Lecture 8 (FW)
February 12, 2007
Gene Expression
Reading: pp.51-62 again; pp. 143-154 of Ch. 10

I. Not all phenotypic characters are encoded in one gene. In fact, most traits are "**polygenic**".

A. Mendel was lucky. Many, perhaps most phenotypic traits, are the result of the action of many genes. They are so-called polygenic traits. Crosses involving polygenic traits may give results that look like "blending". This makes the analysis of their inheritance in experimental animals very difficult, and it also makes the reconstruction of the heredity in human pedigrees very challenging. In the case of skin color in humans, it is know that at least 4 different genes, each with several different variants and differing in degree of expression, can affect skin color. The same is true for height, weight, many congenital malformations (cleft palate) and genetic disorders like diabetes. Many of the traits that we wish to know more about are polygenic, and it is difficult to discern what is the contribution of the environment (nurture) and what the contribution of the genes (nature). We'll look at this issue again later in the course.

II. Genes that are present on the **sex chromosomes** can show unusual modes of inheritance.

A. Gender differences in **X linked** recessives. Hemophilia.

X-linked traits will only have one representative of the gene in males, but two in females.

B.We discussedin lecture 7 the transmission of the hemophilia gene in the deescendatnts of Queen Victoria of Britain, The trait is usually only expressed in males because it is a recessive; since it is on the X chromosome, and males only have one X, the trait is expressed. Since females have 2 X chromosomes, the recessive trait is not expressed if the allele on the other chromosome is normal. Hence, the female is a "carrier". See pp. 183-184 on the book.

III. Variable Expression.

A. Some genes are not expressed in all persons who inherit that gene. This kind of variability is called **penetrance**. If the persons who do have the phenotype caused by that gene are afflicted to varying degrees, this is called a variation in **expressivity**.

B. Some genes are not penetrant early in life, but do show up later in life.

1. Huntington's Chorea is a serious affliction of humans, an autosomal dominant; its effects (loss of mental faculties, psychosis, and death) are usually not seen until age 30-50. Likewise, porphyria, a disturbance of the metabolism of the precursor of heme, is not seen until middle age.

C. The environment may profoundly affect the penetrance and expressivity of a gene.

1 .The presence of a mutant gene does not guarantee its manifestation in the phenotype. In addition to being recessive, there are many other factors that affect whether there is an obvious phenotypic expression. There may be environmental factors that affect expression. For example, both Siamese cats and Himalayan rabbits show darker pigmented hair on the ends of the limbs. This is because the temperature of the skin at the

ends of the extremities is somewhat cooler, and the enzyme responsible for pigment synthesis is somewhat temperature sensitive, only working well at lower temperatures.

The extent to which environment and the genotype contribute to the phenotype of an individual is an important question, but it is very difficult to evaluate. The topic will be considered later in the course.

D. One important environmental factor is the influence of hormones.

1. One example of this is an apparent hermaphrodite in humans, which is an X linked trait called "**androgen insensitivity**", in which chromsomal males (XY) develop as females. This mutation is a "loss of function" mutation of the receptor for testosterone. In afflicted individuals the genitalia and secondary sexual characteristics are female, but no internal female reproductive organs form. The reason for this is that the XY embryo, since it is male, produces a hormone early in development called "anti-Mullerian Duct Hormone", and this hormone causes female reproductive organs like Fallopian tube and uterus to wither away. But, since the tissues of the body cannot respond to testosterone, which is necessary for testis development and differentiation of male secondary sexual characteristics, including genitalia, the external phenotype of the affected individual is female. So, the genes for sexual differentiation work through the action of hormones, and **receptors of hormones**, which are themselves encoded by other genes.

III. The regulation of gene expression

A. There are genes that encode proteins which are part of the chromatin/chromosome.

1. Some of these proteins are necessary for the normal cell cycle and mitosis/meiosis.

2. Still other proteins can serve to interact with the DNA to prevent RNA polymerase from carrying out transcription. This is not a permanent genetic change, but a temporary and reversible one. In other words, these kinds of mechanisms affect the read-out of the DNA instruction booklet, but do not interfere with the inheritance of genes.

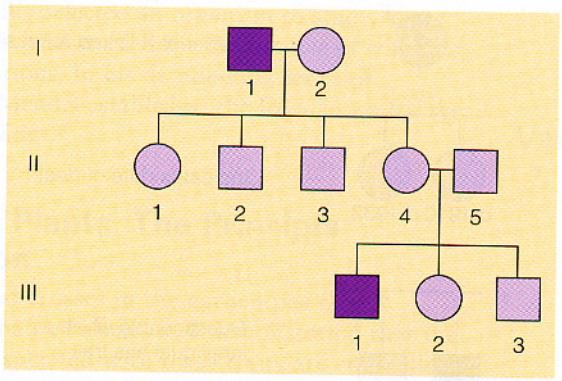
B. There are also many genes that make proteins whose function is to regulate transcription of other genes. In other words, some genes regulate other genes. This works because these protein interact with **RNA polymerase**, and with certain DNA sequences in the regions between promoters, to either **enhance** or **suppress transcription**. This is at the basis of embryonic development and cell specialization.

