Archives of Toxicology
https://doi.org/10.1007/s00204-024-03718-1

LETTER TO THE EDITOR, NEWS AND VIEWS

Muller and mutations: mouse study of George Snell (a postdoc of Muller) fails to confirm Muller's fruit fly findings, and Muller fails to cite Snell's findings

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Received: 27 February 2024 / Accepted: 28 February 2024

Abstract
In 1931, Hermann J. Muller's postdoctoral student, George D. Snell (Nobel Prize recipient—1980) initiated research to replicate with mice Muller's X-ray-induced mutational findings with fruit flies. Snell failed to induce the two types of mutations of interest, based on fly data (sex-linked lethals/recessive visible mutations) even though the study was well designed, used large doses of X-rays, and was published in *Genetics*. These findings were never cited by Muller, and the Snell paper (Snell, Genetics 20:545–567, 1935) did not cite the 1927 Muller paper (Muller, Science 66:84, 1927). This situation raises questions concerning how Snell wrote the paper (e.g., ignoring the significance of not providing support for Muller's findings in a mammal). The question may be raised whether professional pressures were placed upon Snell to downplay the significance of his findings, which could have negatively impacted the career of Muller and the LNT theory. While Muller would receive worldwide attention, and receive the Nobel Prize in 1946 "for the discovery that mutations can be induced by X-rays," Snell's negative mutation data were almost entirely ignored by his contemporary and subsequent radiation genetics/mutation researchers. This raises questions concerning how the apparent lack of interest in Snell's negative findings helped Muller professionally, including his success in using his fruit fly data to influence hereditary and cancer risk assessment and to obtain the Nobel Prize.

Keywords Hermann J. Muller · X-rays · Mutation · Cancer risk assessment · Radiation · Scientific misconduct

Introduction

George D. Snell received the Nobel Prize for Physiology or Medicine in 1980 for fundamental insights concerning histocompatibility genes. However, long before Snell redirected his research to immunogenetics, he had become captivated by the extraordinary findings of Hermann J. Muller in 1927, who claimed that he had induced gene mutations in the fruit fly via the use of X-rays, being the first to do so by any means (Muller 1927). Snell was also excited that Muller produced copious new gene mutations in a short time, with the mutational results not being susceptible to subjective interpretation as previous efforts had been. At the time of Muller's *Science* paper (July 22, 1927), Snell was a Ph.D. student of William Castle at Harvard University, training to become a mouse geneticist. After he received his Ph.D., Snell spent the next 2 years (1930–1931) at Brown University in Providence, Rhode Island, teaching anatomy (Klein 1996).

Snell believed that Muller's discovery of a high rate of induction of recessive mutations, and particularly of recessive lethals, needed to be extrapolated to a mammalian model to have more tangible relevance for humans. Snell (1935) also knew that while X-rays could induce sterility in mice (Bagg and Little 1924; Murphy and de Renyl 1930), the occurrence of heritable variations (i.e., mutations) due to ionizing radiation-induced mutations was uncertain, but suggestive, in mammals. For example, Bagg and Little (1924)

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Published online: 04 April 2024

and Bagg (1925) had found a recessive mutation associated with irregularly affected eyes, feet, and viscera in the third and subsequent generations of two different pairs of X-rayed mice. In the studies of Dobrovolskaïa-Zavadskaia (1928), the well-known dominant mutation known as "tailless" or "short-tailed" occurred several times among the first- and second-generation progeny of treated male mice. The same experiment also revealed an F_1 male with an unhardened top of its cranium, along with an F_2 male with one digit of a front foot missing—these variants failing to survive for any breeding tests—as well as an F_2 male showing a nervous motion of the head. This last variant and the tailless mutation were continued across generations. Strandoskov (1932) had found one male with two penises in the second generation following treatment of male guinea pigs. While the above observations suggested to Snell (1935) the possible induction of mutations by X-rays, he realized that analyzed separately—in view of uncertainties about frequencies of occurrence of such variants in the absence of treatment—there was no statistically significant proof of induction by X-rays. These data, especially in view of Muller's discovery that "X-rays cause an enormous increase in the mutation rate of *Drosophila melanogaster"* (Snell 1935), gave Snell considerable incentive to test whether X-rays would induce mutations in mice.

Snell realized that more powerful methods were available in *Drosophila* to detect the presence of recessive mutations than in mice, thanks to the inventive developments of Muller (Muller 1927). Nonetheless, Snell (1935) devised experimental methods that could be applied in mice that would give "the greatest chance of discovering any mutations that might be induced with the least use of pens and time; or more concisely, to give the maximum probability of mutation detection per pen per week." His proposed breeding scheme focused on recovering recessive visible and recessive lethal mutations. To identify recessive visible mutations, he backcrossed offspring that would have a 50% chance of being heterozygous for a new mutation back to a parent that would have been heterozygous for the same mutation, with the result that, on average, 25% of the offspring would be expected to reveal the presence of a new mutation that was either induced by the X-ray treatment or spontaneous. This was accomplished by mating heavily irradiated males (or control males) with mice homozygous for normal genes to obtain F_1 progeny. F_1 progeny were then outcrossed to mice with normal genes to obtain F_2 progeny, which were then backcrossed to their parents to produce what were called F_3 progeny, with those being carefully observed for different phenotypes.

To identify recessive lethal mutations, Snell (1935) proposed using genetic markers distributed on four of the rather large chromosomes of the mouse, and those recessive markers were homozygous in the stock of mice that he planned to irradiate with a large dose of X-rays. The irradiated males were to be mated with females that were homozygous for the wild-type alleles of the 5 recessive markers used (spread over 4 of the 20 pairs of chromosomes found in mice) to produce the F_1 offspring, all of which would then be heterozygous for all 5 of the markers used. It was expected that some of those four chromosomes would contain new recessive lethal mutations that would then be linked (i.e., physically connected) with the marker(s) on each of these chromosomes. Those F_1 offspring were then to be mated with females that were homozygous for the wild-type alleles of the six recessive markers used, which means that there was a 50% chance that any one of the F_2 progeny would have any one of those markers. Every one of those F_2 progeny was then to be tested by a breeding test (i.e., by mating it with a mouse homozygous for all the six recessive markers) to determine which of the six recessive markers it contained. If, for example, a female F_2 mouse was thereby demonstrated to be heterozygous for the brown (*b*) allele, that mouse would then be backcrossed to its father to determine whether any of the resulting offspring would have the brown coat color showing it to be homozygous for *b*. Failure to find any brown offspring among 20 or more offspring would provide convincing evidence that a recessive lethal mutation had been induced on the *b*-marked chromosome. That is, because of the linkage of the new recessive lethal mutation to *b*, the zygotes from the backcross that were homozygous for the recessive lethal would all die and thereby eliminate all homozygous *b* offspring. It was expected that this method would effectively identify any recessive lethals on the marked chromosomes, at least as long as there were not too many crossover units distant from the recessive marker genes on their respective chromosomes. Importantly, Snell (1935) thought that "because of the relatively simple external anatomy but complex internal anatomy of mammals, many mutations may not be externally visible." As a result, in addition to careful external observation of offspring, Snell (1935) proposed that an autopsy should be performed consisting "of a standardized examination of salivary glands, thyroid, trachea, heart, lungs, thymus, digestive organs, kidneys, testes and ovaries and their ducts, the accessory glands of the reproductive system, and parts of the skeletal and circulatory systems." Although his proposal made no mention of dominant mutations (i.e., those causing phenotypic changes in heterozygotes and thus often showing effects in the offspring of irradiated animals), such mutations could also be found using his proposed protocol.

