MEDICINA NEI SECOLI ARTE E SCIENZA, 29/1 (2017) 189-210
Journal of History of Medicine

Articoli/*Articles*

IMAGING THE *SUPER-FEMALE*: WOMEN, GENDER AND HANDBOOKS IN THE HISTORY OF A GENETIC TERM

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SUMMARY

The concept 'super-female' initially appeared in genetic studies of the common fruit fly, Drosophila, during the 1920s, and in early medical cytogenetic research in 1959. In this paper I present a genealogy of this gendered term and analyse the influence of the genetic concepts formulated by drosophilists on the construction of what would come to be known as medical – human – cytogenetics. While retrieving the participation of woman geneticists, the historical trajectory of this word and its meaning will be traced through the early cytogenetics of sex determination.

Early 20th century human genetics was the study of hereditary processes from a mother and father to their descendants. One research trajectory was conducted at the cell level, in the chromosomes detected during cell division. With their ability to be stained, the shapes of chromosomes during the steps towards cell division illustrated the biological process of hereditary transmission. Therefore, when the practices of cytogenetics were incorporated by the clinic in the 1960s, human genetics was identified with chromosome studies. Four decades had passed since the early *Drosophila* studies, during which an entire cellular epistemology had circulated and survived by providing correlations between bodies and chromosomes at the origins of the biomedical era[1].

Key words: Drosophila genetics - Human genetics - Chromosomes - History

As Helga Satzinger has suggested, the study of heredity has been genderised in various forms during the 20th century, and chromosomes, having being identified as the biological bearers of heredity, become the subject of genetic research. A group led by Thomas H. Morgan began cross breeding *Drosophila* in the 1910s in efforts to locate genes as particular sites in the chromosomes. These studies were hugely influential and provided evidence for the chromosomal theory of heredity[2].

The sex chromosomes had been the focus of cytology and cytogenetics since the late 19th century. Later, in the few years between the late 1950s and early 1960s, a large number of disorders and abnormalities were described in publications on the origin and development of biological research into sex difference[3]. Along with cytology, embryology, botany and zoology were among the disciplines involved in these sex studies[4]. Isabel Delgado has suggested that the development of German microscopy and the circulation of knowledge and practices generated in Germany enabled some research groups in the UK and the US to later take the lead, not only through the migration of those fleeing the Nazis but also by the subsequent stimulus to knowledge dissemination from post and other forms of communication[5]. The XY system was not the only one found in the many species studied by cytologists: a number of other systems were described and in many species sex determination was found to be non-existent. However, as *Drosophila* had the same sex determination system as human beings and *Drosophila* genetics were mutually reinforced, as Delgado has stated. The generalisation of such a system led to the identification of X as the female chromosome and Y as the male, despite awareness that sex development depended on a combination of X and Y chromosomes[6].

By following traces of the super-female fruit fly, in the first part of this essay I will retrieve the early history of the biological understanding of sex. Sex is taken here to be a biological ontology identified in chromosome sets and correlated with bodies, as studied in *Drosphila* and linked to Mendelian trait inheritance. In the second part I focus on human sexes, chromosomes and biology reconstructed around the concept of the super-female, attributed in the clinic to a woman that did not menstruate[7]. In the third part I trace the term super-female in *Drosophila* handbooks. I reflect on the history of sex, gender and women geneticists as part of the contemporary epistemology of heredity, when the laboratory and medical practice interacted in a particular way, characteristic of the biomedical era. The historicity of a genetic term drives this reflection. While providing a reconstruction of the epistemology embedded in such a genetic term, I will show the influences and reciprocal interactions between *Drosophila* and medical genetics.

