**Mendel forever**

**The data**

Expt. 1. Form of seed. -- From 253 hybrids 7324 seeds were obtained in the second trial year. Among them were 5474 round or roundish ones and 1850 angular wrinkled ones. Therefrom the ratio 2.96:1 is deduced.

Expt. 2. Color of albumen. -- 258 plants yielded 8023 seeds, 6022 yellow, and 2001 green; their ratio, therefore, is as 3.01:1.

Expt. 3. Color of the seed-coats. -- Among 929 plants, 705 bore violet-red flowers and gray-brown seed-coats; 224 had white flowers and white seed-coats, giving the proportion 3.15:1.

Expt. 4. Form of pods. -- Of 1181 plants, 882 had them simply inflated, and in 299 they were constricted. Resulting ratio, 2.95:1.

Expt. 5. Color of the unripe pods. -- The number of trial plants was 580, of which 428 had green pods and 152 yellow ones. Consequently these stand in the ratio of 2.82:1.


Expt. 7. Length of stem. -- Out of 1064 plants, in 787 cases the stem was long, and in 277 short. Hence a mutual ratio of 2.84:1. In this experiment the dwarfed plants were carefully lifted and transferred to a special bed. This precaution was necessary, as otherwise they would have perished through being overgrown by their tall relatives. Even in their quite young state they can be easily picked out by their compact growth and thick dark-green foliage.

**Sweet**

Sweet

The Wilted-Seed Character of Pea Described by Mendel is Caused by a Transposition-Exon Insertion in a Gene Encoding Starch-Branching Enzyme

Mendel's dwarfing gene: cDNAs from the Le alleles and function of the expressed proteins

**Mendel's dwarfing gene: cDNAs from the Le alleles and function of the expressed proteins**


Four alleles of the Le locus known:

Le > le-3 > le > le

"gibberellins"

The stature of Le mutants can be restored by application of GA1, but not by GA20

Herr Mendel, meet Drs. Beadle and Tatum

Mendel's green cotyledon gene encodes a positive regulator of the chlorophyll-degrading pathway

Sato et al. PNAS August 28, 2007 vol. 104 14169-14174

**Mendel's green cotyledon gene encodes a positive regulator of the chlorophyll-degrading pathway**

Solely on the basis of statistical analysis of plant crosses, and a full century before the discovery of the structure of DNA, the chemical nature of mutations, the "central dogma (fact) of molecular biology," the notion that genes code for enzymes (or enzyme subunits) -- in essence, before the discovery of anything at all relevant to what is being studied here -- Mendel correctly determined that differences between plants in traits such as seed shape, plant height, and seed color are determined by discrete entities that behave in a distinct, specific way during meiosis, and during ontogeny.

Nearly 150 years later, molecular genetic and biochemical analysis has shown that Mendelian inheritance of the traits Mendel studied is, in precise agreement with his model (take THAT, Karl Nägeli and your stupid apomixing Hieracium; grrrrrr), due to specific lesions (mutations) in unique, single genes coding for enzymes directly involved in the development of the traits that Mendel studied. Furthermore, the nature of the lesions conclusively explains the recessive nature of the alleles Mendel studied. These examples offer wonderful case studies in the effect of genotype on phenotype.

1866 – 2007 – ∞
“It's All in the Genes”
New York Times, 5/2/04

Gene → phenotype
Other genes → epistasis → variable expressivity (sickle-cell anemia)
The environment → “norm of reaction” → variable penetrance (BRCA1-induced breast cancer)

Epigenetic effects

Plant epigenetics 1:
mitotically, but not meiotically resistant inheritance

Persephone, the Greek goddess of Spring

A bit of plant biology – the seeming paradox of vernalization

“Vernalization is the process by which prolonged exposure to cold temperatures promotes flowering. Monocarpic species senesce after flowering and setting seed. … Plants that require vernalization to flower thus typically require two seasons to complete the life cycle and are usually classified as biennials or winter annuals. Many winter annuals and biennials become established in the fall, taking advantage of the cool and moist conditions optimal for their growth. The vernalization requirement of such plants prevents flowering until spring has actually arrived.”


Vernalization

"I think it is reasonable to refer to the vernalization-induced, mitotically stable acquisition of the competence to flower as an epigenetic switch because it is a change that can be propagated through cell divisions in the absence of the inducing signal."


"The vernalization-mediated repression of FLC is epigenetic in the sense discussed above: The repressed state of FLC is maintained after vernalized plants are returned to warm growing conditions. Thus, in Arabidopsis, vernalization provides competence to flower by repressing the expression of a flowering repressor. As expected, FLC expression is on again in the next generation. This resetting of the epigenetic switch during passage to the next generation is reminiscent of genomic imprinting in animals. But the unique aspect of this switch is that the on-to-off direction of the switch is set by perception of the environment, whereas the off-to-on direction is set by passage to the next generation."


"… some might argue that the term epigenetic should be used only for changes that persist from one generation to the next. This of course does not happen in the case of vernalization; if it did, a biennial would only be a biennial for one generation.

One of Lysenko's false claims was that the vernalized state was heritable; that is, a vernalized plant would transmit the rapid-flowering trait to the next generation. This of course does not happen in the case of vernalization; if it did, a biennial would only be a biennial for one generation. Lysenko's false claims were based on the idea that the environment of the members of a Marxist society could produce heritable changes in attitude, and, thus, if the proper environment was provided, future generations would consist of improved citizens. Lysenko's efforts to obtain or fabricate results that supported a political ideology and, with the assistance of Stalin's regime, to force others to accept his views had disastrous consequences for Russian genetics."