The Muller–Snell connection

While at Brown University, Snell established a letter exchange with Muller during which he suggested taking a postdoctoral appointment under Muller's direction with the

goal of trying to extend Muller's research in fruit flies with a mouse model. Snell (1935) described what happened as follows:

> "Communications between the writer and Prof. MULLER revealed that almost identical plans—essentially those outlined in an above section of the paper [as in the present paper]—for an X-ray experiment with mice, had been prepared independently by each of us. Prof. MULLER, with the aid of several of his students, had developed an animal colony at the UNIVERSITY OF TEXAS for the purpose of executing this experiment. I am indebted to him for his kindness in putting this colony at my disposal. I am also indebted to him for valuable suggestions made during the course of the experiment."

Thus, to the delight of Snell, Muller had already recognized this important next step. In fact, Muller had even established a mouse colony within a newly constructed animal facility. Muller (March 10, 1931, letter to Snell) noted that he had about 400 mouse cages and could expand upon this as needed and could arrange to have a permanent university employee provide maintenance of the mouse colony during his research.[1] Snell decided to leave Brown University for a research appointment with Muller at the University of Texas at Austin. He arrived there in July 1931 and stayed for 2 years. We do not know if Snell used some mouse stocks that Muller had already gathered. After arriving in Texas, Snell located and imported some of the mouse stocks that he used from genetics laboratories across the USA to optimize his protocol. He finally selected five stocks of mice to use in his approach. An extremely important stock was the R-stock, which he obtained from Professor William H. Gates of Louisiana State University in Baton Rouge. The mice of that inbred stock were homozygous for the five recessive mutant genes *a*, *b*, c, *se*, and *p*. The *c* and *p* genes are on the same chromosome, tightly linked, and thus these five genes are biomarkers for 4 of the 20 chromosome pairs in mice. All of the X-rayed males were from this stock. An inbred stock obtained from Dr. Gregory Pincus (probably then at Harvard University) was homozygous for A^{w} and c^{ch}. Two other stocks were provided by the Roscoe B. Jackson Memorial Laboratory (Bar Harbor, Maine), and a fifth stock consisted of the first-generation progeny from two of the other stocks. Because it reflects on the high quality of his experimental design, it should be noted that Snell's experiment included a randomization component as well as the coding of animals in the experimental and control groups. The randomization was made with regard to the location of the pens of the experimental and control mice.

It is important to realize that Snell's arrival in Austin coincided with a period of considerable professional and personal upheaval for Muller (Carlson 1981). Muller was being formally challenged by multiple geneticists in scientific meetings/conferences, especially Louis J. Stadler, who claimed that Muller had not induced gene mutation but merely modest to massive gene deletions and other chromosomal changes such as translocations, findings that were far more limited in their biological significance. Stadler had asserted that Muller had confused an observation (i.e., transgenerational changes) with a mechanism (i.e., gene mutations) (Calabrese 2015, 2017a, 2019). In fact, Muller and numerous other geneticists were experimentally unable to support Muller's claim that he had induced gene mutations in research based upon the induction of reverse mutations, despite massive efforts (Calabrese 2019; Lefevre 1949, 1950). Muller was trying to prove that he had not simply "punched" large holes in chromosomes as had been suggested by Edgar Altenberg, his close friend, and others (Muller 1928). Muller was also in a separate conflict with the University of Texas administration and its Board of Directors over his advisory involvement in an unauthorized communist student group at that time. Finally, Muller was experiencing acute marital difficulties that would eventually lead to divorce (Carlson 1981). In fact, the combination of these three pressures is said to have led Muller to attempt suicide on January 10, 1932, only 6 months after the arrival of Snell. This period of great turmoil in Muller's life extended for many years, during which he lived in several other countries including the USSR (Carlson 1981).

Despite these tumultuous affairs in the life of Muller, Snell was fortunate that there was a group of talented geneticists and others with whom to interact, such as Bentley Glass and Clarence Oliver (Ph.D. students of Muller), several notable faculty such as John Patterson and Theophilus Painter, and a few geneticists from the USSR and other countries including Carlos Offermann from Brazil (Snell 1935). Offermann was having an affair with Muller's wife, beginning in the fall of 1931 (Schwartz 2008, p. 248).

Snell's X-ray experiment

In the Snell (1935) experiment, only male mice were X-rayed. Most of the details on the X-ray treatment were described by Snell (1933). During exposure, each mouse

[1] Muller wrote to Snell on February 27, 1931: "Not only I, but also the others in the department, would be delighted at the prospects of having you working with us. It so happens that I have colonies of mice here that have been inbred for some time with the specific purpose of being used in testing the production of mutation in mammals by means of X-rays…..it seems to me, however, that I have enough on my own hands with the *Drosophila* work and I should be only too glad to turn the mouse work over to you if you came here and wished to prosecute it. In fact, I had been hoping that someone would turn up who would want to do it.".

was enclosed in a leaded chamber that was large enough to hold it comfortably without permitting much freedom of movement. The X-rays were directed upward through an aluminum window with sequential aluminum and copper filters making up about 40% of its length. This arrangement allowed the X-rays to reach all parts of the testes and reproductive ducts. A dosimeter was placed in the chamber and showed that the X-ray exposure was delivered at 36.5 Roentgen-units/minute (i.e., a dose rate that was roughly 1.5×10^8 fold greater than the background radiation rate). The difference in treatment group exposures was dependent upon the duration of exposure, with the rate being kept constant across all exposure groups. The dose tested ranged from 400 to 1200 Roentgen-units, but mostly included mice exposed to 600 or 800 Roentgen-units. All offspring were collected from matings that occurred during weeks 1 and 2 immediately after treatment, which meant that the results related to irradiated spermatozoa.

