# NEUR 1520 Neuroscience Study Guide for Exam 2: Lecture 15: Experience and Gene Expression

Sources: the lecture slides and The Mind's Machine, Chapter 4. Nothing else.

Each heading is one book learning objective. [L13 s08] = Lecture 13, slide 8. [MM p124] = book page 124.

*(teal italics) = plain meaning of the word before it.* ⚠ **Do not mix up = a look-alike pair to keep apart.** **Amber dotted words** = names printed on the figure beside them.

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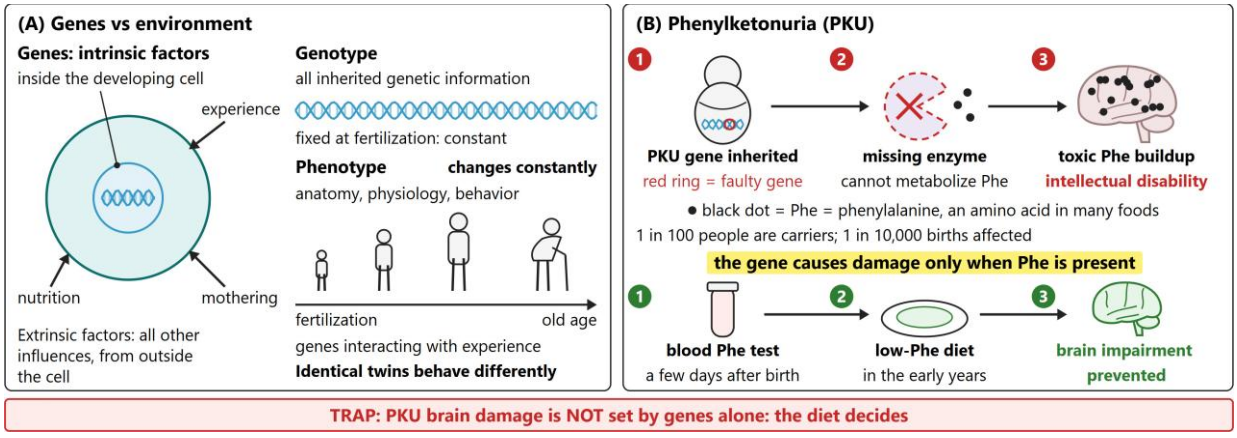
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## 4.3.1 Describe how the environment can regulate gene expression and how experience and genes interact to affect behavior

⚠ **Do not mix up: Genotype does NOT change with experience: phenotype does, through extrinsic effects on genes.** [L15 s05, MM p135]




*Genes against environment, genotype and phenotype over life, and how PKU damage is prevented* [MM p134]

**On the figure:** genotype · phenotype · intrinsic factors · extrinsic factors · identical twins · phenylalanine · intellectual disability · low-Phe diet

**Genotype**: sum of all the intrinsic, genetic information an individual has; constant. [L15 s05, MM p135]

Genotype is all the genetic information one individual has inherited. [MM p135]

Genotype is set at the moment of **fertilization** *(sperm joins egg)* and stays the same for life. [MM p135]

**Phenotype**: sum of an individual's physical characteristics at one particular time. [L15 s05, MM p135]

Phenotype includes anatomical, physiological, and behavioral characteristics. [MM p135]

Phenotype changes constantly, based on extrinsic effects on genes, as we grow up and grow old. [L15 s05, MM p135]

Phenotype changes even in a tiny way with each breath. [L15 s05, MM p135]

Phenotype is set by genotype interacting with **extrinsic factors**, including experience. [MM p135]

**Intrinsic factors**: genes, which originate within the developing cell itself. [L15 s05, MM p134]

**Extrinsic factors**: all other influences, which originate outside the developing cell. [L15 s05, MM p134]

Genes direct the production of every protein a cell can make. [MM p134]

An altered gene makes an altered protein, affecting every cell that uses that protein. [MM p134]

So every neural structure, and every behavior, can be altered by changes in genes. [MM p134]

**Identical twins**: same genotype, but differences in neural phenotypes produce different behaviors. [L15 s05, MM p135]

Identical genotypes do not give identical phenotypes, because extrinsic influences are never identical. [MM p135]

Hundreds of genetic disorders of protein, carbohydrate, or lipid **metabolism** *(body chemistry processing)* harm the developing brain. [MM p135]

Typical defect: a missing **enzyme** *(protein that runs a reaction)* for a key step making or breaking down a body product. [MM p135]

