QUICK FIX

An Algorithm for the Rapid Analysis of Genetic Pedigrees

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Abstract

An algorithm has been developed for the rapid determination of single-gene inheritance patterns from genetic pedigrees.

Key Words: *Genetic pedigrees; patterns of inheritance; single-gene traits; algorithm.*

Teaching and learning inheritance of single genes usually involve the use of Punnett squares and pedigrees. Pedigrees can be a powerful tool for visual learners because one can "see" the pattern of inheritance in a pedigree. However, college biology textbooks and laboratory manuals are often very limited in their presentation of pedigree analysis (Pendarvis & Crawley, 2011, pp. 210–214; Reece & Urry, 2011, pp. 276–277; Johnson, 2012, pp. 207–211).

In a pedigree analysis of a single gene, there are seven possible inheritance patterns: (1) autosomal dominant, (2) autosomal recessive, (3) X-linked or sex-linked dominant, (4) X-linked or sex-linked recessive, (5) mitochondrial or maternal, (6) Y-linked, and (7) inconclusive. Table 1 lists condensed clues, not rules, for the assignment of the first six listed inheritance patterns. The seventh pattern, inconclusive, is the result of none of the first six patterns being borne out in the complete pedigree, or sometimes there are two patterns within different parts of the pedigree. Inconclusive pedigrees are often times the result of a relatively small family size and a trait that is not severe enough to impair fertility (Lewis, 2008, p. 83).

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Over the course of 10 years' experience teaching genetics in college introductory biology courses for majors and nonmajors and in upper-division genetics courses, I have developed an algorithm, shown in Figure 1, for the rapid development of a hypothesis about the inheritance pattern of a single gene from the trait pattern of a pedigree. From the algorithm, a student can create a hypothesis that can then be tested by labeling each person in the pedigree with the hypothesized genotype to check whether the hypothesis is correct. It is important to check because there are a few nontypical cases, which will be discussed below.

The important concept embedded in the algorithm is its attention to order of analysis. The algorithm is based on the sequential

Table 1. Condensed pedigree clues, not rules.

Autosomal dominant
Approximately half of everybody
Males and females affected
All generations
Autosomal recessive
Rare
Skips generations
Males and females affected
Consanguinity (□ = ○)
X-linked dominant (sex-linked dominant)
Some females can have it
All generations (no skipped generations)
Males get it from affected mothers and give it to their daughters
X-linked recessive (sex-linked recessive)
Rare
Males predominantly have it
Generally skips generations
Males generally get it from unaffected mothers
Y-linked
All males, all the time, all generations (must be direct descendent of the family)
Mitochondrial or maternal
Every child of affected mother is affected

