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Appropriate Gene Symbols in Teaching Genetics[1]

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Choice of appropriate gene symbols in teaching general genetics avoids misinterpretation and misleading conclusions that are otherwise frequent. Lack of consistency in textbooks, especially with the wild-type standard concept, misdirects the student into confusing dominance with epistasis, as well as allelism with independence. The similar fallacy of "dominant" white in White Leghorns is clarified as an "interaction" white by appropriate choice of symbols. Use of the wild-type standard method, basic in choosing symbols, allows a drastic reduction in the number of crosses necessary in comparing different stocks for genetic differences. Two related sets of rules are suggested for choosing appropriate gene symbols.
INDEX DESCRIPTORS: Gene symbols, teaching genetics, wild type.

It seems reasonable that gene symbols in higher organisms should imply at a glance whether they are recessive or have some degree of dominance, and whether they are normal or mutant. Consistency is especially important in teaching genetics. However, most of the "official" rules on choosing gene symbols delve into the most sophisticated and special needs of advanced and specialized areas of genetics seldom needed for general genetics. With different individual exceptions, such "official" rules do follow Mendel's lead, and they support in general the rules used in this paper, including the Wild-Type or Standard-Type method. The reader may refer to the report of the International Committee On Genetic Symbols and Nomenclature (1957), to Lindsley and Grell (1968) and Burnham et al. (1974). Use of gene symbols in textbooks, on the other hand, frequently violates these rules and generally is inconsistent and even misleading to the student.

Mendel suggested that recessives be indicated by a lower-case letter and dominants by a capital letter. Not having personally noted intermediate degrees of dominance, Mendel said nothing about them. It seems appropriate that, since partial dominants are phenotypically evident when heterozygous, they should be symbolized by a capital letter also. Pragmatically this works well.

Many authors like to distinguish the various types of intermediate dominants by distinctive names usually differentiated by function: codominance, semidominance, partial dominance, absence of dominance, incomplete dominance, intermediate dominance, mosaic dominance, etc. The distinctions usually depend upon knowing the gene action. Since the function or lack of it is usually not known directly, and since the various texts may disagree in usage, I have found it useful to lump them all together and use the shortest term, codominance, for all such categories. The definition then is recognizability of the genotype by observation of the phenotype; that is, codominance shows an effect of each allele in the phenotype. This really simplifies the difficulties for beginning students, since all genes then are dominant, codominant, or recessive.

Darwin (1868) always referred "to the wild rock pigeon (*Columba livia*) as the standard of comparison" for the numerous breed variations. This was a pioneering approach of general utility.

The *Drosophila* researchers early learned that the wild type, or "normal," analogous to the type specimen of the taxonomists, was not only useful, but sometimes necessary as a standard of reference to distinguish dominance from epistasis and to reduce the number of crosses necessary in testing for dominance relationships. This criterion then answered the otherwise bothersome question about a "gene" being both dominant and recessive: "To what is the gene dominant or recessive?" In the primary or essential analysis, the answer is that a mutant gene is dominant (or recessive) to its *normal allele* (standard or wild-type). Of course, relationships among multiple dominant alleles or multiple recessive alleles are secondary, and must be specified for each combination.

The normal (= standard-type = wild-type) allele then was designated symbolically as + for ease in distinguishing it from frequent alternatives (mutant alleles). *Reasoning* can be applied to designate the standard or wild type, if the criterion "most frequent in the wild population" is not easily noted. For example, in cattle whose actual wild type is no longer extant, which is the preferable standard, horned or polled? Is it more reasonable that wild cattle had horns to fight off predators or joust in dominance conflicts or not? Horned seems reasonable as wild type. Analogy with related species may be helpful, but not necessarily definitive. Bison, water buffalo, kouprey, banteng, yak, gaur, and anoes all have horns, but cattle *might* represent a special adaption. Fossil aurochs, progenitors of the domestic cattle, do have horns as was pictured from ancient through Roman times (Rouse, 1979). Horned, therefore, is conclusively wild type. An arbitrary choice for standard type can work if all else fails.

In order to work many kinds of problems, the beginning students need to be able to easily assign their own symbols to genetic characters regardless of the prior "official" symbol. A wrong or inappropriate symbol can easily mislead students; therefore, the following rules have been listed rather dogmatically. For somewhat more advanced students an alternative in the persuasive style is available.

