Chapter 17

Rebooting the Genome

What makes hybrid male sterility of great current interest is the increasing evidence that the building blocks of this isolating barrier may be radically different from what we had come to believe. ... It is clear that a new paradigm is emerging, which will force us, first, to revised many conclusions ... that had gathered almost unanimous agreement, and, second, to try a completely different experimental approach.

Horacio Naveira and Xulio Maside (1998) [1]

With the notable exceptions of Butler and Miescher, in the nineteenth century the information concept as applied to biological molecules did not extend to information error and the need for its detection and correction (Chapter 2). Miescher in 1892 thought that: “Sexuality is an arrangement for the correction of these unavoidable stereometric architectural defects in the structure of organized substances” (Chapter 3). While referring to “left handed coils” being “corrected by right-handed coils,” at that time he was unable to relate this to “nuclein,” a new substance he had discovered, later known as DNA. However, he appreciated that correction would require some sort of yardstick (i.e. “right hand coils”) to permit the fact of error in a molecule (i.e. “left hand coils”) to be detected, and then appropriately corrected.

If the various degrees of redundancy found among DNA molecules have a single explanation, it is error-detection and correction. This itself might explain another apparent redundancy, the fact that members of most biological species are either one of two sexes. Yes, this certainly makes our lives more interesting. But, the biological advantage is not obvious. Imagine a world without males in which each woman, on average, was able to produce two offspring per generation asexually. Both of these would be female. In the first generation there would be two women. In the second generation there would be four women. In the third generation eight women, and so on. With a similar limit to offspring number, in a sexual world a woman would be likely to produce one male and one female per generation. Only the latter, on being fertilized by a male, would produce further offspring. In the first generation there would be two individuals, male and female. In the second generation,
there would still be two, and so on to the third generation, etc. … . Since the winners in the struggle for existence are organisms that leave the most offspring, sex would seem very disadvantageous [2].

Redundancy

At the outset the two-fold parallel redundancy of naturally occurring DNA duplexes, which contain complementary ‘top’ and ‘bottom’ strands, was recognized as revealing not only how DNA was replicated, but also how it might be corrected. Changes in DNA, manifest as unusual bases (e.g. U instead of T), or damaged bases (e.g. cross-linked Ts), would have provided a selection pressure for the evolution of specific enzymes that could recognize and correct errors. Indeed, many such enzymes were discovered [3].

Sometimes, however, a normal base can change into another normal base (“base substitution”) so that an unusual base-pair results (e.g. A on one strand opposite a C on the other strand). Again, one can envisage a selection pressure for the evolution of enzymes that recognize base mispairing; but after the fact of recognition, how is it known which base to correct (Chapter 2)? Take the following duplex:

CAGGCTATCGTAA
GTCCGATAGCATT

(17.1)

Consider a base change (transition mutation) from T to C (underlined):

CAGGCTATCGTAA
GTCCGACAGCATT

(17.2)

The error might be corrected as:

CAGGCTATCGTAA
GTCCGATAGCATT

(17.3)

Or compounded as:

CAGGCTGTTCGTAA
GTCCGACAGCATT

(17.4)

There is only a 50% chance of actual correction. And there is another actor in the wings. While the ‘rapid response team’ of error-correcting enzymes is