**Phenylketonuria (PKU)** *(inherited protein metabolism disorder)*: an important example of genes and environment interacting. [L15 s05, MM p135]

PKU defect: no enzyme to metabolize **phenylalanine** (Phe) *(amino acid in many foods)*. [MM p135]

Phenylalanine builds up to toxic levels, damaging the brain and causing **intellectual disability**. [MM p135]

About **1** in **100** people is a PKU carrier; **1** in **10,000** births is affected. [MM p135]

PKU was the first inherited error of metabolism linked to intellectual disability. [MM p135]

Blood phenylalanine is measured in children a few days after birth, for early detection. [MM p135]

**Low-Phe diet** *(reducing phenylalanine in food)* prevents brain impairment; most critical in early years. [MM p135]

Low-Phe meal example: fruit and protein-free rice and pasta, without cheese. [MM p135]

Gene plus environment: the faulty gene causes intellectual disability **only** when phenylalanine is present. [MM p135, MM p141]

So genotype alone cannot predict brain development: you must also know the child's diet. [MM p135]

Second reason genes are not the whole story: experience changes the activity of genes. [MM p135]

Adult human intelligence comes from inherited genes plus experience deciding where and when genes are expressed. [MM p137]

The large brain growth after birth is molded by experience and social guidance. [MM p137]

Review: new adult neurons grown with exercise, socializing, and mental stimulation is brain **neurogenesis**. [L15 s02, L15 s03]

Review: synapses that strengthen or weaken by effectiveness driving the target cell are **Hebbian synapses**. [L15 s02, L15 s03]

### Genotype vs phenotype

| | Genotype | Phenotype |
|---|---|---|
| **What it is** | All intrinsic, genetic information | Physical characteristics at one time |
| **Includes** | Genes | Anatomy, physiology, behavior |
| **Over life** | Constant, fixed at fertilization | Changes constantly |
| **Set by** | Genes inherited | Genotype plus extrinsic factors, experience |

Table source: [L15 s05, MM p135]

### Intrinsic vs extrinsic factors

| | Intrinsic factors | Extrinsic factors |
|---|---|---|
| **What** | Genes | All other influences |
| **Origin** | Within the developing cell | Outside the developing cell |
| **Examples** | Inherited gene, altered gene | Diet (nutrition), experience, mothering |

Table source: [L15 s05, MM p134, MM p135]

## 4.3.2 Define epigenetic changes, and explain how they might play a role in the interaction of genes and the environment

⚠ **Do not mix up: Epigenetic changes alter gene EXPRESSION, NOT the nucleotide sequence of the gene.** [L15 s06, MM p135]

**Clones**: asexually produced organisms that are genetically identical. [L15 s06, MM p135]

Cloned pigs vary in behavior and temperament as much as normal siblings do. [MM p135]

Genetically identical mice raised in different laboratories behave very differently on many tests. [MM p135]

Nearly every cell has the full genotype but uses **only** a small subset of genes at once. [MM p135]

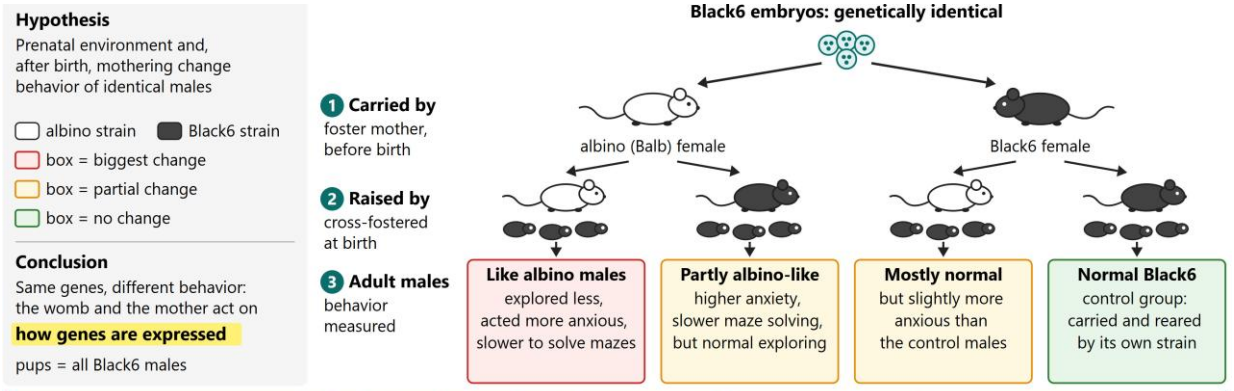
**Gene expression**: a cell uses a particular gene to make that gene's protein. [MM p135]

