In conclusion, these complementation tests demonstrate that *straw* is allelic to *laccase2*. Therefore, we propose that according to established *Drosophila* nomenclature practices, the gene name of CG42345 should be changed to *straw*, as it was first called in the Morgan lab in 1917. Our observation "Bridges" the historical gap in understanding the molecular nature of the *straw* mutants discovered 100 years ago.

References: Gohl, D., M. Mueller, V. Pirrotta, M. Affolter, and P. Schedl 2008, Genetics 178: 127-143; Morgan, T.H., C.B. Bridges, and A.H. Sturtevant 1925, The genetics of *Drosophila melanogaster*. Biblphia Genet. 2: 262pp; Riedel, F., D. Vorkel, and S. Eaton 2011, Development 138: 149-158.

History of the FM7 balancer chromosome.

Merriam, John[1]. Revised by Scott Hawley and Danny Miller, 1-22-2014. Figure courtesy of Angie Miller. [1]Molecular Cell and Developmental Biology, University of California, Los Angeles 90095.

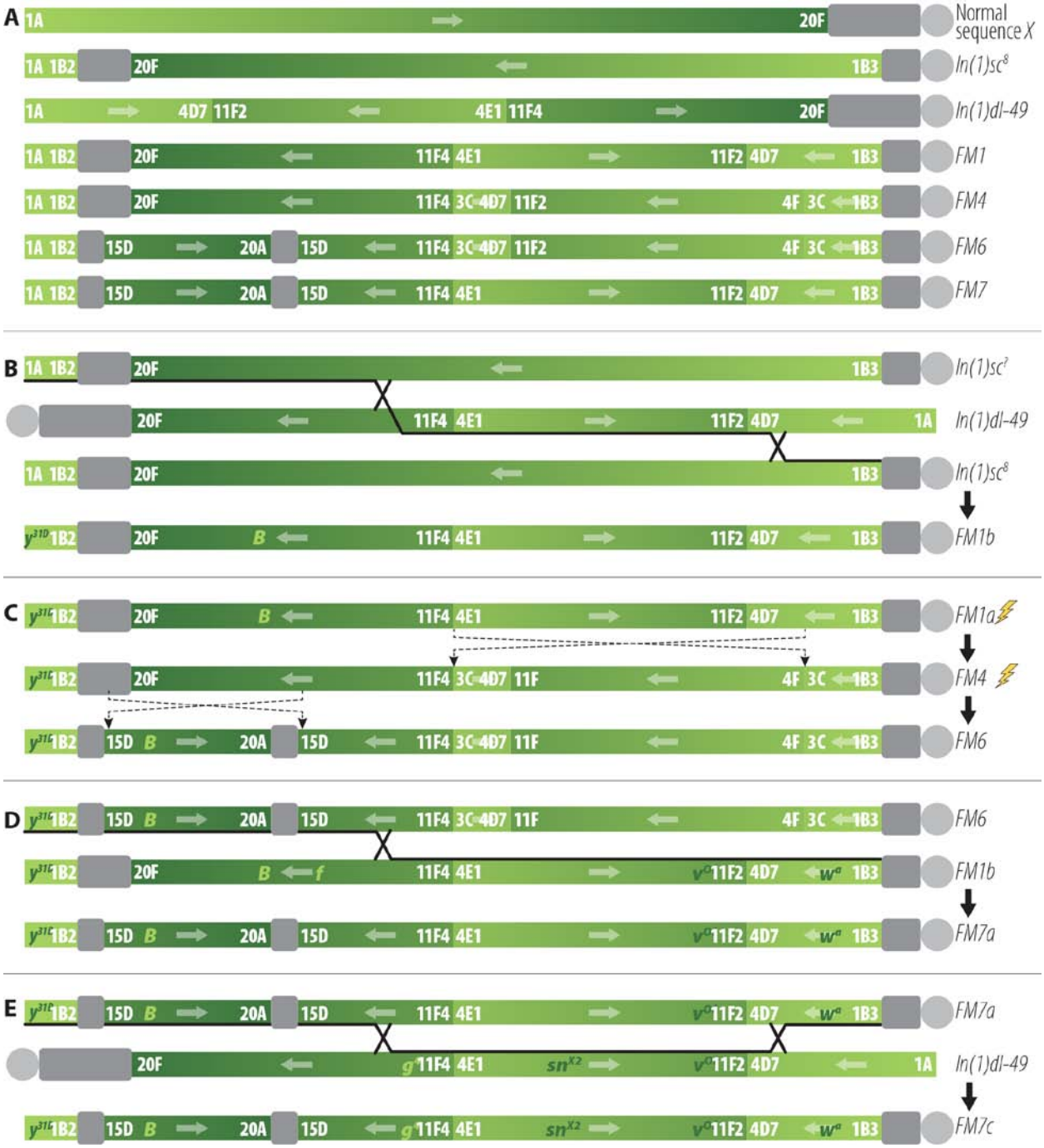
Like all modern balancer chromosomes in *D. melanogaster*, *FM7* was constructed from a series of progenitor balancer chromosomes. Inversion heterozygotes, but not homozygotes, suppress crossing over at the inverted portion of the chromosome. Sturtevant (1913) discovered the first example of an inversion, which he named *In(3R)C*, for crossover suppressor in the right arm of chromosome 3. This inversion reverses much of the distal third of the chromosome (from section 92D1 to 100F2) so that the chromosome sections in the right arm distal to the break at 92D1 are in the order centromere–100F2–92D1–telomere, and it suppresses crossing over for this region (from the marker *Dl* (*Delta*) to the telomere). Muller (1918) used *In(3R)C* to make the first permanent heterozygous stock, or "balanced stock", with the marker *Bd*, an allele of the *Serrate* (*Ser*) gene, that has both a dominant wing notching and recessive homozygous lethality. In the language of its time, this stock was "pure breeding"—all progeny had the same phenotype and genotype of their parents—because *Bd/Bd* and *In(3R)C/In(3R)C* homozygotes did not survive, leaving only *Bd/In(3R)C* heterozygotes each generation. In order for this stock to remain heterozygous each generation there must be suppression of crossing over, as it keeps the wild-type Bd^+ allele from *In(3R)C* from being placed onto the *Bd* chromosome, which would allow for recovery of *Bd+/Bd* non-*In(3R)C* progeny.

