Part III

On So-called Sex-determining Factors and the Act of Sex Determination

Chapter 13

Elucidation of So-called Sex-determining Factors

The chromosomal sex-determining mechanism quite obviously depends upon the presence of female-determining factors on one member and of male-determining factors on the other member of the sex chromosome pair. Yet, the exact nature of so-called sex-determining factors remains a riddle. While sex-linked genes are Mendelian genes which behave in a predictable manner, the sex-determining factors are elusive entities which have not permitted close scrutiny.

In this chapter and the next, an attempt shall be made to elucidate the nature of so-called sex-determining factors and their contribution to the actual act of sex determination. No doubt, each sex-determining factor is a particular DNA molecule, but each may exist as multiples on the sex chromosome. They do not appear to be structural genes; rather, they seem to act upon the embryonic indifferent gonad and decide its developmental fate.

Since we are totally ignorant of the nature of individual sex-determining factors of vertebrates, certain inferences have to be made from what is known in the fruit fly (Drosophila), but even in the fruit fly, the knowledge in this regard is very meager indeed. On the other hand, endocrinological information which is essential to our understanding of sex determination is non-existent in the fruit fly, but abound in mammals. The attempt in these two chapters suffers from an indiscriminate assimilation of fragmentary information. Unfortunately, there seems to be no other choice.
a) Relative Potency of the X and the Y in Drosophila and Mammals

Both in *Drosophila melanogaster* and in *Drosophila virilis*, the XO-individual is a male, while the XXY-individual is a female. Thus, it is evident that whether to be a male or a female is not determined by the presence or absence of the Y, but rather by the number of X-chromosomes present. This is due to the fact that the factors which counteract the feminizing influence emanated by the X, are carried not by the Y, but by the autosomes. The diploid set (2A) of autosomes is sufficient to overpower the single X, but is easily subjugated by the combined action of two X’s (Morgan et al., 1925). When the triploid set of autosomes (3A) competes against two X’s, the stalemate is reached. Thus, the 3AXXY-individual is an intersex (Bridges, 1921). More analytical studies revealed that among three autosomes of *Drosophila*, the third chromosome (second largest autosome) carries most of the male-determining factors (Bedichek-Pipkin, 1959). The Y-chromosome emerges as a “dummy”.

In the mouse (*Mus musculus*), on the contrary, the XO individual is a functioning female (Welschons and Russell, 1959); furthermore, in certain other rodent species, the female is normally XO (Ohno et al., 1963; Matthey, 1965). In man (Jacobs and Strong, 1959), and in the mouse (*Mus musculus*) (Russell and Chu, 1961), the XXY is a male, although sterile. On the basis of the above findings, it becomes evident that relative potency of the X and the Y of mammals is quite the opposite of that of the X and the Y of *Drosophila*. Here, the male-determining capacity of the Y-chromosome is without doubt; it is the female-determining capacity of the X which has to be questioned.

In Jost’s experiment (1947), removal of the testis in the male fetus of the rabbit automatically resulted in the development of female sexual ducts. On this basis, the view may be taken that in mammals, the female is a neuter sex assumed passively in absence of the Y, and that the 2AXO-constitution is not so much the female constitution, but rather the constitution which is an essential minimum for the individual’s development. This, however, appears as an extreme view, for apparent ineffectiveness of the mammalian X as a female-determiner may merely be a reflection of the particular dosage compensation mechanism which inactivates all but one X-chromosome in each somatic cell. Thus, an individual with the 2AXXXXXXY-constitution