Because the studies of Muller (1927) claimed to have found a high rate of induction of X-ray-induced recessive mutations, especially recessive lethals, Snell (1935) focused his experiments on detecting recessive mutations of the presumably vast number of genes (both for mutations that were lethal in homozygotes and those with visible effects—including those detected by time-consuming autopsies). As explained earlier, the finding of no mice with the phenotype of a particular recessive marker among as many as 20 offspring produced in each of the backcrosses of F_2 offspring with their F_1 parents in the recessive lethal test provided a strong presumption that a new recessive lethal mutation was linked (on the same chromosome) to the marked gene of interest in that F_1 offspring. The total numbers of marked chromosomes tested for the absence of a recessive lethal mutation were 209 and 166 in the experimental and control groups, respectively. Snell therefore concluded that "A [recessive] lethal is indicated if mice homozygous for one of the marker genes fail[s] to appear in the F_3 litters produced by the backcross of F_2 mice heterozygous for the marker to their F_1 parent. In no case where the tests were sufficiently extensive to be significant did the homozygous F_3 mice fail to appear." Thus, the disappointing result provided no evidence that what Muller had found for recessive lethals in the fly also occurred in the mouse. It should be noted that there was one female in the control that was not fully tested that provided a suggestion of expressing a recessive lethal mutation. Among her 13 backcross offspring, none had the *b* (*brown*) phenotype. The expectation that each offspring would not be brown in the backcross is 0.75, and 0.75 raised to the 13th power is 0.024, which is less than 0.05. However, Snell recognized that when so many statistical tests are being done, significance cannot be declared at 0.05, and he considered it unlikely that these data indicated that a recessive lethal had been found in the control.

The other backcross experiment, which tested to see whether induction of recessive visible mutations could be demonstrated in mice, provided a similar result. For such mutations, the important number is the number of backcross offspring examined for evidence of visible mutations instead of the number of marked chromosomes tested. There were 50 F_1 sons of irradiated males that produced 615 offspring that were autopsied, and there were 41 F_1 daughters of irradiated males that produced 254 offspring that were autopsied. Thus, for the vast numbers of genes in the mouse genome that could potentially mutate to a recessive mutation that would cause an abnormal phenotype detected externally or by autopsy, there were 869 offspring observed in which there was a 25% chance that any one of those possible mutant phenotypes could appear in each offspring. No evidence was found of a single induced recessive mutation. Similarly, there was no evidence found for the presence of any spontaneous recessive visible mutations in the 740 total backcross progeny in the control that were autopsied. In both the experimental and control groups, there were a few additional offspring that died before the autopsies at about 4 weeks of age. Those offspring were observed for abnormal phenotypes before they died. Snell concluded regarding his attempt to demonstrate induction of recessive visible mutations that "Since no such mutations were found, we must conclude that X-ray treatment of mouse spermatozoa, if it produces them at all, at least produces them with a much lower frequency than it produces translocations." Here, he is referring to a finding in his Texas experiment that was not anticipated when it was begun, namely that "Approximately 33 percent of the immediate progeny of the X-rayed males consistently produced litters of sub-normal size" (Snell 1935). Typically, when mice carrying reciprocal translocations are mated with normal mice, many of the zygotes have a chromosome imbalance, leading to abnormal development, and often resulting in death long before birth. The way in which Snell's experiment was designed provided an excellent method for collecting fertility data essential for the discovery of the radiation-induced reciprocal translocations, which Snell became widely recognized for demonstrating. Much of Snell's 1935 paper was devoted to describing his findings related to translocations. The downside of that unexpected discovery was that the resulting decreased litter sizes in the descendants of a significant number of the F_1 offspring made it necessary to do much additional work to test for induction of recessive mutations.

The backcross experiment did lead to the discovery of one mutation; however, it was not a recessive mutation. It was a dominant mutation with variable expressivity that caused "a reduction in width and a change in shape of the spleen, a considerable reduction in vigor, and frequently a reduction

in size of the animal as a whole." Because it was reported to have been discovered "as a result of the autopsy," it apparently was found in more than one of the offspring from the backcross of a particular F_1 parent because Snell was able to maintain a mutant stock for this mutation for many generations, and he published its pedigree chart extending to four generations after the original F_1 male (Snell 1935). The stock was lost before it could be determined whether the homozygote was viable.

Snell's neutron experiment

Snell only stayed in Austin for 2 years. We know this and other biographical information mentioned here from a paper by Klein (1996). When Snell's postdoctoral funding ended, John T. Patterson—head of the zoology department—offered him a position providing he would shift from working on mice to fruit flies. He was unwilling to do that because he thought that the genetics of mice and other mammals was more important in view of its much more direct application to humans. Instead, he took a job teaching genetics, evolution, and embryology at the University of Washington at St. Louis. Frustrated by not being able to do research, he quit after 1 year. Unable to find a research job—this was during the Great Depression—he spent part of a year barnstorming in Texas with his brother who was a pilot. He then returned to the Bussey Institution in Applied Biology at Harvard University where his mice were being kept temporarily. In 1935, he accepted a job at the Roscoe B. Jackson Memorial Laboratory at Bar Harbor, Maine. When he arrived, there were only six other staff members, no technical assistants, and there was very little equipment in what was then a single building. Interestingly, William L. Russell was one of those staff members. Snell continued to do some experiments related to better characterizing two of his X-ray-induced translocations.