APPROPRIATE GENE SYMBOLS*

(Dogmatic rules for beginners)

1. Let the variant, deviant, or mutant name or condition be indicative of the letter symbol used. Especially use the first letter in the (single) mutant name.
2. Use an upper-case or capital letter of the alphabet for those genes with some degree of dominance (*i.e.*, for dominant or for codominant genes).
3. Use a lower-case letter of the alphabet for a recessive gene.
4. Use a + symbol alone (or as superscript to the base letter) for a gene controlling normal, standard or wild type.
5. Use the same base letter for alleles (to infer multiple alleles when they occur and to avoid confusion with other loci).
6. Use superscript letters or numbers for multiple alleles.
7. When the alphabet is in full use, or where it is appropriate to properly indicate the mutant name, use two or more letters as base symbols for one gene.
8. Use subscript numbers on the same base letter for phenotypically indistinguishable non-allelic mutants (mimics). An alternative now becoming preferred is to use distinctive but synonymous, similar or related mutant names. Another is to add the number 2 (or 3 . . .) following the letter.

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9. Assume the alternative allele to any mutant is normal, and the omission of symbols usually implies (homozygous) normal, unless the data force you to conclude otherwise.

*What's in a name! Any symbols properly identified can be used. These rules of thumb are for beginning students, and for more *accurate communication*. Many historical exceptions with established precedence and usage are contrary to one or more of these rules.

BASIC SYMBOLS IN GENETICS

(For more advanced students)

If we follow the theory that chromosomes are sequences of hundreds or even thousands of functional units, the genes, and if we follow Mendel's lead in assigning letters to genes, won't things get too complex?

We can simplify by starting with a standard type, ordinarily the wild type or normal. With polymorphism or isoalleles in the wild population, the most frequent can arbitrarily be selected. For this type we can agree *not to use letters for its genes*. The genotype for a standard pair of chromosomes may then be represented by ═══.

Mutant or non-standard genes can now monopolize the letter symbols.

Examples:

$\frac{a}{a}$ Homozygous recessive type $\qquad$ $\frac{M}{M}$ Homozygous dominant type

A capital letter indicates at least partial dominance to standard, while a small letter indicates a recessive or so little dominance as to be difficult to identify in the heterozygote.

In the choice of letters ease of remembering is important. Usually the initial of the name of the mutant or non-standard character is convenient. Double or triple letters may be needed.

Examples in the laboratory mouse:

r (rodless retina)
Re (rex = curled hairs)
d (dilute pigmentation)
dw (dwarf = pituitary failure)

Mutants of different origins are not necessarily allelic, even if similar in phenotype. Example: *Re* and *Ca* (Caracul) in mice look identical and both are dominant to their standard alleles, but give free Mendelian recombination.

Heterozygotes of a mutant with standard: The standard allele may be explicitly designated by the symbol +. The locus designation must be included in the symbol for the norml allele if reference is made to a specific normal gene that is not being diagrammed along with a mutant allele (examples d^+ or re^+).

Examples in mice:

$\frac{+}{d}$; $\frac{Re}{+}$; $\frac{+\ +}{bp\ \ a}$ or $\frac{bp\ +}{+\ \ a}$.

If two or more mutants are alleles of one another (multiple alleles), their symbols can be distinguished by superscripts.

Examples in mice or rabbits:

$\frac{c}{c}$, $\frac{c^{ch}}{c^{ch}}$, $\frac{c^{ch}}{c}$

(colorless = albino) (chinchilla color) (heterozygote = light chinchilla)

Complex example of the above in an individual fruit fly (*Drosophila*):

(♀) Sex chromosomes $\frac{y^2\ \ B}{y\ \ +}$ chromosome 2 $\frac{dp\ \ +}{dp\ \ sp}$ chromosome 3 $\frac{e}{e}$ chromosome 4 $\frac{ci}{ci}$

This individual has mutants at six loci of which three are homozygous; the *B*, having some dominance will show a phenotype effect, but *sp* will not.

Note: Some authors use + as a superscript for standard; also multiple alleles may present other complications not mentioned here. And in *Drosophila*, so many mutants are known that letters are conserved by limiting the upper case letter to a given locus, lower case to another. Thus *B* (bar eye) is not allelic to *b* (black body). Since superscripts and subscripts are difficult for the typist or computer, some pragamatic compromises have been used. In corn, for example, superscripts are indicated by a dash after the base letter followed by the "superscript," all horizontally on the same line, while subscripts follow the symbol without a dash.

It will be recognized that for specialized, advanced research and sophisticated needs as in biochemical and microbial genetics, these rules may be insufficient. But let us recognize that some areas *are* specialized, advanced and sophisticated. These areas *ought* to follow basic rules where feasible, but in research pragmatic usages to fit the needs will always evolve and overrun rules which do not quite suit. The beginning student needs general usage guidelines.