**Epigenetics**: study of factors that change gene expression without changing the gene sequence. [L15 s06, MM p135]

The same protein is made, but the amount varies a lot, so brain development varies. [MM p135]

Genetically identical mice raised by different mothers show different behaviors. [L15 s06, MM p136]

Hypothesis: prenatal environment and/or mothering after birth can change behavior of genetically identical male mice. [L15 s07, MM p136]




*Identical Black6 embryos carried and raised by different mothers grow into males who behave differently* [L15 s07]

**On the figure:** Black6 · Balb · cross-fostered · albino · genetically identical

**1.** **Genetically identical Black6** embryos are implanted into a Black6 or **albino** (**Balb**) mother before birth. [L15 s07, MM p136]

**2.** At birth, males are **cross-fostered** *(switched to another mother)* to a Black6 or albino mother. [L15 s07, MM p136]

**3.** Adult male behavior is measured on maze running and anxiety, where the strains normally differ. [L15 s07, MM p136]

Conclusion: same genes, so differences come from prenatal environment and mothering altering gene expression. [L15 s07, MM p136]

Genetically identical individuals may behave very differently because of different epigenetic influences. [MM p141]

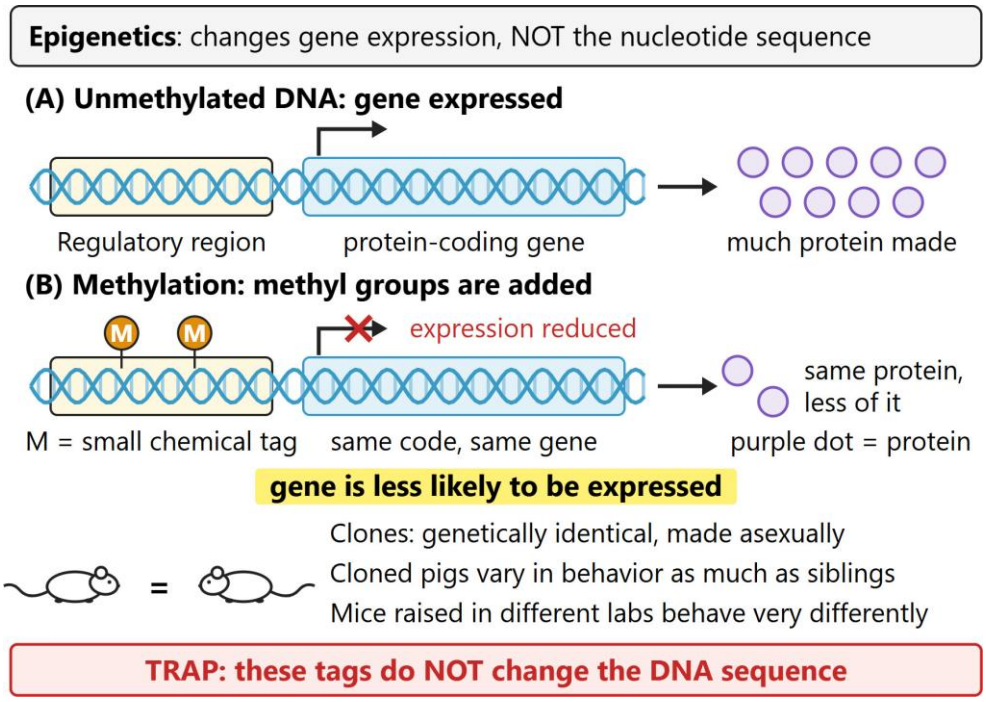
### Cross-fostered Black6 mice

| Carried by | Raised by | Adult male behavior |
|---|---|---|
| **Black6** | Black6 | Normal Black6, as expected |
| **Black6** | Albino | Mostly normal Black6, slightly more anxious |
| **Albino** | Black6 | Partly albino-like: anxious, slow mazes, explores normally |
| **Albino** | Albino | Like albino: explore less, anxious, slow mazes |

Table source: [L15 s07, MM p136]

## 4.3.3 Describe the mechanism by which rodent dams can alter their offspring's lifelong stress response

⚠ **Do not mix up: Poor mothering means MORE methylation, FEWER stress hormone receptors, but HIGHER stress hormone levels.** [L15 s09, MM p137]