With support from the National Research Council, Snell (1939) also completed and published in PNAS a further attempt to detect induction of recessive visible mutations in male mice—this time following irradiation with neutrons. Besides the type of radiation, there were several other differences from the strategy used in his experiment in Texas. Twelve males received a neutron dose of either 110 or 120 "r" and progeny were collected both before and after the radiation-induced sterile period. Offspring born after the sterile period would be relevant to stem-cell spermatogonia, which have much more importance regarding hereditary risks in humans of radiation exposure. A total of 16 females and 25 males were produced in the presterile period and 13 females and 10 males in the poststerile period. Unlike in his experiment in Texas, no attempt was made to detect recessive lethals, with the entire effort regarding gene mutations being devoted to identifying recessive mutations using the same straightforward backcross approach used in his Texas experiment. Also, he used different stocks of mice, with the irradiated males all being from the C-stock, which was described as being homozygous for the recessive mutations *b* and *c*, which were not used as markers for chromosomes. He again tested F_1 offspring for sterility and semi-sterility. Among the 10 female and 23 male F_1 offspring so tested from the presterile matings, he identified 3 sterile males, 3 semi-sterile males, and 1 semi-sterile female. Among the 2 female and 5 male F_1 offspring so tested from the poststerile matings and the 19 female and 3 male F_1 offspring so tested from the poststerile matings, he found no instances of sterility or semi-sterility. The doses of neutrons used obviously induced translocations or other chromosomal damage leading to fertility effects, but to a considerably lesser extent than the doses used for X-rays.

All other F_1 offspring were phenotypically normal and produced litters averaging more than seven offspring in number. An attempt was made to identify any recessive visible mutations among 33 F_1 progeny (13 females and 20 males). Backcrosses between 83 of their offspring (17 sons and 66 daughters) yielded 842 offspring, and the "majority of these were observed at birth and again at about 3 weeks of age." A total of 25 control F_1 offspring were tested in the same way by backcrosses using 39 of their offspring, which produced 467 backcross progeny examined for recessive mutations. Snell concluded that, "In quite extensive tests, no evidence was found for the occurrence of recessive visible mutations with neutrons." It is of interest that F_1 male 8 (in the paper listed as Male $R_1$8, whose father was exposed to 140 "r") was described as "having a tendency to small litters … transmitted to about one-half his progeny." Also, it was noted that in addition to his normal and semi-sterile offspring, "5 out of 63 offspring that have been raised to maturity have shown conspicuously slow growth and have remained stunted throughout life." PBS, who has much experience inducing dominant mutations in mice that cause skeletal malformations and stunted growth, considers it highly likely from this description that F_1 male 8 was heterozygous for a dominant mutation (induced or possibly spontaneous) with incomplete penetrance for stunted growth. Because Snell referenced the procedures from his Texas experiment, it seems likely that all backcross progeny living to about 3 weeks of age were autopsied; however, Snell's paper on neutrons never mentioned autopsies. Without doing autopsies, Snell would have been much less justified in stating that "In quite extensive tests, no evidence was found for the occurrence of recessive visible mutations with neutrons." Snell (1939) did not report how many of the F_1 progeny tested for recessive visibles were drawn from the presterile and poststerile samples. Although it would be interesting to know how many backcross progeny were related to

irradiated stem-cell spermatogonia, that is not a crucial piece of information when assessing whether neutrons can induce recessive lethal mutations in mice. Vast numbers of genes were irradiated, regardless, and the backcrosses provided no evidence of induction of such mutations. It seems curious that Muller is never mentioned or cited in the neutron paper.

Was much interest shown by other geneticists in Snell's results on recessive visible and recessive lethal mutations in mice?

The 1935 paper of Snell has been cited in the Web of Science database 74 times to date. Muller never discussed the findings of Snell (1935) in the published literature as far as we have been able to determine. Muller acknowledged this paper one time in 1950 (Muller 1950). However, this 1950 paper of Muller listed the Snell (1935) paper as a citation in the references section of the paper but failed to acknowledge it in any manner in the text.

It is of particular interest to note the treatment of Snell's (1935, 1939) papers by certain geneticists for whom it seems that the data should have had considerable relevance. William Russell (1952) presented a paper at a symposium at Oberlin College in 1950 at which Muller also presented a paper. This would have been rather soon after Russell had initiated his first specific locus test (SLT) experiment and before he had any preliminary data to report. The goal of Russell's paper was said to "survey most of what is known and pass on to a consideration of what is needed next." He stated in his section on "Experimental Work: Gene Mutations.–Mutations produced by X rays have been reported in mice (Snell 1935; Hertwig 1939, 1941, 1942), but the data are not adequate for a reliable estimate of mutation rate…. Chromosome Aberrations.–Much is already known about the induction by X-rays of chromosomal aberrations in the mouse. The pioneer work was done by Snell (1933, 1935), Snell and Ames (1939), and Hertwig (1935, 1938, 1940)." Thus, he cited Snell's (1935) paper, but because Snell's paper only reported evidence showing induction of one irregular dominant mutation affecting the spleen, it is apparent that Russell is not referring to the part of Snell's paper related to visible and recessive lethal mutations. Later, Russell stated that "It would be out of place here to consider in detail the possible ways of measuring mutation rate [in mice] in other whole groups of genes." He then briefly described the SLT test approach being used in his present research at Oak Ridge in which he explained that recessive mutations at specific loci (number not stated) will be detected in the first generation and noted that: "This method has not been suggested before, for mice, presumably because of the relatively large number of animals needed. It was calculated, however, that, with the facilities offered by the Atomic Energy Commission, reliable mutation rates might be obtained in a reasonable time if they were not lower, or much lower, than the *Drosophila* rates." Without mentioning any specific experiments using such methods, he stated that "…methods for obtaining autosomal recessive visible mutations as a group require at least three generations and then only recover a portion of the total. The mutants [in the SLT] can be recognized at a glance, in contrast to the detailed examination, by highly trained observers, necessary when searching for mutations at all loci." Russell then, when discussing chromosome aberrations in much detail, cited two papers by Snell including the 1935 paper, but only with reference to sterile and semi-sterile males, and he emphasized the importance of Snell's findings regarding reciprocal translocations. In this paper, Russell did not mention that Snell found no evidence of induction by radiation of recessive mutations in mice in his 1935 and 1939 papers.

Russell (1951) presented extensive preliminary data from his first SLT experiment along with his initial claim that mice are much more sensitive to induction of recessive mutations than fruit flies. Snell was never mentioned in that paper. It is also now known than Russell was aware of the presence of a very large cluster of mutations in his control group of that first experiment before the symposium at which he presented those data; however, he chose to keep that a secret (Selby and Calabrese 2023).

Russell (1954) wrote a detailed review paper in which he cited 14 papers by Snell, including the 1935 and 1939 papers. Extreme detail was provided on Snell's results related to reciprocal translocations and sterility. Russell, when citing Snell's (1935, 1933) papers, reported that no dominant mutations with externally visible effects were found in 178 offspring of male mice given a mean X-ray dose of 681 r. He noted that Snell had identified one dominant mutation with incomplete penetrance that affected spleen shape, which had been identified in autopsied F_3 mice and that "as the descendant lines were not always large enough to give near certainty of recovering even dominant mutations, the mutation rate must be taken as one mutation in something less than ninety-one sperm for a dose of approximately 700 r." In the section of Russell's review (1954) on "RECESSIVE LETHALS, SEMILETHALS, AND VISIBLES," the emphasis was mainly on induction of recessive mutations in the preliminary results from his first SLT experiment, and Snell was never mentioned.

