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EDITORIAL

Our Genetic Patrimony

Since the turn of this century, geneticists have become increasingly involved in localizing human genes, especially those implicated in disease. A great deal has been learned about genetic mapping from model organisms such as the drosophila, the mouse, *Caenorhabditis elegans*, and *Saccharomyces cerevisiae*. Mapping the human genome is a laborious task, and substantial progress has been made, especially with the use of molecular techniques involving manipulation and analysis of DNA.

In 1980, it was proposed that polymorphisms of lengths of DNA restriction fragments (RFLPs) be used for systematic genetic mapping of the human genome. This approach had to be applied to family material containing numerous siblings and, if possible, grandparents, in order to establish allelic phase. It was evident that the efficiency of mapping would be enhanced if the family material to be genotyped was unique and common to laboratories involved in constructing genetic maps. As a result of a generous legacy, the Centre d'Étude du Polymorphisme Humain (CEPH) was able to organize the distribution of DNA, free of charge, from members of 40 large French, North American, and Venezuelan families (more than 500 individuals) to, now, over 100 laboratories throughout the world. Thus, an international collaborative mapping effort was launched which has continued for 10 years.

Another step forward was the discovery of mini- and microsatellites whose varying numbers of sequence repetitions allowed the definition of many new and informative hereditary polymorphisms. The frequency and the relatively homogeneous distribution of microsatellites in the human genome make them a remarkable tool for genetic mapping, especially since their polymorphism tends to be greater than that of the RFLPs and they are easily genotyped by means of the polymerase chain reaction. Microsatellites often are represented by 10 to 15 alleles, whereas RFLPs predominantly are defined by two or three alleles. Genotypes for approximately 4000 RFLPs have accumulated in 10 years of studying the CEPH family material, which has become the international reference panel for genetic mapping; in 3 years genotypes for over 2000 microsatellites, many of which were developed at Généthon, have been accumulated from the CEPH panel. These highly informative markers provide an efficient source of genotypes, rapidly obtained, for building the human genetic map.

This issue of *Science* assembles current knowledge on the state of human genetic mapping. The mean interval between the various markers of the genetic maps presented here is 0.7 cM. Of course, it is possible to go farther, to refine even more, and to fill many of the gaps that remain by means of genetic and physical mapping techniques.

However, as it is now, the genetic map of the human genome is a great achievement. It has played a considerable role in constructing a physical map, whether regional or covering the genome, making it possible to detect overlapping DNA fragments and form contigs. It will be even more useful in establishing the integrated map of the human genome, in which each DNA fragment will be defined not only by its position, but also by the genes and markers it carries, thus forming the basis for a computerized library that contains the present knowledge of our genetic patrimony. These cloned fragments must be freely available to the entire scientific community. We look forward to the addition to the library of coding sequences of the human genes and, eventually, of the complete sequence of the genome.

Finally, and perhaps most importantly, the genetic map of the human genome has already played a precious role in the localization, isolation, identification, and functional study of genes implicated in human disease and their normal counterparts. One has only to refer to the almost weekly discoveries in the field of genetic disease research to recognize the exceptional contribution of the mappers in close collaboration with clinicians in the fight against disease and suffering. This quest, in fact, has only just begun. Its relentless pursuit will lead to specific treatments that are based on detailed information from cloned genes, particularly by somatic gene therapy. These new therapies should be developed and provided in an ethically sound environment where the respect for the integrity and dignity of the human individual is paramount.

Jean Dausset and Howard Cann

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