*Unmethylated gene makes much protein; methyl groups on the regulatory region reduce expression* [MM p135]

**On the figure:** unmethylated DNA · methylation · methyl groups · regulatory region · protein-coding gene

**Methylation**: chemical change to DNA; same nucleotide sequence, but gene is less likely to be expressed. [L15 s08, MM p136]

**Unmethylated DNA**: no **methyl groups**, so the gene is expressed and much protein is made. [L15 s09, MM p137]

**Methylation**: same code, same gene, expression reduced; same protein, less of it. [L15 s08, MM p135, MM p136]

A **protein-coding gene** *(DNA stretch that makes a protein)* sits next to its **regulatory region**. [L15 s09, MM p134, MM p137]

Methyl groups attach at the gene's **regulatory region** *(stretch that controls the gene)*. [L15 s09, MM p137]

Pups with inattentive mothers, or interrupted maternal care, secrete more **glucocorticoids** *(stress hormones)* under stress as adults. [MM p136]

Poor maternal care induces methylation of the **glucocorticoid receptor gene** *(stress hormone receptor gene)* in the brain. [L15 s08, MM p136]

Result: rodent pups become hyperresponsive to stress for the rest of their lives. [L15 s08, MM p136]

1. Mother gives **low licking and grooming** to pups. [L15 s09, MM p137]
2. **Methyl groups** are added to the **stress hormone receptor gene**'s **regulatory region**. [L15 s09, MM p137]
3. **Gene expression** is reduced, so fewer hormone receptors are expressed in the brain. [L15 s09, MM p137]
4. Adult has high **stress hormone levels** and high anxiety. [L15 s09, MM p137]
5. Adult daughter gives low licking and grooming to its own pups. [L15 s09, MM p137]

Attentive mothers prevent methylation, so their daughters grow up to be attentive mothers too. [L15 s09, MM p137]

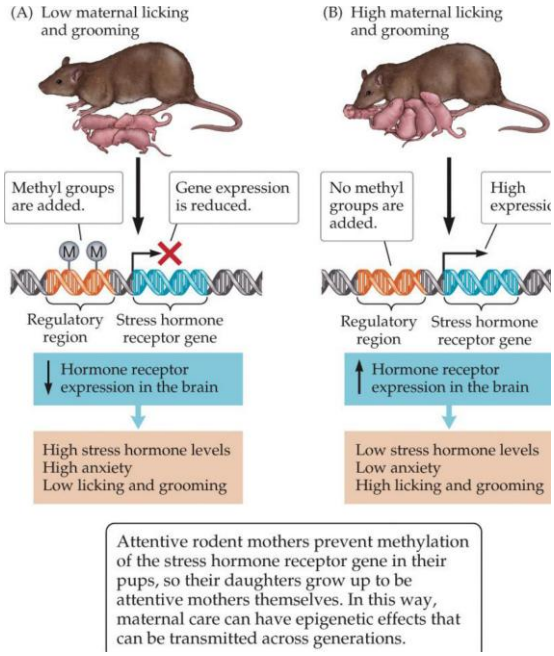
So maternal care has epigenetic effects that can be transmitted across generations. [L15 s09, MM p137]

In humans, the same gene is methylated in people who suffered childhood abuse. [L15 s08, MM p136]

The gene is more often methylated in postmortem brains of suicide victims abused as children. [MM p136]

Suicide victims not abused as children were no more likely than controls to have it methylated. [MM p136]

Suggests methylation in abused children may make them hyperresponsive to stress as adults. [MM p136]




*Low licking adds methyl groups and lowers receptors; high licking does the opposite* [L15 s09]

**On the figure:** **methyl groups** · **regulatory region** · **stress hormone receptor gene** · **stress hormone levels** · **low licking and grooming** · **high licking and grooming** · **gene expression**

Mothering is an environmental factor that can affect gene expression. [MM p141]

### Low vs high licking mothers

| | Low licking and grooming | High licking and grooming |
|---|---|---|
| **Methyl groups** | Added | Not added |
| **Receptor gene expression** | Reduced | High |
| **Brain hormone receptors** | Decreased | Increased |
| **Stress hormone levels** | High | Low |
| **Anxiety** | High | Low |
| **Daughters as mothers** | Low licking and grooming | High licking and grooming |

Table source: [L15 s09, MM p137]