Earl Green had been a colleague of, and shared an office with, W. Russell at The Roscoe B. Jackson Memorial Laboratory, and he was the Director of that laboratory from 1956 to 1975. In Green's (1968) extensive review on the "Genetic Effects of Radiation on Mammalian Populations," there are no citations for Snell. Snell is only mentioned along with others for "classical studies" related to fertilizing capacity of

irradiated sperm and dominant sterility and dominant semi-sterility. Green referred readers to the summary of data and citations related to reciprocal translocations provided by Russell (1954).

In the paper by Lyon et al. (1964) entitled "The overall rates of dominant and recessive lethal and visible mutation induced by spermatogonial irradiation of mice," Snell's (1935, 1939) papers are never mentioned. The Lyon and Morris (1966) paper "Mutation rates at a new set of specific loci in the mouse" addresses the question of how representative the seven loci studied by W. Russell are of mouse loci as a whole. They pointed out that Russell had "found a 35-fold range of difference in sensitivity from the most to the least sensitive locus after a dose of 600 r. of X-rays to spermatogonia" (Lyon and Morris 1966). They stressed that this question was of importance when "considering the overall mutagenic effect of radiation in the mouse, and in comparing the mouse with other organisms" (Lyon and Morris 1966) and, in this regard, they noted Russell's claim that the mouse is 15 times more sensitive than the fruit fly to induction of mutations by an acute X-ray dose. They referred to the Lyon et al. (1964) paper in suggesting "that the mouse was only four to five times as sensitive as *Drosophila* and that the average mouse gene locus was less mutable that the seven studied until then." They reported that their new group of six loci was substantially (by a factor of four to five times) less sensitive to mutation induction than the group of seven loci studied by Russell, and they stressed that "it cannot be assumed that the new loci are accurately representative of mouse loci as a whole." While Snell's data from the 1935 and 1939 papers seem to be extremely relevant to this topic, those papers were not mentioned.

In Searle's (1974) long review "Mutation Induction in Mice," Snell is only mentioned once and that was just in regard to showing that dominant lethality and hereditary semi-sterility occurred following X-irradiation of postmeiotic stages in male mice. Udo Ehling and Randolph (1962) and Ehling (1965, 1966) only mentioned Snell twice in his three papers dealing with induction of presumed dominant mutations affecting the skeleton. In Ehling's earliest paper (Ehling and Randolph 1962), Snell (1935) is mentioned only in regard to demonstrating the reduction in fertility of irradiated male and female mice. Ehling (1965), when referring to Snell's (1935) paper and two other papers, wrote that those studies "yielded some information about the frequency of X-ray induced dominant visible mutations in mice, including those detected by autopsy." There was no mention that Snell's autopsies included parts of the skeleton and that the purpose of Snell's experiment was to detect recessive visible and recessive lethal mutations in mice. Liane Russell (2013) never mentioned Snell in her detailed history on the development and contributions of the mouse research program at ORNL. While some of these authors may not have been aware of Snell's attempts to demonstrate induction of recessive visible and recessive lethal mutations, others certainly were and may have purposely avoided the topic.

Why were Snell's findings on recessive mutations ignored?

Several important questions emerge regarding the above seeming lack of interest in Snell's (1935, 1939) papers:

- **Why did Muller fail to cite/discuss the research of** Snell (1935) **which was designed to replicate his famous fruit fly research with mice and research that was performed under his supervision following a study design that he apparently approved?**
- **Why did Snell fail to cite/discuss the 1927 breakthrough paper of Muller that provided the scientific foundation for the research he conducted under Muller and that his 1935 paper was based on?**
- **Why didn't other researchers acknowledge that** Snell (1935) **had failed to detect apparent X-ray-induced gene mutations, thereby not being able to extend the fruit fly findings of Muller to a mammalian model?** As discussed in numerous papers (Calabrese 2019, 2021), during the years between 1927 and 1946 when Muller was awarded the Nobel Prize, he was involved in much controversy regarding whether his major discovery actually related to gene mutations. Thus, it is puzzling why so little interest was shown in whether his discovery about gene mutations extended to mice.

A review of each of the papers citing Snell (1935) indicates that the mutagenicity findings were generally not evaluated (see the limited comments of Charles 1950; Dubrova 2016), with the vast focus of these 74 papers citing Snell (1935) commenting on the translocation findings. Some especially important examples were provided in the previous section.

Scientific and other literature reviews offer no explanation for this lack of interest in Snell's (1935, 1939) papers. In fact, the present paper appears to be the first time that this relationship between Snell and Muller has been explored, with attention being given to the puzzling lack of interest shown in the findings of Snell when he tried to replicate in mice the findings from Muller's *Drosophila* experiments that had commanded so much interest. However, Evans (1949) noted the significance of the Snell findings (1935), emphasizing that acute doses of X-rays at 600 rads could produce chromosomal breakage and translocations but "not by gene mutation" (Evans 1949). In fact, Evans sent his manuscript/paper to many leading geneticists and health physicists in late 1948 and early 1949, including Muller. Very curiously

in the Evans–Muller exchange on the Evans paper that cited Snell's findings, Muller appears to have dodged this question because his long letter to Evans made no reference to the Snell work (Calabrese 2023). That Muller failed to discuss the key findings of Snell in his own published papers and in his letter exchange with Evans represents an important historical finding that could potentially affect the historical foundations of LNT.

