Biology

Rick Weiss reports from San Diego at the Human Genome 1 meeting

Many faces of a gene-mapping project

Only 36 years after scientists discovered the structure of DNA, molecular biologists now seek the exact sequence of all 3 billion nucleotide pairs that together encode every inherited human trait. The 15-year project promises to revolutionize disparate specialties within the life sciences. Among them:

• *Medicine.* An understanding of the molecular basis of inherited diseases may lead to improved diagnosis and treatment. Leroy E. Hood of the California Institute of Technology in Pasadena, for example, makes synthetic bits of protein that resemble myelin — the protective coating around nerve cells. By injecting these proteins into mice, he induces a white blood cell response against the rodents' natural myelin, causing a syndrome resembling multiple sclerosis. Recently he has found that synthetic proteins featuring minor molecular alterations have different effects when injected. For instance, one variety performs the first step necessary to induce myelin damage but cannot convince white blood cells to finish the job. Another analog gets white cells so excited they overreact to the protein, inducing vaccine-like protection against subsequent exposures to myelin-damaging injections. Hood aims to use such experiments to reveal the critical differences between myelin-destroying white cells and their innocent cousins. Later, scientists might develop drugs that destroy only the former to halt the progression of multiple sclerosis.

• *Evolution.* Since DNA mutates at a fairly constant rate, DNA comparisons among different organisms provide a historical record of evolutionary changes over time. Further, a portion of each cell's DNA — called mitochondrial DNA — is inherited only from one's mother, allowing researchers to trace human maternal lineage to the one "modern" mother from whom we all descend. New work by Allan C. Wilson of the University of California, Berkeley, now indicates this original mother lived 140,000 years ago — 60,000 years later than was thought — and her closest living relatives are today's !Kung tribe in southern Africa. Wilson's genetic studies suggest the first major human migration northward from that region occurred about 70,000 years ago; 35,000 years later they brought their genes to Europe. All the world's populations "are just twigs on an African tree," Wilson says. "Basically, we are all !Kung."

• *Comparative biology.* The human body harbors about 100,000 proteins, and differences in a very few of these can account for all the recognizable variations among us. Indeed, DNA studies of bacteria, yeast, mice and cows indicate living things are much more alike than they are different. Scientists suggest that just as research findings in mice can shed new light on humans, other organisms may prove genetically enlightening and even easier to experiment with. For example, tomato cells and mouse cells have a lot in common, each featuring the same number of chromosomes and chromosomal arms. Moreover, says Eric S. Lander of the Whitehead Institute for Biomedical Research in Cambridge, Mass., a tomato "is roughly the same size as a mouse and is substantially easier to catch."

• *Technology.* The genome project will require significant technological advancements in areas of information storage and automated DNA analysis. Improvements made to date rate as a mixed blessing, however. For example, as techniques have become increasingly simplified, much of the DNA sequencing work traditionally performed by postdoctoral fellows has become intellectually mundane and repetitive. Unless robotic devices take over many of these tasks, says C. Thomas Caskey of the Baylor College of Medicine in Houston, "it's clear the postdocs are going to burn out very quickly."

Sydney Brenner of the MRC Molecular Genetics Unit in Cambridge, England, jokes that researchers convicted of scientific fraud should be sentenced to produce DNA megasequences in laboratory-equipped penal colonies.

Biomedicine

Hypertension, heart disease and diuretics

An estimated 7 million people in the United States may have inherited a syndrome of hypertension and elevated blood lipids that puts them at high risk of a heart attack, according to study results reported last summer. And Swedish research suggests that a class of drugs commonly used to treat hypertension may also heighten the threat of heart disease.

Roger R. Williams, Steven C. Hunt and their colleagues at the University of Utah in Salt Lake City first described the syndrome, called familial dyslipidemic hypertension, in the June 24, 1988 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. In that report they detailed a study of 131 hypertensive siblings from 58 families and concluded that a pattern of hypertension and abnormal blood lipid levels seems to run in families.

Scientists know that people with hypertension have alterations in the transport system that carries sodium and other ions across cell membranes. But new work by the Utah team shows that people with this syndrome have more ion-transport abnormalities than do hypertensives with normal blood lipid levels. The researchers described their latest findings Sept. 28 in Cleveland at the 43rd Annual Fall Conference and Scientific Sessions of the American Heart Association Council for High Blood Pressure Research.

Williams and Hunt found that people with the greatest ion-transport problems had high blood levels of insulin, a hormone produced by the pancreas. High blood insulin values suggest that people with this syndrome may have a disorder called insulin resistance, in which the body doesn't respond properly to insulin (SN: 9/16/89, p. 184). Some researchers believe insulin resistance is at the core of a lethal process leading to heart disease. Hunt says his team doesn't know whether insulin resistance or some other factor underlies familial dyslipidemic hypertension.

Most people with the syndrome get treatment for their high blood pressure, but physicians often ignore their high blood lipids, the researchers find. "When physicians see high blood pressure develop early in a patient, they should check the lipid levels and blood pressure of that patient's brothers and sisters," Williams says. If scientists can find a genetic marker for the disorder, it might enable physicians to identify affected children and start treatment before cardiovascular damage occurs, the researchers say.

Most scientists agree that people with hypertension and lipid disorders can lower their heart disease risk by losing weight, exercising and cutting down their consumption of saturated fats. Scientists disagree, however, on when such patients need to start taking medication to lower their high blood pressure.

Hunt notes that many people with the newly identified syndrome take diuretics, which treat hypertension by reducing water in the body. But a new report by a team of Swedish researchers suggests diuretics may boost the risk of heart disease for all people with hypertension.

Thomas Pollare and his colleagues at Uppsala University studied 50 patients with hypertension, finding that when subjects took the diuretic drug hydrochlorothiazide they had significantly higher blood levels of cholesterol than did subjects receiving placebo pills. When the researchers gave these same patients captopril, one of a class of drugs known as ACE inhibitors that reduce blood pressure by reducing blood vessel constriction, their blood lipid levels were no higher than those of patients on the placebo.

The team reports in the Sept. 28 NEW ENGLAND JOURNAL OF MEDICINE that hydrochlorothiazide made body tissues less responsive to insulin. Some scientists say such evidence argues against diuretic treatment for certain people with hypertension, especially those with insulin resistance.