Chromosome Distribution

- Errors in chromosome distribution can result in cells containing too many or too few chromosomes.

- For example, Down's syndrome results from an extra chromosome 23. Most of the time an incorrect chromosome number leads to embryonic death, accounting for 40% of spontaneous abortions and 6% of stillbirths

- Radiation is *more effective at breaking chromosomes* than in **causing errors in chromosome distribution**.

- Such a chromosome imbalance, if it does not cause the death of the embryo, leads to physical abnormalities, usually accompanied by mental deficiency.

H. J. Müller' Studies

- He studied the Drosophila fruit fly by observing mutations on the X chromosome.
- The results showed a linear non-threshold response of the mutation rate to radiation dose.
- This type of response is also known as stochastic response. (This type of response has been used by the National Council on Radiation Protection to model the human response to low doses of radiation.)
- ***Müller also concluded that the observed mutations were of the same quality as those which occur spontaneously.***
- The response observed was independent of dose rate, indicating that the damage is due to a single hit on a gene.

Megamouse Project

- After World War II, L.B. and W.L. Russell began a large mouse colony which was exposed to radiation dose rates from 0.001 to 0.90 rad per minute and total doses of 1000 rad (10 Gy).

- They observed specific expressions of genetic information, i.e***., the coat color and eye color.***

- These studies have continued with over one million mice, giving the project the common name of the **Megamouse Project**.

Megamouse Project: Major Conclusion

- A major conclusion of this study is that there is a dose-rate effect for mammals.
- This study observed that the mutations were more frequent for mice exposed at a high dose rate than in mice which received the same dose but at a lower rate.
- This is termed a dose-rate effect, as the mutation rate depends upon the rate at which the dose is given, not on the total dose.

Correlation of Sensitivity with DNA Content

- As has been shown in numerous studies in addition to Russells', there is a relationship between radiation-induced damage and the size of the nucleus, chromosomes, or DNA content.
- As the DNA content increases between species, the mutation rate per gene multiplies by almost the same factor.
- This correlation may result from an increased amount of DNA associated with regulating the gene activity as the DNA content increases.

Megamouse Project: Implied Repair Mechanism

- The study implies a repair mechanism for radiation damage in mammals.

- It is important to note that the mutation rate found in mice is about 15 times greater than that found in fruit flies. In the target model, this would imply that the actual size of the genome on the chromosomes is about 15 times larger in mammals than in fruit flies.

Megamouse: Genetic risk

- There are two ways to describe the estimated genetic risk of radiation:
- The first method is to compare radiation-induced mutations with those that occur spontaneously. The results are expressed in terms of doubling-dose. This is the relative mutation risk.
- The second way of describing the direct or absolute mutation risk quotes the incidence of disorders resulting from mutations in the first generation.

Megamouse Project: Relative Mutation Rate

- The following major conclusions were reached as a result of these experiences:

1) The radiosensitivity of different mutations ***varies by a factor of 35—it*** is only possible to speak of average mutation rates.

2) The male mouse is much more sensitive to radiation than the female. At a low dose rate, almost all the radiation-induced genetic burden in a population is carried by the males.

3) The genetic consequences of a given dose can ***be greatly reduced if a time interval is allowed between irradiation and conception.*** Consequently, if persons are exposed to a significant dose of radiation, it is recommended that six months be allowed to elapse between the exposure to the radiation and planned conception to minimize the genetic consequences.