adrenal gland) in animals.

Cortisol

A hormone produced by the adrenal cortex (outer layer of adrenal gland) in humans.

Cytosine

One of five nucleotide bases present in nucleic acids. Cytosine always pairs with guanine in DNA, and may become methylated where it occurs consecutively to guanine in the DNA sequence (see 5-methylcytosine).



Developmental Origins of Health and Disease (DOHaD)

This is a concept or theory that suggests that exposure to environmental factors, such as nutritional components, during key stages of prenatal or early postnatal development may 'program' an individual's metabolic response to nutritional components in adulthood and enhance risk for chronic conditions such as heart disease, diabetes, obesity, and high blood pressure. This theory is founded on human population-based studies. Recent studies in animal models suggest that metabolic programming may involve epigenetic mechanisms.

DNA (deoxyribonucleic acid)

DNA is the molecular material of which our genes are made. It has a double-helically coiled sugar-

phosphate backbone, held together by organic base pairs (adenine with thymine, cytosine with guanine). This generates 2 complementary strands of base-pairs. The entire sequence of the human genome contains more than 3 billion base-pairs.

DNA methylation

A reversible biochemical modification of DNA apparently universal to vertebrates. Methyl groups can be enzymatically added to or removed from cytosine (C) bases in the DNA molecule. Associated with regulation of gene expression, and especially silencing of gene expression.

DNA repair genes

Normal metabolic activities and environmental factors can cause DNA damage (e.g. mutation of an A to T). DNA repair genes make enzymes that fix such mishaps (e.g. DNA glycosylases).

DNA sequence

The sequence of bases along a strand of DNA. There are four organic bases, adenine (A) pairs with thymine (T), cytosine (C) pairs with guanine (G). The DNA sequence of a gene will determine the amino-acid composition of a protein.



Embryo

A term used to describe the early life stage of a developing organism after fertilisation. In humans, the embryo begins after fertilisation and persists up until week 8 of pregnancy.

Endocrine disruptor

Some endocrine disruptors prevent hormones from interacting with certain receptors by blocking the receptor site on a cell. Others directly stimulate or inhibit the endocrine system and cause overproduction or underproduction of hormones.

Endocrine system

Refers to the system of glands and tissues in the body that secrete hormones.

Endosperm

The nutritive tissue surrounding the developing embryo within the seeds of flowering plants. Formed from a double-fertilisation event involving two female nuclei and one male nucleus.

Enzyme

A protein that facilitates a specific biochemical reaction. Many enzymes work together to build and break down biomolecules within the cell. Enzymes also affect the transcription and translation of DNA into RNA and protein.

Epigenetic code

Both DNA methylation and histone modifications specifically modify the way that genes are expressed. This has led to the theory that, in addition to the genetic code, there is an epigenetic code which serves to modify the underlying instructions.

Epigenetic marks

Features not governed by the genetic code, which include methylation of DNA and covalent modification of histone proteins. The latter may be tagged with methyl, acetyl, ubiquitin, phosphate and some other biochemical groups, which modify their behaviour and influence the way genes are expressed.

Epigenetic mechanisms

For example, DNA methylation and histone modifications.

Epigenetics

The study of heritable changes in gene function not controlled by changes in the DNA sequence. Epigenetic phenomena are thought to play a significant role in development and evolution, and include histone modifications and DNA methylation.

Epigenome

Refers to all epigenetic features of an organism.



Fetal Alcohol Spectrum Disorder

This term describes the range of physical, physiological and behavioral disabilities that may affect people whose mothers drank alcohol while they were pregnant.

Fetal programming

The concept that prenatal (in utero) exposure to maternal/environmental factors can affect fetal development, leading to altered physiological and behavioural responses in later life. (see DOHaD)

Folate or Folic Acid

A dietary essential nutrient (the body cannot make it) and one of the water-soluble B-vitamins. There are three main sources of folate in our diet: (i) the naturally occurring form found in foods such as leafy green vegetables (eg spinach) and meat, especially liver; (ii) fortified foods including enriched flour and cereal products; (iii) vitamin supplements. Folate is important for DNA replication, normal production of red blood cells, and methylation reactions. Folate deficiency presents clinically as megaloblastic anemia and poor folate status is associated with hyperhomocysteinemia and disrupted methyl group metabolism.



Gene

The basic unit of the genetic code, composed of DNA. Required for production of a functional product (eg. RNA, protein).