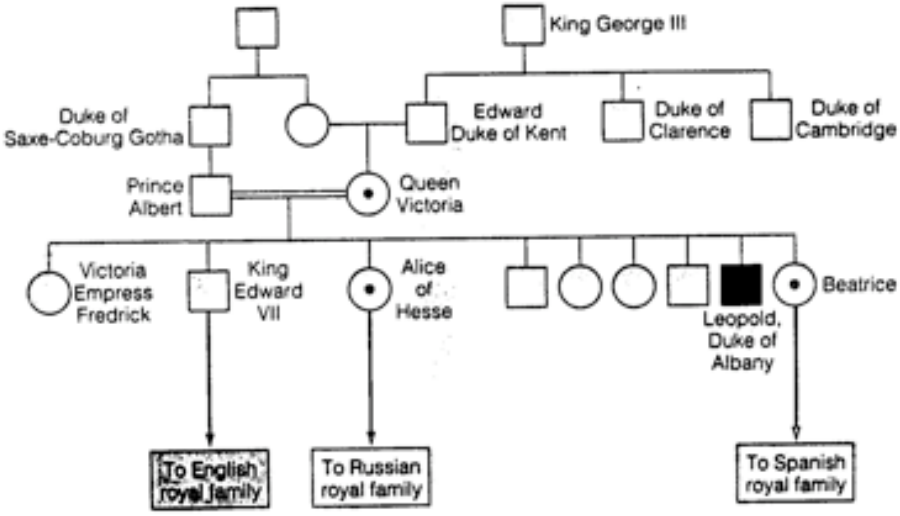
1. For example, even though there are hemoglobin genes in all cells of the body, only the developing red blood cell transcribes those genes. That is because there are other protein, present only in developing red cells, necessary for Hb gene transcription. The question then becomes: why are these special factors necessary for Hb gene transcription only present in developing red cell, and not in all cells. That complicated question is now one of the leading research fields in biology, and answers are starting to come in. The general answer is that factors in the environment, mainly signals being sent to and from other cells in the embryo, stimulate expression of many of the "**regulatory" genes**.

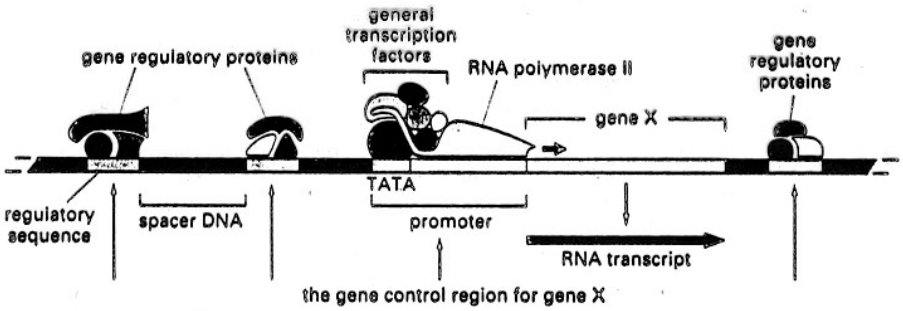
IV. Some terms to know.

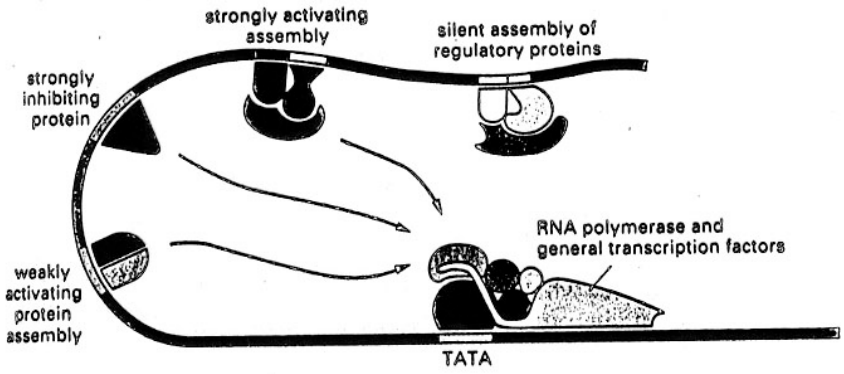
Polygenic, sex chromosome, autosome, X-linked, penetrance, expressivity, androgen insensitivity, hormone receptor, RNA polymerase, enhancer, suppressor, regulatory gene.

V. Reading: pp. 143-154 again.






general transcription factors
gene regulatory proteins
RNA polymerase II
gene regulatory proteins
gene X
TATA
regulatory sequence
spacer DNA
promoter
RNA transcript
the gene control region for gene X


strongly activating assembly
silent assembly of regulatory proteins
strongly inhibiting protein
RNA polymerase and general transcription factors
weakly activating protein assembly
TATA