The findings of Snell (1935) clearly had the potential to challenge the 1927 mutational report of Muller with fruit flies with regard to their extrapolative relevance to mammals/humans. However, Snell was in a professionally precarious situation. His findings of no evidence of X-ray-induced recessive lethal and recessive visible mutations using very high doses/dose rates contrasted with the findings of Muller for similar gene mutations. Yet, Snell had been graciously integrated into Muller's famous research team, surrounded by colleagues who would strongly endorse the Proportionality Rule/LNT. Snell most likely realized that he was in a difficult situation. How would he have managed it? As noted above, one of the most striking aspects of the Snell's (1935) paper was that it failed to cite the original *Science* publication by Muller (1927) (or other relevant Muller publications) even though it was designed to confirm and extend those findings by Muller. Snell (1935) clearly chose not to emphasize in his discussion the surprise that he must have felt in finding no support for the view that Muller's results in the fly would apply to mammals. The beginning of his Acknowledgements section in his 1935 paper seems particularly noteworthy in view of this situation. He began by stating that "The investigation reported in this paper was conceived under the stimulus of the discovery by Prof. H. J. MULLER that X-rays cause an enormous increase in the mutation rate of *Drosophila melanogaster*." That sentence was followed by the three revealing sentences concerning the converging radiation research interests of Muller and Snell included earlier in our paper in the long quotation found near the beginning of the Section "**The Muller–Snell connection**."

Snell's (1935) paper also failed to address its potential implications for the Proportionality Rule (Hanson 1933). In fact, while Snell could have challenged the public health implications of the Muller fruit fly mutagenicity findings, he left this strikingly obvious issue unaddressed. It seems likely that it was in Snell's best interest to avoid potential conflict with Muller and others in his sphere of influence. It seems remarkable that Snell, after being in such a precarious situation regarding his career, would—a few years later—initiate his neutron experiment (Snell 1939). Again, he found no evidence of radiation-induced recessive visible mutations. He also dodged the rather obvious implications of those findings related to the development and application of the Proportionality Rule/LNT. In this paper, Snell (1939) never even mentioned Muller, *Drosophila*, or fruit flies. At this point, Snell perhaps realized that he had almost jumped from the frying pan into the fire regarding possible negative effects on his career. As noted earlier, with urging by his Jackson Laboratory supervisor, Clarence C. Little (Klein 1996),[2] Snell then developed other interests that, with his obviously great abilities, led him to explore other areas of genetics research, and eventually led to his being awarded the Nobel Prize.

Discussion

Carter (1957) noted that the research of Snell (1935) represented "the only search for induced recessive autosomal lethals in the mouse" which he affirmed was negative. He cited Haldane (1956) who had "recently suggested that a further search should be made, and has proposed a technique based on the use of recessive visible marker genes." Citing the research of Snell (1935, 1939) and Charles (1950), he noted that at that time "gene mutation rates [in mammals] are not very reliable, since they are calculated from a few mutations in a small number of tested cells." Charles directed a major effort in the Manhattan Project during World War II to address these concerns, but that project is viewed as a significant failure due to the complexities of project, the death of Charles, and the loss of some of the data (Calabrese 2019). An attempt was made to salvage as much as possible of the project by former staff members 5 years after the death of Charles, but with limited success, in part, due to an incomplete dataset/lost data (Charles et al. 1960, 1961). Further, this effort was greatly overshadowed by the massive research program of W. Russell (Russell 2013). Similar types of general shortcomings of the earlier mutation research in mice were noted by Dubrova (2016), but without providing any detailed analysis. It is not known whether findings from Snell's X-ray and neutron studies were considered when key decisions were made regarding the initiation of W. Russell's massive mouse mutagenesis program, which used over five million mice just within approximately the first two decades. The Russell research would also discover the occurrence of repair of genetic damage in spermatogonia and oocytes, and it would become the mainstay of the mammalian hereditary and cancer risk assessment program for radiations and chemicals in the USA and internationally (Selby and Calabrese

[2] Little was a prominent mouse geneticist who was a rival of Muller to be the first to induce gene mutation. Little would later become a member of the US NAS BEAR I Genetics Panel. Little was one of three of the BEAR Genetics Panelists who did not provide estimates of genetic damage to the US population over 1 to 10 generations as requested by Panel Chairman, Warren Weaver, due to unacceptable levels of uncertainty (Calabrese 2019).

2023). Applications of the Russell data to genetic and cancer risk estimation have recently been severely criticized (e.g., Calabrese 2017a, b; Selby and Calabrese 2023) due to Russell's **failure to report** the occurrence of spontaneous gene mutations found in often large clusters of recessive mutations produced by masked mosaics (Russell and Russell 1996) **throughout the entirety of their research**. This problem first came to the attention of other scientists when it was reported to the US Department of Energy by Selby in 1995 (Selby 2020). The Russells (1996, 1997) were compelled to publish corrections due to an external expert panel review, and on the basis of those corrected data—as well as a much better understanding of their previously published data after the Russells' 1996 and 1997 papers were examined closely—it was demonstrated that the Russell findings for both male and female mice supported a threshold rather than a linear dose response (Calabrese 2017a, b, c; Selby and Calabrese 2023). A detailed reanalysis of massive amounts of data on mice showed that there appears to be a threshold dose response in both sexes (Selby and Calabrese 2023) and that, as a result, W. Russell was incorrect when he shared his published findings with the US NAS Biological Effects of Ionizing Radiation (BEIR I) to support the LNT. Snell's (1935) results are certainly consistent with the view that a threshold dose would be remarkably large even for irradiated spermatozoa.

In retrospect, ideally (but likely putting his career at great risk), Snell (1935) should have discussed his mutational findings within the context of Muller's (1927) groundbreaking findings that X-rays induced gene mutations at high frequencies in fruit flies. Likewise, the same type of scientific obligation should have been felt by Muller, especially because these findings—based entirely upon his methodology, conducted in his own laboratory, and by his own postdoc—provided no support for the view that his discovery carried over to mammals. While the study had a mixture of strengths and limitations, it was published in the top genetics journal (i.e., *Genetics*), and had thus satisfied review processes of that era. Nonetheless, the paper appears to have been written in a deliberate attempt to avoid discussing the strengths, limitations, and implications of the mutational findings and how the results related to Muller's work. By neglecting to properly address these critical issues, Muller had one less hurdle to get over in being awarded the Nobel Prize and there was a prolonged gap in the literature as noted by Carter (1957) that would eventually be addressed in earnest by the massive research efforts of Russell. It took 20 years (from 1927 until the AEC agreed in 1947 to support Russell at Oak Ridge) after Muller's discovery about X-ray-induced mutations in fruit flies before it was decided that a massive expenditure was needed to determine whether Muller's findings applied to humans. There is no reason to think that Snell's results contributed to the delay because they were largely ignored. Some individuals, including Muller, had expressed grave concerns about possible hereditary harm from exposure to radiation in medicine. The dropping of the atomic bombs likely made some people realize that the society needed to know whether radiation had any similar effect in humans. Russell's (1951) surprisingly quick discovery that recessive visible mutations (many of which were homozygous lethal—and thus recessive lethals) were very effectively induced in male mice by X-rays likely brought great relief to Muller, in case he ever wondered whether he had been wrong in suggesting that his discovery also applied to humans.