The importance of this example was instantly recognized, leading to the identification of dominant crossover suppressor lines for all the linkage groups, and it was applied to maintaining mutant alleles with poor viability and/or multiply-marked chromosomes. Because *Drosophila* stocks cannot be maintained through frozen lines, essentially all of the thousands of mutant alleles in different genes now available must be maintained in balanced stocks without selection. The balancer chromosomes responsible have improved to contain multiple inversions for more complete crossover suppression, as well as a dominant marker for identification and recessive lethal or sterile mutants to prevent the stock from becoming homozygous for its balancer and losing the mutant allele.

Along with balancing mutant alleles, the inverted chromosomes also became essential in screens for new mutants. Muller (1928) recovered a balancer on the *X* (or 1^{st}) chromosome, *In(1)Cl*, also carrying the visible markers *sc v f* (all recessive) and *B* (dominant), as well as a lethal allele in an unknown gene. The middle two-thirds of this chromosome was inverted from 4A5 to 17A6. Maintained as the "ClB" stock, it formed the basis for Muller's assay to determine the fraction of sperm that carried a new *X*-linked lethal mutation after exposure to X-rays, work for which he received the Nobel Prize in 1946. Balancers were also used to identify lines with segregating recessive lethal mutations following mutagenesis, which could be identified as stocks which only gave heterozygous mutagenized-chromosome/balancer progeny. One highlight example is a 1980 paper by Nusslein-Volhard and Wieschaus describing their identification of the embryonic patterning genes through lethal alleles, for which they received the Nobel Prize in 1992.

Both the stock-maintenance and selective-screening uses of balancers depend on their effectiveness in suppressing crossing over. The goal of balancer construction has, therefore, been to add multiple inversions in order to cover as much of the chromosome as possible. *In(1)Cl* suppressed crossing over for most *X* regions except most proximally, but was less useful because of its own recessive lethality. *In(1)dl-49*, the second *X*

inversion discovered, is homozygous and hemizygous viable and fertile, although it inverts only the middle third of the *X* so it acts in a polar fashion, suppressing crossing over in the middle and distal thirds but allowing crossing over proximally. Muller led an extensive effort to generate X-ray induced variants for altered phenotypes of genes and for altered chromosome rearrangements. Often the examples were both—the frequent *scute* (*sc*) mutations turned out to be inversion or translocation rearrangements through breakpoints in the centric heterochromatin that repaired next to the distally located *sc* gene, inactivating the *sc* gene through position effect. One example is *In(1)sc*^{8}, an entire-arm inversion that eliminated all single crossovers but allowed the less frequent double crossovers to survive, which facilitated the movement of markers such as w^{a} and *B* into and out of *In(1)sc*^{8}. This, of course, meant it was not a very good balancer by itself.