Gene expression

The process by which the heritable information encoded by a gene (contained in the DNA sequence) produces a physical and biologically functional gene product such as RNA or protein. Epigenetic mechanisms play an important role in regulating gene expression.

Gene regulation

The modulation of gene expression. Genes are regulated at the level of DNA, RNA and protein, whose interactions are a direct consequence of their immediate biochemical environment.

Genetic code

The genetic code is comprised of codons. Genes are frequently tens of thousands of base-pairs long. This makes for some fairly long chains of amino acids, and a wide variety of different possible proteins.

Genetic information

The “code” contained within the DNA sequence.

Genome

The entire DNA sequence of an organism. This information is replicated in the nucleus of nearly every body cell but not every gene is switched on in every cell. Full genome sequences are available for human (cf. human genome project) and other organisms such as mouse, frog, roundworm and fruit fly.

Genomic imprinting

Describes asymmetrical inheritance of alleles (activation or silencing). ~200 mammalian genes are inherited in an active/silent manner depending on whether they are inherited from the mother or father.

Gestation

The period of *in utero* development during pregnancy.

Guanine

A nucleotide base found in nucleic acids. Guanine always pairs with cytosine in DNA and RNA.



Hdac

Histone deacetylase (HDAC) is an enzyme that influences the process of transcription (DNA to RNA). It removes the acetate groups from the lysines (amino acids) within histone proteins, causing genes to switch off. In diseases such as cancer, lupus and Huntington's disease, the regulation of histone acetylation is out of balance. HDAC inhibitors have been shown to be effective in cancer chemotherapy.

Hdac inhibitor (HDACI)

Small molecules used as anti-cancer drugs. They bind to HDAC enzymes and inhibit their activity. HDACs are all out of kilter in cancer cells; HDACIs can help to redress the balance between these enzymes and their histone acetyltransferase (HAT) counterparts.

Heterochromatin

Highly condensed parts of chromosomes (see chromatin), where genes are generally inactive. Further sub-divided into constitutive (stably inactive) and facultative (inertia reversible). Certain epigenetic marks (e.g. DNA methylation, histone hypo-acetylation, methylation of lysine 9 on histone H3) are features of this inactive form of chromatin.

Histone

The most common protein in the nucleus, around which DNA is wrapped. There are five major types of histone. Along regular intervals of the genome, histones H2-H4 are arranged into nucleosomes (bundles). These proteins may be modified by enzymes, which affects gene expression and chromatin state (euchromatin vs. heterochromatin).

Homocysteine

A non-protein forming, sulphur-containing amino acid generated during the metabolism of methionine or the 'methionine cycle'.

Hormone

A chemical messenger that carries signals from one cell to another.

Housekeeping genes

Genes required throughout development for the smooth running of the cell. Housekeeping genes are always switched on.

Hypothalamic-pituitary-adrenal (HPA) axis.

One of the major stress regulation systems of the body. Describes the cascade of hormone responses (from hypothalamus [area at base of brain] to pituitary gland [in brain] to adrenal gland [on kidney]) that result ultimately in release of stress hormones (cortisol or corticosterone) from the adrenal cortex.

Hyperhomocysteinemia

Elevated blood levels of homocysteine that occur in certain health conditions such as kidney disease and hypothyroidism, and also as a result of poor B vitamin nutritional status, especially folate. Hyperhomocysteinemia is associated with several adverse health conditions such as heart disease, stroke, birth defects, Alzheimer's disease, and osteoporosis. Disrupted methyl group metabolism occurs in hyperhomocysteinemia.

M

Methionine

A sulphur-containing dietary essential amino acid found in fish, meat, eggs, and sesame seeds. Methionine has two important biological functions: (i) required component of proteins; and (ii) synthesis of S-adenosylmethionine or SAM, which serves as a methyl donor in methylation reactions.

Methylation

Enzymic addition of a methyl group(s) to a molecule.

Mitochondrial DNA

The DNA in the circular chromosome of the mitochondria. mDNA is present in many copies per cell, is maternally inherited, and evolves 5 to 10 times as rapidly as does genomic DNA.

Monozygotic twins

Twins derived from a single fertilized ovum. MZ twins are identical genetically, but diverge epigenetically.

MTHF - Methyltetrahydrofolate

This is a biological derivative of folate or folic acid that serves as a methyl group donor during the recycling of homocysteine to methionine.