Most texts give "lip service" to the + or wild-type usage. But they fall far short of applying it widely when applicable. One text on a left-hand page says + is customarily used for wild type and on the right-hand page fails to use it. Particular texts really ought not be singled out because most differ only slightly in their inconsistencies. Generally, the wild type is used appropriately with *Drosophila* and physiological characters of microorganisms, often with tomatoes and corn, and sporadically elsewhere. Most teachers also *are not* consistent. Texts and teachers seem oblivious to the generalization and appropriate usage with cats, rabbits, and rats, dogs and doves, chickens and cucumbers, peas and petunias, radishes and raspberries, etc. (see review by Hollander, 1953).

Students deserve reasonable consistency. But if teachers and texts can not get together on general usage, genetics will continue to be regarded as a confounding subject by many.

Let us use chickens to demonstrate some fallacies perpetuated if this method is ignored.

EXAMPLE 1. Jungle Fowl, *Gallus gallus*, wild-type ancestor of domestic chickens, is similar to the Brown Leghorn in plumage color, and can be briefly described as "black and red".

Question: In the following pedigree, Figure 1, is white recessive to black?

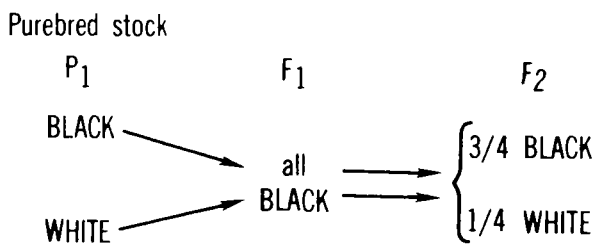

Fig. 1. A plumage-color cross in chickens, such as "Rose Comb" Bantams.

The usual answer is yes, *but* try assigning appropriate gene symbols. You will discover the data are insufficient to answer the question, since no wild type (black and red) appears in the problem! Besides allelism of mutants as a possibility, domestic species frequently carry more than one mutant. Mating each P_1 stock to wild type should clarify the matter. (Fig. 2).

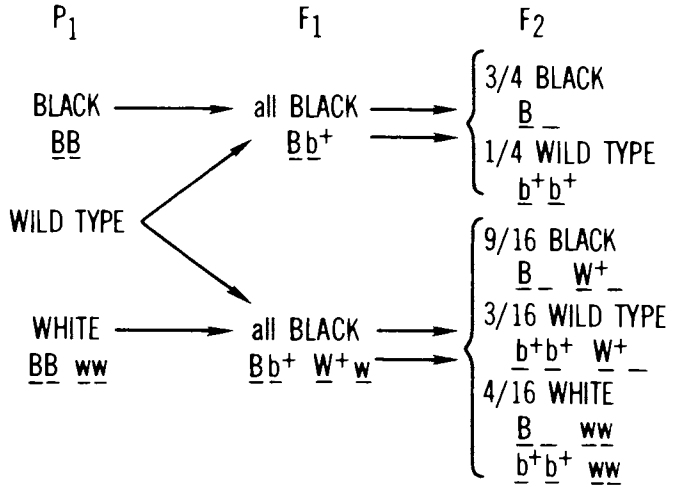

Fig. 2. Clarification of the previous cross (Fig. 1) by inclusion of wild type.

Assigning appropriate gene symbols now is easy. *B* controlling the dominant black in the upper monohybrid segregating family, and *w* controlling the recessive white is epistatic (rather than recessive) to the dominant black mutant in the bottom dihybrid segregating family (the F_1 color and 9:3:4 ratio being basic clues). It will be noted that the pedigree style is not found in most textbooks. This style is not new, but has been explained again recently (Miller, 1983).

Black and albino rabbit stocks (wild type = "agouti") may be substituted instead of chickens and yield similar results. Many other alternative choices of examples may be used.

If this usage of a standard type or wild type were ignored, there would seem to be nothing wrong in assigning the gene symbol *W* for the "walnut" comb shape in chickens. Then from purebred P_1 stocks, Walnut × Pea comb, one could obtain an F_2 segregating as ¾ Walnut, *W*_ , and ¼ Pea comb, *ww*, a simple monohybrid. Most teachers of genetics, however, would admit that this is misleading. Walnut represents an interaction of two dominant and independent *mutants*, Pea comb and Rose comb, and is a classical example of interaction genetics. The two mutants, *P* and *R*, collaborate to control the walnut phenotype (see Miller, 1983, for the problem diagram, or Altenburg, 1957, for appropriate use of the Punnett square for comb shape). How can gene *W*, one locus, be two interacting independent genes? By including the "single comb" = wild type in the crosses, the two dominant interacting *mutants* are easily disclosed.

EXAMPLE 2. A frequently used example of a partial dominant in a problem that wrongly implies allelism of two independent mutants, see Figure 3.