Although some multiply-inverted combinations were induced by irradiation, *X* chromosome balancer design and construction took a major step forward through the use of crossing over to place the centrally located *In(1)dl-49* inside of *In(1)sc*^{8}. This was not easy and somewhat paradoxical, because *In(1)dl-49* does not allow double crossovers to occur on the X, yet it takes a double crossover, one on each side of *In(1)dl-49*, to get it into the *In(1)sc*^{8} chromosome. Muller found a way, however, possibly by using a triploid line carrying a metacentric attached *X* chromosome isogenic for *In(1)dl-49* with *In(1)sc*^{8} as the free *X* chromosome (Muller, 1934). Alternatively, triploid females are known to have elevated rates of crossing over, particularly at the terminal and centric ends of chromosome arms, so it is not unlikely that the necessary double crossover occurred in triploids (Dan Lindsley, personal communication); this latter alternative is shown in Figure 1B.

By 1953, the doubly inverted chromosome *In(1)sc*^{8}*+In(1)dl-49* marked with y^{31d} sc^{8} w^{a} lz^{s} and *B* existed; its synthesis was credited to Schultz and Curry by Lindsley and Grell (1967) and it was named *First Multiple 1* (*FM1*) by Lewis and Mislove (1953). *FM1* functions well as a balancer except in the presence of additional chromosome rearrangements, such as heterozygous autosomal inversions, which will boost crossing over elsewhere [the "interchromosomal effect" (Joyce and McKim, 2011)], that increased the frequency of double crossovers proximal to the *dl-49* interval inside *sc*^{8}. Attempts to improve its crossover suppression by X-irradiation succeeded only in forming a partial reinversion of the *dl-49* interval, the *FM4* variant (Figure 1C), which looks complex in cytology but does not suppress double crossovers for most of the arm inside the *sc*^{8} inversion. Further irradiation of *FM4* produced a better version, the *FM6* variant, which contained a new inversion from 15E to 20A that suppressed double crossovers proximally but still allowed them distally (Figure 1C).

To expedite the production of an effective balancer chromosome, *FM1* was crossed to *FM6* and a recombinant was chosen that merged the best features of both (Figure 1D). The process was not difficult, because the *FM1/FM6* genotype is homozygous for *In(1)sc*^{8} and has normal levels of crossing over for most of the *X* (Sturtevant and Beadle, 1936). From *FM1,y* w^{a} v^{Of} *f B/FM6,*y^{31d} *dm B* females, only a single crossover (distal to the *dl-49* interval and recognized by the differential markers w^{a}, v^{Of} and dm^{+} from *FM1* and f^{+} from *FM6*) was required to obtain the stock referred to as *FM7a* [*i.e.*, *In(1)sc*^{8}*+In(1)dl-49+In(1)15E-20A,*y^{31d} w^{a} v^{Of} *B*] (Merriam, 1969). In the presence of autosomal rearrangements, *FM7a* effectively suppresses crossing over along the entire *X*, but because both *FM7a* males and homozygous females are viable and fertile, a sterile balancer (*i.e.*, without fertile homozygotes) was needed. To that end, *FM7a* was further converted by recombination with *In(1)dl-49* lz^{s} to produce *FM7b* [*In(1)sc*^{8}*+In(1)dl-49+In(1)15E-20A,* y^{31d} w^{a} lz^{s} v^{Of} *B*] and with *In(1)dl-49,* sn^{X2} v^{Of} g^{4} *f* to produce *FM7c* [*In(1)sc*^{8}*+In(1)dl-49+In(1)15E-20A,*y^{31d} w^{a} sn^{X2} v^{Of} g^{4} *B*] (Figure 1E) (Merriam and Duffy, 1972). The lz^{s} and sn^{X2} female sterile mutants were induced on *In(1)dl-49*-bearing chromosomes, so their entry into *FM7* was possible by a double crossover between homozygous *In(1)dl-49* sequences. The *FM7a* and *FM7c* balancers (plus customized reporter additions) are the two most widespread *X* chromosome balancers in use today.

References: Use the references section in FlyBase to identify the cited literature.