MTHFR - Methylenetetrahydrofolate Reductase

An enzyme that functions to produce MTHF. A genetic variant (mutation) in the *MTHFR* gene, referred to as C677T, results in diminished ability of the enzyme to produce MTHF. This variant is very common, found in about 10-20% of Caucasians. Individuals with this variant have increased blood homocysteine levels, disrupted methyl group metabolism and require more folate in their diet.

N

Neuroendocrine

Neuroendocrine cells are a specialized group of nerve cells that produce hormones. The hormones are packaged in small vesicles and sent via long processes to blood vessels. The hormones then travel to their target cells and may stimulate, inhibit or maintain function of these cells.

Nucleosome

A small bundle of histones (H2-H4) around which DNA is wrapped at regular intervals within the nucleus of the cell.

Nucleotide

A molecule composed of a nitrogenous base, a 5-carbon sugar, and a phosphate group. A nucleic acid is a polymer of many nucleotides.

Nucleus

Organised membrane-bound compartment within eukaryotic cells that contains the genome and associated histone proteins.

P

Placenta

Temporary membranous vascular organ that develops in mammals when young are developing in the womb. Attaches to the foetus via the umbilical cord, and is expelled after birth.

Prion

An infectious agent composed only of protein. Prions are believed to be heritable and can infect or propagate by refolding abnormally into a structure which is able to convert normal molecules of the protein into the abnormally structured form, e.g. mad cow disease.

Protein

A polypeptide chain or complex of polypeptide chains, each consisting of a long string of amino acids. Amino acid sequences are specific to each protein, and are specified by the underlying DNA sequence of the gene that encodes that protein.

R

RNA (Ribonucleic acid)

A nucleic acid formed upon a DNA template, containing ribose instead of deoxyribose, and uracil instead of thymine. Messenger RNA (mRNA) is the template upon which polypeptides are synthesized. Transfer RNA (tRNA), in cooperation with the ribosomes, brings activated amino acids into position along the mRNA template. Ribosomal RNA (rRNA), a component of the ribosomes, functions as a non-specific site of polypeptide synthesis.

RNA interference

A recently discovered mechanism of gene silencing. Small double-stranded RNA sequences made naturally or artificially introduced can interrupt the process of translation (mRNA to protein), thus preventing gene expression.

S

Sex Chromosomes

The X and Y chromosome are a unique pair of chromosomes with the Y being sex-determining such that 46,XY = male and 46,XX = female (the 46 refers to the total number of human chromosomes = 2 of each of 22 autosomes, and 2 sex chromosomes).

Sir2

A protein found in yeast (with versions in other organisms) that has been found experimentally to increase lifespan. At the molecular level Sir2 removes chemical (acetyl) groups from histone proteins and has the overall effect of silencing regions of the genome.

SiRNAs

Small-interfering RNAs (involved in RNA interference). A process that both naturally occurs in cells and is being used as a technology to switch certain genes off.

Stem cell

A cell that has the ability to divide for indefinite periods in culture and to give rise to specialized cells.

- *Adult stem cells:* Adult stem cells are undifferentiated cells found throughout the body that divide to replenish dying cells and regenerate damaged tissues. These cells are able to generate all the cell types of the organ from which they originate.
- *Embryonic stem cells:* Self-renewing cells isolated from the inner cell mass of a developing embryo (compare adult stem cells).
- *Hematopoietic stem cell:* Precursors of mature blood cells that give rise to all red and white blood cells and platelets.

Stress

A state of threatened homeostasis or balance in the body.

T**Thymine**

One of five nucleotide bases found in nucleic acids. Thymine always pairs with adenine in DNA.

Teratogen

An agent that causes a birth defect.

Transcription

The transfer of genetic information from DNA into RNA. This is the first step in the process by which the information encoded by a gene (DNA sequence) is translated into a functional protein or peptide.

Translation

The process of converting the genetic information in the RNA into proteins.

Uracil

One of five nucleotide bases present in nucleic acids. Uracil is found only in RNA, and pairs with adenine.

X**X-chromosome**

One of the two sex-determining chromosomes in many animal species, including mammals (the other is the Y chromosome).

X-inactivation

Phenomenon whereby one of the two X-chromosomes in female mammals is randomly inactivated in every cell.

Y**Yeast**

Cellular and/or filamentous fungus. There are two kinds (fission and budding yeast) that are used extensively for genetic research.

Some definitions have been selected from a webpage dedicated to epigenetics (<http://epigenome.eu/>)