Perspectives

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The "Genesis of the White-Eyed Mutant" in *Drosophila melanogaster:* A Reappraisal

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THE science of genetics is, in all probability, unique among the biological sciences in that it is possible to pinpoint precisely the date of its inception. The rediscovery of MENDEL's laws in 1900 independently by DE VRIES, CORRENS, and VON TSCHERMAK marks the start. During the subsequent decade, the universality of MENDEL's laws among plants and animals was demonstrated, the Danish geneticist JOHANNSEN gave the name *gene* to MENDEL's factors, and the British geneticist BATESON coined the term *genetics.* However, while the arithmetic of Mendelian genetics was quickly established, the cellular mechanism was unclear. Without experimental evidence, SUTTON and MONTGOMERY each independently speculated on the correlation between meiotic chromosome disjunction and gene segregation. *Sensu stricto,* modern genetics began in 1910 with the discovery of the white-eyed mutant in *Drosophila melanogaster* by T. H. MORGAN and his demonstration of the correlation between the inheritance of this mutation and the transmission of the *X* chromosome. Experimental proof for the linkage between gene and chromosome came with the publication in 1916 (in Volume 1, page 1 of GENETICS) of BRIDGES' monumental doctoral dissertation on nondisjunction of the *D. melanogaster X* chromosome.

The recent publication of a detailed, instructive, and valuable history of the roots and proliferation of Drosophila genetics by ROBERT E. KOHLER, intriguingly titled *Lords of the Fly,* has reopened two issues of historical interest. When exactly was the *white* mutation in *D. melanogaster* discovered, and did MORGAN really find this mutation?

When considering the first question, it is important to note that the first sentence in MORGAN's seminal publication describing the inheritance of *white,* published July 22, 1910 in *Science,* reads as follows: "In a pedigree culture of Drosophila which had been running for nearly a year through a considerable number of generations, a male appeared with white eyes." No date of discovery is given, nor is the finder specifically named, although presumably this must have been MORGAN because he is the sole author of the brief paper, only a bit more than three pages long. It should be noted that the paper is dated July 7, 1910. In his discussion of MORGAN's first mutation experiment with *D. melanogaster,* KOHLER emphasizes the discovery of a putatively first mutation called *with* ("with trident") in which a pigmented triangular area appears on the thorax just anterior to the adult fly's scutellum. The following quotation (pp. 41–42) is relevant: "Ross Harrison recalled visiting Morgan's lab in the first days of January, 1910. 'There's two years work wasted,' he (Morgan) exclaimed, having his hand on rows of bottles on shelves. 'I've been breeding these flies for all that time and have gotten nothing out of it.' But, just a few days later, Morgan observed a few flies with a darker pattern than any he had seen before. Inbreeding quickly produced a mutant strain, *with,* which had a distribution of pigment that was distinctly darker than wild type which further selection did not alter . . . Visiting his wife and newborn daughter in the hospital in the second week of January, Morgan could talk of nothing but his new mutant." Was MORGAN really talking about *with* or was he talking about *white*? Three pages later in his narrative, KOHLER writes, "When Lillian (*sic*) Morgan recalled her husband's visit to the hospital in January, 1910, she remembered him talking about the *white* mutant. It must have been *with,* since *white* turned up in May!" While it is not always necessary for historians of science to understand the intricacies of the sciences about which they write, there are instances when some comprehension is useful in interpreting or explaining relevant historical events. Had KOHLER appreciated fully the vagaries of the *with* phenotype, he probably would not have dismissed Mrs. MORGAN's recollection out of hand. Accordingly, several compelling reasons militate against the May, 1910 date and support a date in January, 1910.