An illustration of how Muller used his fame to promote the importance of Russell's discovery that ionizing radiation induced recessive mutations in mice is provided by the audio recording of his speech at the Lindau Nobel Laureate meeting in (1955), which was attended by numerous Nobel Laureates and many others.[3] Muller (1955) made the following statements during his 71-minute lecture, in which he referred to both the spontaneous and induced mutation frequencies from the preliminary results of Russell. At about the 7:40 minute mark: "Observations on the frequency of certain mutant characteristics in man, supported by recent more exact observations on mice by Russell working at Oak Ridge, indicate that any one given gene on the average—that is one gene—undergoes one mutation of a given type per generation out of 50,000 to 100,000 human germ cells. That is the mutation frequency for one gene, which we call μ." Then at about the 21:00 minute mark: "Let's now see how a given dose of ionizing radiation would affect the population. Radiation induces mutations similar to the spontaneous ones. … Now Russell's data on mice—the organism studied for this that is closest to man—shows that it would take about 40 Roentgen units—40 R of radiation—to produce mutations at a frequency equal to the natural frequency." Muller used these numbers from Russell in calculations that he made—on a blackboard—for his audience that related to his ideas of how to estimate hereditary risks. The important point is that Muller obviously wanted his audience to know that Russell had clearly demonstrated the induction of recessive mutations in mice following treatment of male mice with X-rays, making the negative (and uncited/not discussed) findings of Snell (1935) even more irrelevant.

[3] The following quotation is from the beginning of the "Comment" found at the website with the audio recording: "For the Lindau meeting on chemistry in 1955, the physicist Werner Heisenberg had proposed that invitations should go out to all Nobel Laureates working on nuclear problems, such as radioactivity and ionizing radiation. As a result, the meeting attracted Laureates from physics, chemistry and physiology or medicine. Because of this particular circumstance, the American biologist and geneticist Hermann Muller attended a Lindau meeting for the first and only time and gave a long and brilliant lecture (in English with a short polite introduction in German).".

The puzzling and troubling situation that we have described regarding Snell's data seems to be another example of the now nearly century-long battle to "save the LNT-single hit" model, a history that has now been carefully documented (Calabrese 2015, 2017a, 2019, 2022). The present paper about the Snell experience provides yet another example of how the desire to promote the acceptance of LNT within the scientific and regulatory communities was used by leaders like Muller to manipulate the field and governmental agencies in a manner that is strongly ideological, contradicting their scientific obligations. The recent documentation of the conflicts within the Health Physics Society, high-level advisory groups such as the NCRP, NAS, and also the US EPA concerning their ideological biases to support an LNT framework, show that these leadership efforts of Muller are still resonating at the highest levels of science in the USA (https://junkscience.com/).

Conclusions

This paper highlights the research of George Snell, working under the direction of Hermann J. Muller, showing that high doses/dose rates of X-rays did not induce recessive and recessive lethal mutations in his experiments with mice. The paper showed that Snell chose to work under Muller's direction to try to extend Muller's famous fruit fly mutation findings to a mammalian model. Yet, Snell never cited the underlying findings of Muller nor did Muller ever cite these negative mouse mutation findings of Snell throughout his entire career, nor did other leading contemporary geneticists, despite its acceptable quality, publication in the leading genetics journal (i.e., *Genetics*) and the profound importance of the findings which challenged the X-ray-induced gene mutation claims of Muller. The apparent "shunning" of the Snell findings by Muller and other leaders of the radiation genetics research community strongly suggests that the field of radiation genetics had started to be dominated by a controlling politicized ideology as early as the mid-1930s, a characteristic that became strikingly apparent by the mid-1950s and beyond (Calabrese 2019). In addition, the negative findings of Snell had the capacity to directly challenge the significance and generality of the Muller mutation findings and impact his being awarded the Nobel Prize. If Muller had not received the Nobel Prize, and thereby not used this international platform to aggressively promote his LNT perspectives, one might speculate on how this would have affected the adoption of LNT by regulatory agencies. Thus, the shunning of the Snell findings by Muller and other leaders of the radiation genetics community may have had a profound effect on the evolution of hereditary and cancer risk assessment policies and practices worldwide.

Acknowledgements EJC acknowledges longtime support from the US Air Force (AFOSR FA9550-19-1-0413) and ExxonMobil Foundation (S18200000000256). The U.S. government is authorized to reproduce and distribute for governmental purposes notwithstanding any copyright notation thereon. The views and conclusions contained herein are those of the author and should not be interpreted as necessarily representing policies or endorsement, either expressed or implied. Sponsors had no involvement in study design, collection, analysis, interpretation, writing, and decision to and where to submit for publication consideration.

Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

References

Bagg HJ (1925) Right Atari abnormalities of the viscera. 1. A morphological study with special reference to abnormalities of the kidneys of in the descendants of X-rayed mice. Am J Anat 36:275–311

Bagg HJ, Little CC (1924) Rotatory structural defects in the descendants of mice exposed to Roentgen ray irradiation. Am J Anat 33:119–145

Calabrese EJ (2015) On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith. Environ Res 142:432–442

Calabrese EJ (2017a) Flaws in the LNT single hit model for cancer risk: and historical assessment. Environ Res 158:773–778

Calabrese EJ (2017b) The threshold VS LNT showdown: dose rate findings exposed flaws in the LNT model. Part one period the Russell-Muller debate. Environ Res 154:435–451

Calabrese EJ (2017c) The threshold vs LNT showdown: Dose rate findings exposed flaws in the LNT model. Part 2. How a mistake led BEIR to adopt LNT. Environ Res 154:452–458

Calabrese EJ (2019) The linear no-threshold (LNT) dose response model: a comprehensive assessment of its historical and scientific foundation. Chem-Biol Inter 301:6–25

Calabrese EJ (2021) Ethical failings: the problematic history of cancer risk assessment. Environ Res 193:110582

Calabrese EJ (2022) Linear non-threshold (LNT) historical discovery milestones. Med Del Lavoro 113:e2022033

Calabrese EJ (2023) Thresholds for radiation induced mutation? The Muller Evans debate: a turning point for cancer risk assessment. Chem-Biol Inter 382:110614

Carlson E (1981) Genes, radiation, and society. The life and work of H.J. Muller. Cornell University Press, Ithica