The action of the blue mutant segregating here is a dilution of eumelanin. But again where is wild type? While minor modifiers may be present, basically, *two* mutants are present as crosses to wild type would disclose. Dominant black is again present homozygous in the stock. Then the codominant blue (or call it splashed, or dilution of eumelanin) segregates with its normal allele. Therefore, the blue chickens are genetically *BB B1B1*$^+$, and the "white" segregants are

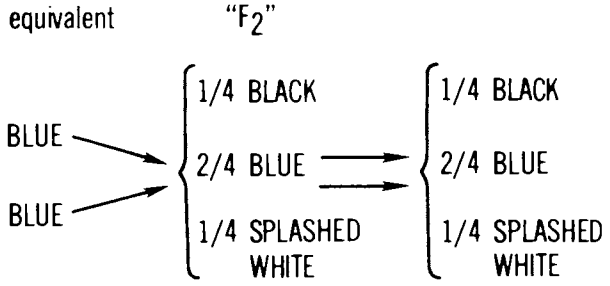

Fig. 3. Blue Andalusian chickens never breed true!

BB B1B1 (*S* for spashed or *D* for dilution would be quite acceptable in place of *B1*). The gene controlling black is *not* allelic to that controlling white in this or in the previous example with a different kind of white.

Roan cattle are another example of this sort frequently used and confused in the textbooks, which usually imply red is allelic to white, and then give a lower-case letter of the alphabet in spite of the *three* phenotypes exhibiting monohybrid intermediate dominance (codominance) segregation. And then often they use the symbol for the recessive red gene *not* segregating in the problem: e.g., *r* instead of *W*, although *R* for roan may be accepted. In cases of codominance, convenience may decide whether the symbol chosen refers to the homozygous mutant type or the heterozygous type. The inheritance of cattle colors is not fully analyzed (see Searle, 1968). Wild type has been designated by Olson (1975, 1980) as blackish brown in bulls and reddish brown in cows. Red Shorthorn cattle are likely genotype *rr*, (but preferred symbolization in mammaliam genetics is *ee*), roan shorthorn are *rr*, *WW*$^+$, and white are *rr WW*. Obviously the whole breed is homozygous recessive red and will not segregate at this locus. Different textbooks partially correct the prior difficulties in different directions. Similar textbook fallacies occur with palomino horses and tortoiseshell cats. For graduate students reference to preferred symbols in the research literature should be recommended.

EXAMPLE 3. In chickens, "Dominant white", *I*, is cited in texts as demonstrable in crosses of White Leghorns x recessive white, *cc*, Wyandottes (or Silkies) yielding a 13:3 F_2 ratio. Has anyone actually demonstrated this conclusion? It is hard for me to understand why Hutt and Rasmusen (1982) support this model. Tests as early as that by Punnett (1923) appropriately interpreted have shown White Leghorns to possess 5 or 6 mutants affecting plumage color (see Somes, 1980):

1. Sex-linked dominant "silver", *S*, (black and white plumage), which inhibits most phaeomelanin (reds and yellows).
2. Sex-linked "barred", *B*, which produces transverse sections of the feather alternately well pigmented and diluted of eumelanin pigment.
3. Dominant "pile", *I*, (red and white plumage) which inhibits eumelanin.
4. Blue, *B1*, codominant (homozygous = red and splashed white) dilutes eumelanin.
5. "Dominant black", *E*, (top dominant of "extension" series of alleles) which extends eumelanin in place of phaeomelanin. *E* was simplified to *B* in the previous problems.
6. *Sometimes* present is "recessive white", *c*, which blocks both kinds of melanin.

The phenotype white is accomplished by the *interaction* of the dominant mutants silver and pile blocking both melanins; or by the dominant black excluding (replacing) phaeomelanin and then being

blocked by pile (again interaction); as well as *E* and *B* plus the homozygous blue diluting the eumelanin to near white. The biochemical sequence of events is not known.

Many other color mutants in chickens are known, in many domestic stocks (breeds). If, say 50 stocks are extant, how many crosses are necessary to test each for genetic differences? (Data from F_1, F_2, and backcrosses = one test.) Let n = the number of stocks; then $\frac{n\,(n-1)}{2} = \frac{50\,(50-1)}{2} = 1225$. By contrast, if one uses the wild type method, then only 50 crosses are necessary to identify the mutants or the different genes involved. The only drawback is that these 50 will not necessarily inform you of all the mutant relations. *But even adding* some crosses for this purpose leaves the necessary tests far less than 1225.

I believe this system is unsurpassed in classical application. It increases consistency, is widely suitable, clarifies manipulation and analysis and reduces confusion.

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