Early Drosophila chromosomes

In 1905, Nettie Stevens identified the "heterochromosomes" XY of the common mealworm, *Tenebro molitor*. Stevens' studies, alongside those of E. B. Wilson and Thomas H. Morgan, established the chromosomal theory of sex determination; historians have noted that Stevens' work and presentation of evidence not only preceded the efforts of Wilson and Morgan, it was also more comprehensible[8]. Stevens had graduated at Bryn Mawr College and collaborated with Theodor and Marcella Boveri during her stay in Germany, taking an active role in the influential community searching for evidence of Mendelism. Stevens contributed to the concept of sex as a Mendelian trait and participated in the controversy surrounding sex determination, along with Morgan and other geneticists and zoologists of the time, constructing a theory of sex determination based on her own findings[9].

Nettie Stevens was the first to describe and draw the chromosomes of *Drosophila* (known initially as *amphelophila* and from some point, *melanogaster*)[10]. In a 1908 paper, she identified the chromosomes of a wide set of flies and midges from the genus *Diptera*. Among the four plates of chromosome drawings she published, twenty seven figures showed *Drosophila* chromosomes at different stages of cell division. Three of these are reproduced in figure 1. Following a detailed procedure for preparing the slide, images of chromosomes were characterized as "camera lucida drawings", produced by the projection onto paper of what was revealed to the eye by microscopic magnification of the slide. At that time, chromosome images of *Drosophila* and other species were usually created using this method: I have found this largely taken for granted, as publications rarely mention the method by which these drawn images - which became scientific evidence - were manufactured.

Nettie Stevens died in 1912. Her studies of "sex-limited" inheritance in *Drosophila* helped persuade Thomas H. Morgan to accept the chromosomal theory of heredity. In the laboratory that would come to be known as 'the fly room', Morgan worked in collaboration with many women, the names of whom were included in Morgan's acknowledgements of some of his publications: in addition to Edith Wallace (see below), these included M.B. Abbott, Anna Bergner,

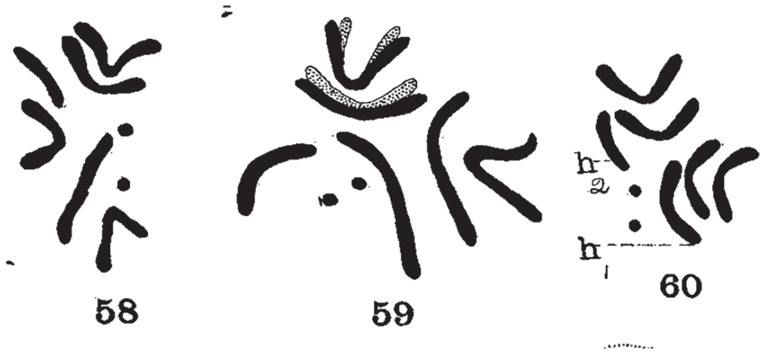

Fig. 1. Stevens, N. M. 1908, A study of the germ cells of certain *Diptera*, with reference to the heterochromosomes and the phenomena of synapsis. *Journal of Experimental Zoology*, 5 (3), 359-374, from Plate III.

Eleth Cattell, Clara Lynch, Ann Elizabeth Rawls, Helen Redfield, Shelley Safir, Mary Stark, and Sabra Tice[11]. It was immediately after Morgan gained a number of male colleagues, that these "boys" names would join Morgan's as the leading scientific members of the *Drosophila* group at Columbia University, New York: Calvin Bridges, Alfred Sturtevant and Hermann J. Muller. No woman's name was included in the earlier drosophilists, as described by the team members, despite many early contributions having been made by women[12]. As Helga Satzinger has pharased it, "gender is at work in the establishment of the fragile balance of innovation and stabilization of scientific knowledge"[13].

X and Y stabilised as sex human chromosomes from the 1950s on, and the subcellular organelles became genderised, female and male respectively. Human cells were also genderised according to their chromosomes. Sex determination theory was influenced by the history of hormones, the steroids that as chemical compounds had also received gender identity, either the female or male adjective according to the person from whom the samples were extracted[14].