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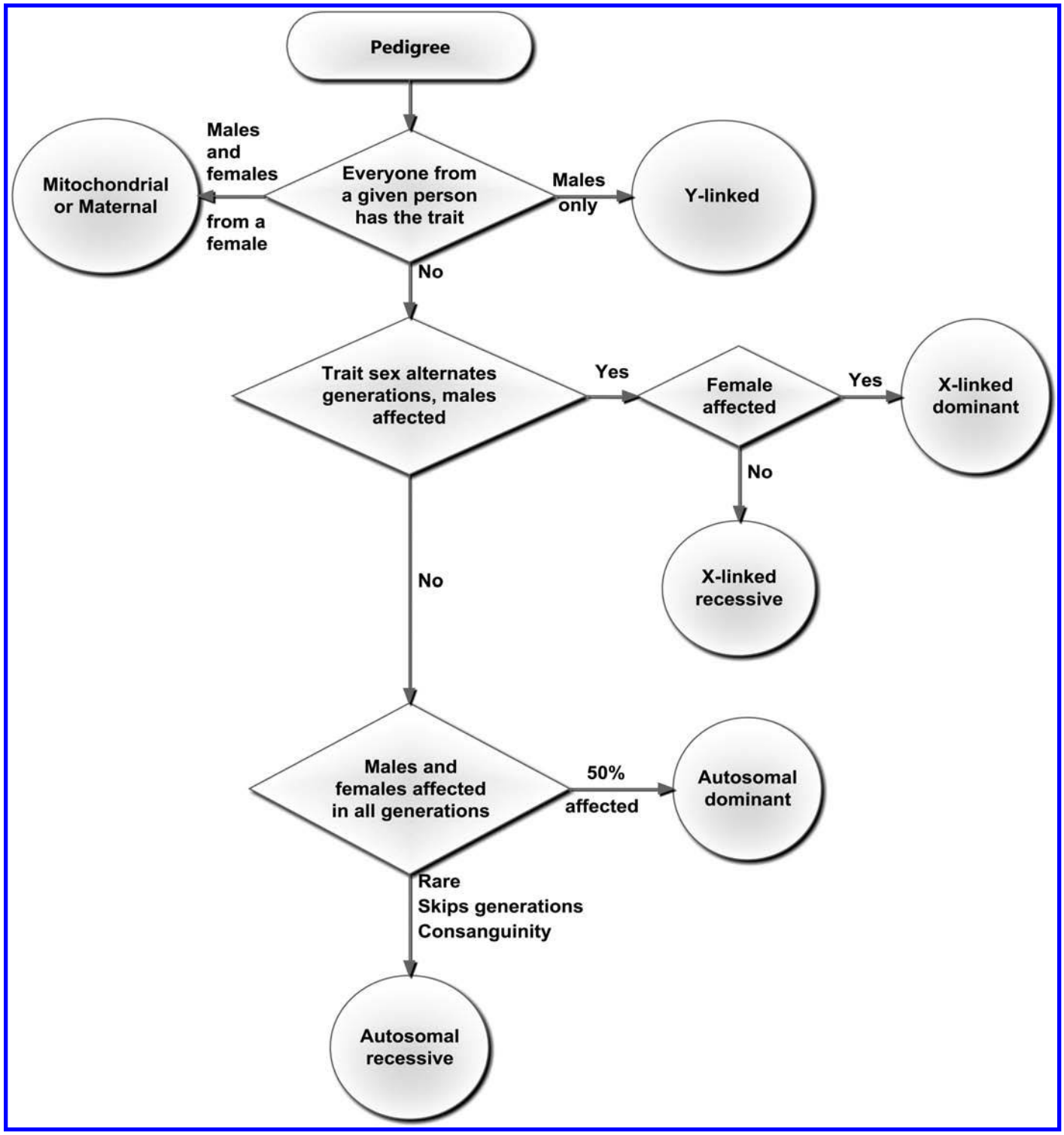

Figure 1. Algorithm for the rapid analysis of genetic pedigrees.

elimination of recognizable inheritance patterns in order to narrow down the possibilities. The easily detectable patterns of mitochondrial/maternal and Y-linked inheritance patterns are disposed of first. X-linked inheritance is considered next, because of its unique sex-alternating generational pattern. The remainder is autosomal inheritance. Dominant and recessive patterns are each determined after the X-linked/autosomal choice is made. The algorithm has a maximum of four steps, or four questions.

Question 1 is whether every female or every male exhibits the trait, beginning from a given female or male. If every male or female descendant of an affected female is affected, it is mitochondrial or maternal inheritance; whereas if every male descendant from an affected male is affected, the inheritance pattern is Y-linked. If neither pattern is present, we proceed to the second question.

Question 2 is whether the trait alternates sexes from generation to generation, with only males (no females) being affected by the trait.

If so, the inheritance pattern is X-linked or sex-linked, and we proceed to question 3: If there are no affected females, the trait is X-linked or sex-linked recessive. If there are affected females that alternate generations with affected males, the trait is X-linked or sex-linked dominant. These generalizations are based on common assumptions and hold for the majority of pedigrees; however, there can be exceptions. Here are three (Michael J. Dougherty, pers. comm., 2013):

(a) Imagine a woman with an X-linked dominant trait: Half of her offspring, regardless of sex, will be affected (no sex alternation).

(b) If she is an X-linked carrier for the recessive trait, half of her sons will have the trait and half the daughters will be carriers. If a carrier daughter reproduces with a noncarrier male, half the sons will be affected (affected males in successive generations; no sex alternation).

(c) In cases where an affected son produces offspring with a woman carrying the same allele (violating the common "assumption" that people who marry in carry no mutant alleles), both sons and daughters with the trait may result.

Finally, if the results of trait determination are negative to this point, it means that males and females are affected in all generations. We now come to question 4: if approximately half of all males and females are affected, the inheritance pattern is autosomal dominant. If the trait is rare, skips generations, and often includes consanguinity, the inheritance pattern is autosomal recessive. Students should be made aware of, and take into account, incomplete dominance and incomplete penetrance, in which a gene is not always expressed in an individual's phenotype.

In my experience, students using this algorithm significantly reduce their learning time for pedigree analysis and make fewer mistakes in determining the correct inheritance pattern of a given pedigree. The ease of use and immediate success rate encourage their enthusiasm for genetics. Many students spontaneously construct pedigrees of their own families with regard to traits. This algorithm is a powerful tool for the teaching of inheritance patterns.

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