even if they had no prior clues about the gene's function [14]. By late 1979, the first such DNA marker was found by Arlene Wyman and Raymond White, working in Worcester, Massachusetts[15].

These heterogeneous DNA markers were quickly used to hunt for disease genes, demonstrating the utility of the gene mapping idea. Suppose, for example, that some adult progeny of the same mother (or father) Huntington's disease also developed it, while other children did not. If the affected children all inherited DNA from the same region of chromosome 4, while those unaffected inherited the other copy of that DNA, this would be strong statistical evidence that DNA in that chromosome 4 region contained the Huntington's disease. This is exactly what James Gusella and others discovered in 1983, when they linked Huntington's disease to the tip of chromosome 4[16]. The DNA marker they used to track the passage of chromosome 4 in families was not the gene itself, but a nearby region that just happened to differ among family members so that the investigators could tell the chromosomes apart. Finding the gene itself took another decade of arduous work, but it was ultimately successful, made possible only because genetic linkage narrowed the zone of DNA to scan for the offending mutation[17].

The second cluster of mapping techniques centered on structural catalogs of DNA fragments, rather than markers to track inheritance through pedigrees. The general idea was to take native chromosomal DNA, break it into fragments that could be copied by various cloning techniques, and then put the DNA fragments (now plentiful enough to study in the laboratory) back in order. If this could be done for all the chromosomes, then once a gene's location were narrowed to a particular region by genetic linkage, then the DNA from that region would already be available in a test tube for direct analysis.

The techniques for physical mapping were again derived from work on viruses and bacteria, and by the mid-1980s, pioneering groups had moved into constructing physical maps of larger and more complex organisms. Maynard Olson and his colleagues at Washington University were working on a physical map of yeast, which was a very powerful model for the