Maize (corn) – Zea mays

Maize is monoecious – distinct male (tassel) and female ("corn silk") flowers on the same plant.

Courtesy of Prof. Jay Hollick, MCB Department
What is going on?

1. The green maize plant is not outcrossing, it is selfing.
2. The red allele is incompletely penetrant, except when in a homozygous state.
3. This is actually two-locus inheritance, and the green locus exhibits full dominant epistasis to the red locus.
4. This is actually two-locus inheritance, and the green locus exhibits full recessive epistasis to the red locus.
5. Mmmmm ... Milla ...

What IS going on

This is paramutation: a meiotically heritable change in the phenotype of a plant that results not from the physical alteration of the primary DNA sequence of the underlying genes, but from an effect on their expression.

Recall Mendel's "compromise that the two alleles of a gene reach in a heterozygous organism for the life of a plant." In this case, the compromise is not reached. The Pl' allele somehow causes the epigenetic silencing of the Pl allele -- silencing that persists through meiosis.

Transcriptional Regulation of Anthocyanins

Other genes involved in maize pigment synthesis can be paramutated

A critical aspect of the paramutation process -- one that is shared by many epigenetic processes

It is sensitive to the environment: paramutation can be variably expressive (in other words, the extent of paramutation can vary, and how variable it is can be specified by the environment).
Environmental Programming of Heritable Epigenetic Changes in Paramembranous Expressions Using Temperature and Light at a Specific Stage of Early Development in Maize Seedlings

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ABSTRACT

Different developmental stages and environments in the growth of maize plants under different temperature conditions applied during a developmental period which is sensitive to the environment predict the possibility of the occurrence of a disease. The results of 10 independent experiments revealed that the maize plants derived from the treatment of short wavelengths (22C) and constant light conditions differ significantly from those derived from 22C (somatic) and 10 independent experiments were performed in the same conditions. The experiments provided the first evidence that higher epigenetic changes can occur in maize plants grown under constant conditions than in those grown under variable environmental conditions. The epigenetic traits of enhanced homologous recombination could be transmitted through both the maternal and the paternal crossing partner, and proved to be dominant. The increase of the hyper-recombination state in generations subsequent to the treated generation was independent of the presence of the transgenic allele (the recombination substrate under consideration) in the treated plant. We conclude that environmental factors lead to increased genomic flexibility even in successive, untreated generations, and may increase the potential for adaptation.

Three processes

Vernalization: Environment → epigenetic state that is mitotically heritable

Paramutation: “Dialog” of two alleles → epigenetic state that is meiotically heritable and sensitive to the environment

Transgenerational memory of stress: environment → epigenetic state that is meiotically heritable

Transgeneration memory of stress in plants – Barbara Hohn et al. Nature 442, 1046-1049

*Owing to their sessile nature, plants are constantly exposed to a multitude of environmental stresses to which they react with a battery of responses. ... Here we show that in Arabidopsis thaliana plants treated with short-wavelength radiation (ultraviolet-C) or flagellin (an elicitor of plant defenses), somatic homologous recombination of a transgenic reporter is increased in the treated population and these increased levels of homologous recombination persist in the subsequent, untreated generations. The epigenetic trait of enhanced homologous recombination could be transmitted through both the maternal and the paternal crossing partner, and proved to be dominant. The increase of the hyper-recombination state in generations subsequent to the treated generation was independent of the presence of the transgenic allele (the recombination substrate under consideration) in the treated plant. We conclude that environmental factors lead to increased genomic flexibility even in successive, untreated generations, and may increase the potential for adaptation.*

Great-grand-grand-children

1. Plants are engineered to have a "reporter gene" – if the gene undergoes recombination, blue sectors appear.
2. Irradiation of the plants increases the number of blue sectors (not surprising).
3. Most surprisingly, the offspring of the irradiated plants show increased recombination frequency.

Molinier et al. Nature 442, 1046-1049
Influences of the environment on the plant genome have been documented, and have been interpreted as 'genomic shock'. Here we demonstrated that environmental influences, specifically ultraviolet radiation and a bacterial elicitor, change the flexibility of the plant genome in somatic tissue of treated plants and in somatic tissue of their progeny. As these influences persist in the entire population of plants, the basis for the change is epigenetic rather than genetic. Plants carrying the transgene locus do not have to face the environmental challenges themselves in order to transmit the epigenetic change to the offspring; the stimulus for an increase of recombination can be imposed in trans by a single treated parent.

An important point
Paramutation and across-generation memory of stress are both epigenetic phenomena: the loci they affect do not change DNA sequence. This does not mean, however, that the mediators of these epigenetic effects are fundamentally "magical" — there are genes, the products of which are required for epigenetic effects.

Arabidopsis thaliana

Epigenetics:
from phenomenon to mechanism

Some mutations that affect flower structure
S. Jacobsen and E. Meyerowitz

“Superman”

Wild-type flower: 6 stamens (♂).

superman null mutations: 12 stamens.

No comment on the nomenclature

There are two ways to mutate the SUPERMAN gene and get the same phenotype (12 stamens):
1. Just delete the gene.
2. Keep the gene as it is and METHYLATE it!

The methylated form is an “epi-allele” of SUPERMAN and is called clark kent.

Suppressors of clark kent

kyp (kryptonite) codes for an H3K9 histone methyltransferase!

From plants to mice


An evolutionary perspective