Carter TC (1957) Recessive lethal mutation induced in the mouse by chronic y-irradiation. Proc Roy Soc Lond Ser B Biol Sci 147:402–411

Charles RD (1950) Radiation induced mutations in mammals. Radiology 55:579–581

Charles RD, Tihen JA, Otis EM, Grobman AB (1960) Genetic effects of chronic X-irradiation exposure in mice. US Atom Energy Comm Res Dev Rept UR 565:1–354

Charles RD, Grobman AB, Otis EM, Tihen JA (1961) Genetic effects of chronic X-irradiation exposure in mice. Genetics 46:508

Dobrovolskaia-Zavadskaia N (1928) L'irradiation des testicules et l'heredite chez la souris. Arch De Biol 38:457–501

Dubrova YE (2016) Mutation induction in the mouse and human germline. Russian J Gen 52:17–28

Ehling UH (1965) The frequency of X-ray induced dominant mutations affecting the skeleton of mice. Genetics 51:723–732
Ehling UH (1966) Dominant mutations affecting the skeleton in offspring of X-irradiated male mice. Genetics 54:1381–1389
Ehling UH, Randolph ML (1962) Skeletal abnormalities in the F_1 generation of mice exposed to ionizing radiation. Genetics 47:1543–1555
Evans RD (1949) Quantitative inferences concerning the genetic effects of radiation on human beings. Science 109:299–304
Green EL (1968) Genetic effects of radiation on mammalian populations. Ann Rev Genet 2:87–120
Haldane JBS (1956) The detection of autosomal lethals induced by mutagenic agents: with two text-figures. Genetics 54:327–342
Hanson FB (1933) Radiation genetics. Physiol Rev 13:466–496
Hertwig P (1935) Sterlitätserscheimungen bei röntgenbestrahlten Mäusen. Z Induct Abstamm-u Vererb Lehre 70:517–523
Hertwig P (1938) Unterschiede in der Entwicklungsfähigkait von F_1 Mäusen nach Röntgenbestrahlung von Spermatogonien, fertien und unfertigen Spermatozoen. Biol Zbl 58:273–301
Hertwig P (1939) Zwei subletale rezessive Mutationen in der Nachkommenschaft von röntgenbestrahlten Mäusen. Erbarst 4:41–43
Hertwig P (1940) Vererbbare Semisterilität bei Mäusen nach Rontgenbestrahlung, verursacht durch reziproke Chromosomentranslokationen. Z Indukt Abstamm-u Vererb Lehre 79:1–27
Hertwig P (1942) Neue Mutationen und Kippelungsgruppen bei der Hausmaus. Z Induct Abstamm-u Vererb Lehre 80:220–246
Hertwig P (1941) Erbänderungen bei Mäusen nach Röntgenbestrahlung. Proc 7th Int Cong Genet 1939; J Genet Suppl 145–146
Klein J (1996) George D. Snell (1903–1996). The last of the just. Immunogenetics 44:409–418
Lefevre G Jr (1950) X-ray induced genetic effects in germinal somatic tissue of *Drosophila melanogaster*. Amer Nat 84:341–365
Lefevre G Jr (1949) A comparison of x-ray induced generic effects in germinal and somatic tissue of *Drosophila melanogaster*, Degree of Doctor of Philosophy Graduate School of the University of Missouri
Lyon MF, Morris T (1966) Mutation rates at a new set of specific loci in the mouse. Gen Res 7:12–17
Lyon MF, Phillips RJS, Searle AG (1964) The overall rates of dominant and recessive lethal and visible mutation induced by spermatogonial x-irradiation in mice. Genet Res Camb 5:448–467
Muller HJ (1927) Artificial transmutation of the gene. Science 66:84
Muller HJ (1928) The production of mutations by x-rays. PNAS 14:714–726
Muller HJ (1950) Some present problems with genetic effects of radiation. J Cell Comp Physiol 35:9–70
Muller HJ (1955) The effect of radiation and other present day influences upon the human genetic concentration. An audio recording of Muller's lecture at the 5th Lindau Nobel Laureate Meeting on 14 July 1955. https://mediatheque.lindau-nobel.org/laureates/muller
Murphy DP, de Renyl M (1930) Postconception pelvic irradiation of the albino rat (Mus norvegicus) its effect upon the offspring. Surg Gynecol Obstetr 50:861–863
Russell WL (1951) X-ray-induced mutations in mice. Cold Spring Harbor Symposia on Quantitative Biology 16:327–336
Russell WL (1952) Mammalian radiation genetics. In: Nickson JJ (ed) Symposium on Radiobiology (Oberlin in 1950). John Wiley & Sons, pp 427–440
Russell WL (1954) Genetic effects of radiation in mammals. In: Hollaender A (ed) Radiation biology, vol 1. McGraw-Hill, New York, pp 825–859
Russell LB (2013) The mouse house: a brief history of the ORNL mouse-genetics program, 1947–2009. Mut Res 753:69–90
Russell LB, Russell WL (1996) Spontaneous mutations recovered as mosaics in the mouse specific-locus test. PNAS USA 93:13072–13077
Russell LB, Russell WL (1997) Corrections. PNAS USA 94:4233
Schwartz J (2008) In pursuit of the gene: from Darwin to DNA. Harvard University Press, p 248
Searle AG (1974) Mutation induction in mice. In: Lett JT, Adler H, Zelle M (eds) Advances in radiation biology. Academic Press, New York, pp 131–207
Selby PB (2020) The Selby-Russell dispute regarding the nonreporting of critical data in the mega-mouse experiments of William and Liane Russell that spanned many decades: what happened, current status, and some ramifications. Dose-Response 18:1559325819900714
Selby PB, Calabrese EJ (2023) How self-interest and deception led to the adoption of the linear non-threshold dose response (LNT) model for cancer risk assessment. Sci Total Environ 898:165402. https://doi.org/10.1016/j.scitotenv.2023.165402
Snell GD (1933) X-ray sterility in the male house mouse. J Exp Zool 65:421–441
Snell GD (1935) The induction of X-rays of hereditary changes in mice. Genetics 20:545–567
Snell GD (1939) The induction by irradiation with neutrons of hereditary changes in mice. PNAS 25:11–14
Snell GD, Ames FB (1939) Hereditary changes in the descendants of female mice exposed to roentgen rays. Amer J Roent Rad Ther 41:248–255
Strandoskov HH (1932) The effects of X-rays on an inbred strain of Guinea pigs. J Exper Zool 63:175-202