In describing the *with* mutation, KOHLER wrote, "It was just what Morgan expected the process of speciation would look like!" By and large, almost every neophyte Drosophila geneticist used to make an attempt at delin-

eating the genetics of *with* but gave it up as a hopeless task. The reason is simple: the *with* phenotype is variable, overlaps wild type, and is precisely the kind of mutant phenotype not readily amenable to Mendelian analysis. In fact, in the first compilation of the mutants of *D. melanogaster* by MORGAN, BRIDGES, and STURTEVANT (1925), the linkage, map position, and phenotype of *with* are described as follows: "With III 48±. M. (B and M '23). Semi-dominant dark trident pattern on thorax. Discarded." (Note: M = MORGAN; B and M = BRIDGES and MORGAN.) It hardly seems possible that MORGAN would discard a mutant with the qualities KOHLER describes. More importantly, those who knew LILIAN MORGAN knew that she was a superb Drosophila geneticist in her own right, the discoverer of the famous attached-*X* female, and certainly one who would not confuse *with* and *white*. In this connection, it is interesting to relate here the following anecdotal story concerning the white eye mutant, extant in the MORGAN family and disclosed during a visit my colleague C. M. RICK and I recently made to the home of Mrs. LILIAN M. SCHERP, the MORGAN daughter whose birth was noted above as January, 1910. In the course of our lively conversation, Mrs. SCHERP was asked whether she knew anything about the Drosophila white eye mutation. She related the following story, paraphrased here. At the time of her birth, obstetricians commonly mildly anesthetized women in labor in order to ease the pain of delivery. When Mrs. MORGAN recovered from the ether, her first words were, "Oh, I do hope the white-eyed fly is still alive." This story was confirmed by her older sister, Mrs. EDITH WHITAKER, also participating in the conversation. Taking this story together with the quotation from KOHLER, apropos Mrs. MORGAN and the white mutant (see above), *white*, not *with*, was the crucial mutation of January, 1910.

What is the source of the date "May, 1910" noted by KOHLER? In the first catalog of *D. melanogaster* mutations (MORGAN *et al.* 1925), the origin of *white* is given only as 1910. In their 1916 compendium of sex-linked inheritance in *D. melanogaster*, MORGAN and BRIDGES date the finding of *white* as May, 1910. (It should be noted here that this monograph includes a table of sex-linked mutants found up to that time in the MORGAN laboratory. Here, it is explicitly stated that the white-eyed mutant was found by MORGAN.) Subsequently, BRIDGES and MORGAN (1923), in describing the third-chromosome eye-color mutation *pink*, wrote, "The first eye-color, and the character *first* clearly recognized as a sharp mutation was 'white', found in *April* 1910, by Morgan" (emphasis mine). Note the date and note, too, the statement that *white*, not *with*, was the first sharp mutation! There is yet another good reason to believe that neither May nor April is correct and that the actual date is January. The data contained in the 1910 paper involve four generations of flies. Under optimal culture conditions, the generation time for *D. melanogaster* is two weeks. As described by KOHLER, conditions in the MORGAN lab in 1910 were hardly optimal. Thus, for MORGAN to find the mutant in May, complete and score the crosses, prepare the manuscript, and move the family and menagerie from New York City to Woods Hole between, at the earliest, May 1 and July 7, is highly unlikely. An April date is possible but, for the same reasons, improbable. However, the discovery of *white* in January satisfies all necessary conditions. Can the April and/or May dates be rationalized with January? It is only possible to speculate, but one possibility is that the date of origin as April or May was given for the time the genetic analysis was completed, not the specific day the mutant male was found.