According to the Mendelian theory of chromosomes and sex determination, human sex, along with that of some insects, was genetically based: a random biological event during cell division. The 1922 edition of the well-known book by Morgan, Sturtevant, Muller and Bridges, *The Mechanisms of Mendelian Heredity*, which presented an extensive and powerful statement about the evidence supporting the chromosome theory of inheritance – proposed a decade earlier by the Boveris and Walter Sutton – also included the super-female in a long revised chapter on sex inheritance: super-females were described as "Individuals that have 3X" [15].

Inspired by the concepts and reasoning of drosophilists from the first third of the 20th century, medical geneticists in the 1950s and early 1960s employed the new images of human chromosomes – karyotypes – to find not only explanations for their observations, but also names to be reused in medical diagnosis. This has led me to consider the extent to which 20th century human genetics relied upon earlier genetic findings from other species. A gender approach to the historical trajectory of the term "super-female" enables me to show that biological sex has always been a historically contingent and culturally grounded concept. The concept of sex itself was manufactured during the early days of research into the sex hormones and chromosomes of a variety of species.

This reconstruction is based on images of both chromosomes and bodies. The ontology of the super-female is shown as a visual epistemology: a history of scientific images produced in the everyday practices of geneticists. These images are regarded as epistemic images that are part and parcel of the way of producing, perceiving and knowing human medical genetics. Produced through the cytogeneticist's craft at the laboratory bench, these images were based on the creation, reproduction, and circulation of shapes, names and meanings; the super-female joined in this epistemological set composed of a combination of body anatomies and chromosomes.

Drosophila geneticists from Morgan's research group coined the term super-female as a way of reasoning that established a correlation between what was observed in the fly, and what was observed in their chromosomes[16]. The first instance of the label I have found occurs in Calvin Bridges' 1921 paper on what he termed triploid intersexes. He describes among these "the condition 3X" to which he gave the name "super-female". He added: "Triplo X individuals ordinarily die, although in certain lines they occasionally survived"[17]. In a longer report, Bridges developed the concept of the super-female: although resembling females, they are "sterile and sections of the gonads show abnormal ovaries" (the whole fly is in figure 2)[18].

The following year, Lillian Vaughan Morgan, wife of T.H. Morgan, described a female fly with two X-chromosomes linked together so as to exhibit a larger one, which was then "transmitted to the next

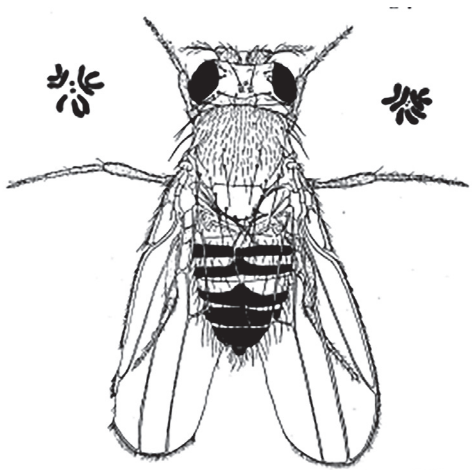

Fig. 2. Bridges 1922: 62; drawn as usual by Edith Wallace

generation" to produce "their rare wild type XXX sisters". Having graduated at Bryn Mawr in 1891, Lillian Vaughan spent many summers at the newly created Marine Biological Laboratory in Woods Hole (MBL), received a Master's degree at Bryn Mawr in 1894 and returned to MBL as an investigator. She married Morgan in 1904 and although continuing her research, devoted most of her time to raising their children. When they were grown she returned to research, and was given a working area of her own in Morgan's laboratory at Columbia[19].

