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Embargoed for Release:
6 PM Eastern Time, Thursday, September 29,1994

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First Human Genome Project Mapping Goal Is Met

An international team of researchers has published a detailed linkage map of the human genome, meeting one of the project's scientific goals a full year ahead of schedule.

The map and an accompanying article will appear in the September 30 issue of *Science*.

"We can no longer say tracking down a specific disease gene is made difficult by lack of a good map," said Francis Collins, M.D., Ph.D., Director of the National Center for Human Genome Research (NCHGR). "We have a good map."

NCHGR is the component of the National Institutes of Health charged with overseeing its role in the Human Genome Project.

Linkage maps consist of an array of DNA patterns, called markers, positioned on chromosomes. They are the first tool gene hunters use in the search for a disease gene because they tell the scientist which general area of the chromosome contains the gene.

Four years ago, Human Genome Project planners established specifications for the quality of linkage map they wanted to produce during the coming five years. Those specifications

called for high-quality markers to be established between 2 and 5 centimorgans apart throughout the genome. (A centimorgan is roughly 1 million bases.) Markers on the new map contain high-quality genetic information, are located on average less than 1 centimorgan apart, and are available to the research community a year sooner than planners expected. Information about the markers is available in public databases.

Coordinated by Jeffrey C. Murray, M.D., and his coworkers at the Cooperative Human Linkage Center (CHLC), the published map is the result of work by four major groups in the United States and Europe and hundreds of individual scientists worldwide. Headquartered at the University of Iowa, CHLC is one of NCHGR's Genome Science and Technology Centers.

"Determining the location of genes, including altered genes which cause disease, on human chromosomes is the first step in determining the causes of genetic disorders, whether it's a rare disease or a common one such as diabetes, heart disease, or cancer," said Dr. Murray.

In addition to CHLC, major contributors to the map include the French company Genethon, NCHGR grantees at Yale University and the University of Utah, and the NCHGR (NIH)-Centre d'Etudes du Polymorphisme Humain mapping consortium.

The new map is a compilation of linkage data generated during the past decade. In addition to the high density of markers, the new map and has several technological advantages over older maps. First, most (36~~11~~ 17) of the 5840 markers are of

the type known as short tandem repeat polymorphisms (STRPs), which are easy to trace in DNA samples from extended family members. Second, these markers are easy to use in the laboratory; they can be amplified in DNA by the polymerase chain reaction. And third, the markers are close enough together to bridge to a more detailed map, known as a physical map, which consists of cloned DNA pieces.

"A particular strength of current human genetic linkage maps is that their construction...allows for the immediate integration of linkage maps with the developing physical maps," the authors say.

Scientists first linked a disease to a human chromosome in the 1930s when they associated both color blindness and hemophila with the X chromosome. Since then, several types of linkage markers have been developed and improved. In 1986, the gene for the immune disorder chronic granulomatous disease was the first gene to be isolated using linkage maps in the process. That procedure for isolating genes is now termed "positional cloning." Since then, 36 genes have been isolated using linkage mapping and positional cloning methods.

The map and the report, "A Comprehensive Human Linkage Map with Centimorgan Density," will appear in the September 30, 1994 issue of Science. Authors are: Jeffrey C. Murray, Kenneth H. Buetow, James L. Webber, Susan Ludwigsen, Titia Scherpbier-Heddema, Frank Manion, John Quillen, Val C. Sheffield, Geoffry M. Duyk, Jean

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