Did MORGAN find the first *white* mutant? Although not stated in his 1910 paper, the discovery of the *white* mutant was attributed to MORGAN and first explicitly so stated by MORGAN on page 63 of his 1913 book, *Heredity and Sex*, as follows: "In my culture, a male appeared that had white eyes." (No date of origin is given.) The attribution was brought into question with the publication in 1941 of a book by F. E. LUTZ entitled *A Lot of Insects: Entomology in a Suburban Garden*. In this book, LUTZ describes the insects collected in the garden surrounding his residence and includes the following statement, which occurs on page 238 and is quoted verbatim: "Meanwhile, something far more worthwhile happened, more worthwhile even if my results are not to be explained by wild flies 'contaminating' my 'pure line' of pedigreed Drosophila. Professor T. H. Morgan visited the station and I told him that a white-eyed Drosophila had appeared in one of the pedigreed strains, but that I was too busy with abnormal veins to attend to it. *He took live descendants of this white-eyed 'sport' and bred them. Eventually, he got the white eye back*" (emphasis mine). Thus, LUTZ asserts that it was he who found the white mutant, and MORGAN isolated white-eyed flies from among the progeny of the wild flies given to him. The situation is confounded further by a review of the LUTZ book by RAMSEY SPILLMAN, which appeared in the *Journal of Heredity* (1942). In his review, SPILLMAN wrote as follows, again verbatim: "It is surely of scientific historic interest that, while studying Drosophila for variations in the wing veins, Dr. Lutz found a white-eyed mutant, but having his hands full with the wing-vein problem, gave over five descendants of the white-eyed sport to Professor T. H. Morgan." In a brief note in the *Journal of Heredity* entitled "Genesis of the White-Eyed Mutant," MORGAN (1942) rebuts SPILLMAN by noting first that SPILLMAN's statement is not quite what LUTZ wrote. He notes further, "It is not obvious from this statement that the flies Lutz gave me were the descendants of the 'white-eye sport' since it was dead when found, unless the bottle had contained a virgin female and the white-eyed male. Moreover, if it had mated before death to a female, many white-eyed males would have appeared in the next generation which was not

the case." On equivalent genetic grounds, MORGAN points to the inconsistency in SPILLMAN's statement. Finally, as MORGAN emphasizes, the *white* mutation occurs frequently, and the white-eyed male he found is independent of LUTZ's dead male. In this connection, it is important to note that MORGAN was quite correct in the matter of *white* mutations. Between March, 1915 and April, 1942, the independent occurrence of 27 white-eyed mutants is recorded in the second published catalog of *D. melanogaster* mutants (BRIDGES and BREHME 1944). This number is in all likelihood an underestimate because not all such mutants are reported. Thus, conceivably LUTZ did find a white-eyed mutant which, however, left no progeny. Without progeny, there is no genetics! Whether LUTZ's observation alerted MORGAN to be on the lookout for the white-eye mutation is a question that cannot be answered.

Finally, it should be noted that *white* was not the first sex-linked mutation discovered. In the currant moth Abraxus, DONCASTER and RAYNOR (1906) described a trait called *lacticolor* segregating among wild females but not among males. The sex-linked, recessive inheritance of *lacticolor* was not understood until it was recognized that, in Abraxus and other Lepidoptera, the female is the heterogametic sex, not the male (BRIDGES 1916).

To sum up: the beginning of modern genetics can best be dated to January, 1910 with the discovery by T. H. MORGAN of a white-eyed *D. melanogaster* male.

For the science of genetics, the portent of the white mutation was enormous. Quickly, additional sex-linked mutants were discovered by MORGAN and his students. By 1913 STURTEVANT, with unsurpassed intuition, constructed the first linear genetic map of the *X* chromosome, followed by BRIDGES' (1916) cytogenetic proof of the chromosome theory, already cited. Crucial for the demonstration of *D. melanogaster* as the genetic organism par excellence was MULLER's (1918) establishment of the principle of balanced lethals, the implementation of which made routine the recovery, maintenance, and analysis of all classes of mutations, genic and chromosomal. By 1925 the vast amount of information accumulated by MORGAN and his students in less than 15 years was summarized in the monograph *The Genetics of Drosophila.* Documented therein are those fundamental principles of genetics derived from the study of Drosophila, principles that have withstood the test of time and that are included in all contemporary textbooks of genetics.

Readers of this series may note the irony that has been identified by LEWIS (1995): A. H. STURTEVANT and G. W. BEADLE found that they could not agree whether the *white* gene was the specific *white* mutant (STURTEVANT) or the entire set of alleles including wild-type (BEADLE).

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