In her research on XXX chromosome flies, Vaughan Morgan stated that the "genetic behaviour of the line of flies having the two inseparable sex chromosomes is in entire accord with the condition of the chromosomes as seen in cytological preparations". She called these specimens "X-triploid" flies. They provided cytological evidence of the chromosome theory of heredity, confirmed the theory of sex determination and became an established tool within genetic research. In the same paper she also described XXY flies that she identified as "female" (fig. p 273) and in so doing Vaughan Morgan participated in the research agenda of her husband's group[20]. While taking care of the household and contributing to the group's achievements, she did not obtain an official appointment herself until much later, at the California Institute of Technology (Caltech) in 1946. The Morgan's had relocated to Caltech in 1928 for what would be an extremely fruitful period for Vaughan Morgan, and where she still worked alone. At that time, during the Morgan's long research careers, *Drosophila* chromosomes were drawn so as to show particularities of a fly or a given line. These chromosome images, along with other materials originating from *Drosophila* cultures and practices, contributed to positioning the work of Morgan, Sturtevant, Muller and Bridges as references. When Vaughan Morgan presented her chromosome images, references to those drawn by Bridges enabled her to correlate her images with her analysis of the genetic "behaviour" of this line. From very early on, both cytological practices and images of chromosomes created references and standards, against which new images and mutations would be contrasted. Figure 3 shows three drawings included in Vaughan Morgan's paper in which her double-yellow females g and h are presented next to the wild type drawn "after Bridges", to illustrate the thicker shape of the inseparable double X chromosome.

Fig. 3. Lilian V. Morgan 1922 "Non-criss-cross inheritance in Drosophila melanogaster" *Biological Bulletin* 42: 267-274, on p. 273.

It was later, in her 1925 detailed revision of the cases of *Drosophila* with two attached X chromosomes, that Vaughan Morgan used the term super-female for the stocks she found of flies with two attached chromosomes and an additional X chromosome: one-fourth of the off-spring expected from the flies with two attached chromosomes were 3X, "and though poorly viable, a few in fact appeared"[21].
The detailed images of *Drosophila* mutants and wild types that had been in circulation since the early days of T. H. Morgan's research were all drawn by Edith M. Wallace, who was also "Morgan's personal technician"[22]. This woman scientist, sometimes called the "artist" of Morgan's group, had graduated from Mount Holyoke College in 1903, received a master's degree in Biology, and worked at Columbia in the fly room since 1908. Although Wallace is usually seen as an artist, she is named the "discoverer" of many mutants by the *Drosophila* handbooks published from 1944 on. Her discoveries are represented in an extensive number of images drawn by Wallace herself, in both books and original papers, demonstrating not only her biological contributions but also the power of her images, and the direct participation of these images in the *Drosophila* genetic work[23]. So far I have found no evidence of who drew the chromosomes for the group's publications[24].
The fly group at Columbia did draw *Drosophila* chromosomes, or at least they included chromosome drawings and not only flies in their publications, following the examples in Nettie Stevens' work. In order to further develop skills in correlating chromosomes and genes, a number of other cytologists began to collaborate or even compete with the Columbia group, among them Theophilus S. Painter and Theodosius Dobzhansky[25]. Obtaining good chromosome preparations provided evidence of the super-female. The historicity of these images shows that 'chromosome' was a term for a biological image plus a biological entity: heredity was becoming morphological, and this cellular morphology constructed a correlation between chromo-

somes and bodies. Biological terms spoke of shapes, the contours and profiles of living beings. It was by means of images that the super-female was defined, characterised and researched.

During the 1920s, X-rays were used to induce mutations in plants and *Drosophila* to check for Mendelian behaviour and chromosomal features. Hermann Joseph Muller's research, published in 1927, into artificial transmutation of the gene by X-rays in *Drosophila* - that is, X-rays producing mutations in *Drosophila* that were transmitted to off-spring - included evidence of the linear order of genes and of pieces of chromosomes being rearranged. In 1928 Muller examined the effect of temperature on the viability of *Drosophila* super-females: use of the term was being stabilised[26]. Theodosius Dobzhansky regarded the *Drosophila* super-female as a semi-lethal form and claimed the considerable variability of their frequency in the progeny of flies of similar genetic constitution could be explained by changes in temperature. Dobzhansky claimed X-chromosome breakage occurred due to environmental influences and summarized that "the highest frequency of the super-female was observed" at 20ºC. At 30ºC, he found "practically a complete non-occurrence of this kind of individuals", while at 24 $^{1}/_{2}$ºC they "were not rare and usually could be found in each culture bottle". He suggested that super-female flies hatched at 20ºC were stronger than those at any other temperature[27].

