CATALOGING GENETIC DISEASES AND MAPPING THE GENES ON CHROMOSOMES

Victor A. McKusick, M.D.
William Osler Professor and Director, Department of Medicine
The Johns Hopkins University School of Medicine, and
Physician-in-Chief, The Johns Hopkins Hospital, Baltimore, Maryland 21205

Introduction
Over a period of more than twenty years, we have assembled a catalog of known genetic traits of man which exists as a computer database and is published in the form of a handbook every few years [1]. For the last few years, work has been in progress on a Human Genetics Knowledge Base, in collaboration with the National Library of Medicine.

The Information Content of the Knowledge Base

The Catalogs of Genetic Traits. The Catalogs and computerized database contain the same basic information. Each genetic trait is an entry. (Conversely and more precisely, each entry relates to a single genetic locus. For many loci, only one mutant form of the genetically variable trait is known, but when various disorders or traits are due to different mutations at the same locus, only one entry is created.) Whenever available information permits, each entry consists of five parts: (1) a preferred designation for the genetic trait and frequently used synonyms; (2) a brief description of the phenotype(s); (3) the nature of the basic defect; (4) a resume of genetic information; and (5) key references. As of July 1, 1982, there were 17,309 references, mainly to the periodical literature, and 28,311 authors are cited.

Two indices are provided for the published handbook. The Author Index is intended to help the reader find a particular entry. The Title Index includes alternative designations and distinctive symptoms or signs that do not appear in the titles of entries. Terminology often presents an obstacle for computer-based systems. The terminology related to many genetic disorders presents difficulties, especially when the basic defect is unknown. Optimally, the name for a genetic trait or disorder should have some relation to the basic defect. Unfortunately, some seven methods of naming are presently in use. For this reason, the Title Index with its full range of alternative designations is extremely important.

Mendelian disorders potentially lend themselves particularly well to precision in nomenclature. By the year 2000, for example, it will probably be possible to look at the phenotype and at the laboratory data and come up with a diagnostic label that is a statement of the specific abnormality in the genome. It might be something like 1q-d164-17TA, meaning that on chromosome 14 both alleles of cistron no. 164 have adenine substituted for thymine as base no. 17 [4]. This is by no means far-fetched, especially now that gene diagnosis, a contribution of molecular genetics, is a reality -- e.g., in the hemoglobinopathies, including the thalassemias, in familial isolated growth hormone deficiency, and in other disorders.

The Gene Map of Human Chromosomes. As part of the genetics of each entry (locus), information on chromosomal localization and linkage to other loci is summarized insofar as known. A pictorial synopsis with key is also provided in the Catalog. References to the evidence for each assignment are given in the entry for the locus. In the gene map, about 600 loci are now (August 1983) assigned to a specific chromosome [1,2,3].

The Future: A Human Genetics Knowledge Base

Since 1979, through contracts with the National Library of Medicine, a Human Genetics Knowledge Base has been established as a major effort of the Lister Hill National Center for Biomedical Communications' Knowledge Base Research Program. In collaboration with the Library of Medicine, we are using the catalogs as the nucleus of an on-line information system in human genetics. Incorporating expert consensus and based on extensive study involving retrieval, analysis and selection of material, the content of the database is clarified and organized in a way that facilitates subsequent knowledge representation. It is believed that the resulting knowledge base system will assist health practitioners in the medical decision-making process.

References