Muller and the University of Texas expert cytologist, Theophilus S. Painter, published detailed studies of the *Drosphila* X chromosome from 1929 on. Awareness of the effect of X-rays on *Drosophila* chromosomes prompted them to conduct a methodical experimental survey. Painter employed his cytological skills to provide an account of the procedure and their conclusions, and together with Muller produced a detailed illustration of the X chromosome: their joint practices contributed to the set of evidence for the chromosome theory of heredity and sex determination (Figure 4)[28].

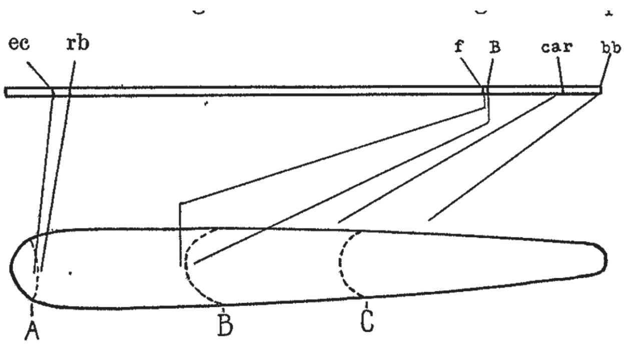

Fig. 4. The X – chromosome of Drosophila melanogaster by Painter 1931, p. 647.

The X chromosome was increasingly being drawn in a standardised shape, thus supporting the argument that visual cultures in *Drosophila* genetics and chromosome images were stable genetic ontologies. “Deficiencies” were correlated with chromosomes: Bridges correlated “diminished” individuals with the loss of an entire chromosome[29]. For drosophilists - once the chromosome theory of heredity had been accepted - a gene meant a piece of chromosome to which a character had been assigned through observation of a correlation, represented by the practice of drawing flies, chromosomes and gene maps. Image trajectories suggest visual cultures, or even cultures of creating visuals: images as evidence that made genetics and Mendelism reliable.

In the consulting room

In 1956, after almost a decade of collaboration, Polynesian cytogenetist Joe Hin Tjio, at the Aula Dei experimental agricultural station in Zaragoza, Spain, and Swedish botanist Albert Levan, from the of Institute of Genetics, Lund University, published their results determining the number of human chromosomes to be 46, rather than the accepted number of 48[30]. Charles Ford and John Hamerton, cytogeneticists at the Harwell laboratory of genetics in the UK, immediately confirmed the new number by reproducing the experiment. As Ford and Hamerton were renowned geneticists their support appeared to have contributed to the rapid acceptance of the new number. It was from 1960 on, however, when a new method for analysing chromosomes from blood samples was devised, that karyotyping became common practice in the clinical laboratory[31].

In 1959, a group of British medical geneticists and clinicians led by Patricia Jacobs published an article on "the existence of the human superfemale", retrieving the term for what the authors qualified as a "sex chromosome anomaly"[32]. The paper included two photographs of a naked 35 year-old woman taken from the front and side - eyes covered, arms straight down by her sides - whose "present appearance" was evidently that of a woman. Of "average height and weight, her breast was underdeveloped", said the text, and her last "spontaneous menstruation" had occurred 15 years earlier. Her chromosome set was shown as a karyotype obtained from a sample of her bone marrow; a sternal marrow sample extracted by biopsy and cultured according to the methods established in Britain the previous year. Taken from a magnified photograph of a single cell chromosome during mitosis, the chromosomes being cut out and re-ordered in pairs by size, the karyotype displayed the additional X chromosome. A growing group of cytogeneticists were collecting chromosomes, constructing the normal number and finding and classifying exceptions, including cases with both additional chromosomes and the lack of one of the pair assigned to sex chromosomes. For many years, correlations would be sought with the chromosomes to account for what were regarded as medical disorders[33].

Back to Drosophila: the handbooks

The story of the term super-female also suggests that although it originated from *Drosophila* genetics, drosophilists themselves reacted accordingly. The trajectory of the word in successive handbook editions reveals the "epistemological concerns" of the field: handbooks not only function as guides for students, they also materialize an entire area of knowledge and practices[34]. It is the set of concepts and their meaning that handbooks and textbooks show, as well as those they do not - the set of presences and absences - that articulate history, genealogy and scientific authority.

Drosophila handbooks produced a corpus of definitions and images, stabilising a space of knowledge and authority. This set of publications joined the aims of the Drosophila Information Service as a space to exhibit and share the practices of the fruit fly geneticists as an expert community[35]. The first handbook, published in 1944, was authored by Calvin Bridges and Katherine Brehme. Under the title, *The Mutants of Drosophila melanogaster*, it was based on a list initially elaborated by Bridges[36]. Following his death in 1938, the project was completed, updated and edited by the geneticist Katherine Brehme, of Wellesley College. The 253-page book described a collection of *Drosophila* "mutants and aberrations" listed by symbols in alphabetical order. It also described a number of wild stocks and included many figures produced by Edith M. Wallace, whose accuracy and artistic touch, according to Brehme's preface, had become "a standard all over the world". The collection characterized hundreds of mutants, at times over ten per page. Among these was a description of the super-female fly; Bridges is credited as the "finder" of the condition and Brehme herself cited as the author of the second reference. This particular fly mutant XXX, or triple-X, is described as a sex chromosome type classification, whose "rare adult survivors are small, wings frayed, ovaries underdeveloped" and produce a "high mortality of offspring".

A revised version of the handbook was published in 1968 entitled *Genetic Variations of Drosophila melanogaster*, by Dan L. Lindsley and E. H. Grell, from the Biological Division at Oak Ridge

Laboratories[37]. It was in the interim between these handbook editions that the human super-female appeared, named and described by the British group in 1959 as discussed above. The *Principles of Human Genetics* by Curt Stern, published in the late 1940s, was the first book on such a subject[38]. It did not include a mention of the term super-female in any of the editions from the 1950s that I have found[39]. Born in Germany, Stern moved to the US to join Morgan in the fly room. Although he returned to Germany to work with Richard Goldschmidt, he left Nazi Germany for the US again, joining the Department of Zoology at the University of California, Berkeley[40]. He reacted against use of the new genetic term super-female within human genetics immediately after the 1959 publication and in the same British journal. Stern underlined the fact that "unlike *Drosophila*, the influence of the X chromosome on sex determination in the human is not known", concluded that use of the term presented an "unproven implication that a 3X person is at least genetically more female than a 2X person" and declared super-female an inappropriate way of characterising an "abnormal woman". Stern also took advantage of the issue of discussing a gendered genetic concept to remark on species differences regarding sex chromosomes. In "man", as he phrased it, "both one X (that is X0, no Y) and two XX are females" while in *Drosophila* one X (no Y chromosome) individuals were male and 2X individuals female. He suggested another word: metafemale. Super-female, he stated, already had unsuitable connotations in *Drosphila* and this "inappropriateness" was "emphasised" when applied to the human case. This brief text by a respected and recognised geneticist suggests the powerful influence of *Drosophila* genetics on the way of thinking about human chromosomes[41]. Despite challenging use of the term, Stern's comments contributed to stabilising the over-riding role attributed to sex chromosomes in both *Drosophila* and human beings[42].

As a neologism, metafemale was also taken seriously by drosophilists. The 1968 version of the *Drosophila* genetics handbook revised by Lindsley and Grell, *Genetic Variations of Drosophila melanogaster* (and a second printing in 1972) accepted Stern's suggestion. It contained a section covering anomalies and disorders entitled "Departures from diploidy". In the alphabetically ordered collection of "departures", "superfemale" is described as "synonymous" with the term "diploid metafemale". The case of a female fruit fly with three chromosomes is listed in the "d" section, and although superfemale is included under "s", the instruction is "see diploid metafemale". Although the mutant's description remained practically the same, the term superfemale is not included in the index, and barely appears throughout the publication. Additional information under the diploid metafemale epigraph gives credit to Stern for suggesting the "term metafemale instead of superfemale". Wallace's drawing of the mutant fly, originally published in Bridges' paper of 1922, appears on the same page.

In the 1992 re-titled handbook *The Genome of Drosophila melanogaster*, by Dan L. Lindsley and Giorgianna J. Zimm, known as 'the red book of *Drosophila*', super-female is again found as a synonym of the first term that appeared in the section "departures from *drosophila*" under the word metafemale[43]. The trajectory of the term in *Drosophila* handbooks shows superfemale to be a stabilised synonym of what became an accepted term, diploid metafemale.

The process that led to the general acceptance of metafemale shows that Stern's proposal was taken seriously by drosophilists, the term remaining in use until at least 1992. It was after the super-female woman which led him to express his dissatisfaction with the term.

Final reflections

When Patricia Jacobs and her colleagues published the case of a super-female woman in 1959, they stated that "this condition is analogous to the super-female found in *Drosophila* melanogaster". In *Drosophila*, they added, such super-females were "often unviable" and that in their patient, only the genital tract was affected[44]. Indeed in *Drosophila* specimens rarely survived, and when they did were small, "wings frayed, ovaries underdeveloped"[45]. Later the same year in the same journal - the British *Lancet* -Curt Stern reacted to what he qualified as the "inappropriateness" of the term, which he considered carried "unsuitable connotations" both for *Drosophila* and for women with three X chromosomes. The prefix "super" did not correlate with the body of a woman shown to have an "underdeveloped breast" and a "small vagina"[46]. Stern suggested "meta-female" instead - meta, as he made clear, meaning beyond - which carried, in his own words, a "neutral quality". *Drosophila* handbooks included super-female among the genetic terms collected, described and finally discarded in the index and names of mutants, while keeping it as a synonym.

Changes in successive editions of *Drosophila* genetics handbooks - designed for students training, for consultation by experts researchers, and to help stabilise a disciplinary space - contribute to trace the development of the term super-female. The "inappropriateness" of the term for a woman might well have been the inspiration to discard the original word, but the gendered meaning remained. Stern specified that the term metafemale "avoids the unproven implication that a 3X person is at least genetically more female than a 2X person". Concepts of bodies and sexes pervaded the construction of genetic terminology. One X-chromosome too many did not mean an over accumulation of femaleness, rather it was the otherness of the unusual, beyond normal, which became embedded in the metafemale. The feedback between *Drosophila* and human genetics is reflected through the handbooks.

Image-making has been one of the most influential practices in human genetics, as shown by following the term super-female from *Drosophila* to human genetics, to the metafemale and back to *Drosophila*. Women and gender were materially engaged in the trajectory of the field: alongside the female *Drosophila*, women participated as both the observed and the observers at the very origins of contemporary genetics as a biomedical space. Between the laboratory and the medical practice, *Drosophila* terms and their meanings became an inspiration and a reference for the increasing authority of medical genetics.

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Acknowledgements
This paper has received valuable comments and suggestions from the participants of the Convegno MEG 2015, "Medical Terminology and Epistemology for a Dictionary of Genetics and its Degenerations from Hippocrates to ICD-10", held in May 2015 at the Universitá degli Studi di Palermo. I am also grateful to Joanna Baines for her careful copyediting. Research funded by the Spanish Ministry of Economy and Competitiveness (FFI 2012 – 34076).

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