

PROSTATE CANCER GENE LOCATION FOUND ON CHROMOSOME 1

From National Center
for Human Genome Research

■(BETHESDA, MD) Researchers at the National Center for Human Genome Research (NCHGR), Johns Hopkins University (JHU) and Umea University, Umea, Sweden, have identified the location of the first major gene that predisposes men to prostate cancer. The gene, named HPC-1 (hereditary prostate cancer 1) by the researchers, is situated on the long arm of chromosome 1. The finding, to be published in the Nov. 22 issue of the

journal *Science*, is the first proof that genes conferring hereditary predisposition to prostate cancer exist.

Scientists discovered the gene location through an international study involving 91 families in which at least three members suffered from prostate cancer. The region implicated represents about 0.3 percent of the human genome and will now be the subject of intense scrutiny to identify the gene responsible. Once the HPC-1 gene itself is identified, it is expected to shed light on how and why prostate cancer develops and also suggest strategies for preventing and treating it.

"The application of genetic tools to the understanding of common disorders is becoming a state-of-the-art strategy in biomedical research," said Donna Shalala, Secretary of the U.S. Department of Health and Human Services. "Discoveries such as this one continue to bear out the wisdom of our national investment in genetics technology for understanding human illness."

Although the disease has been known to run in families, genetic analyses of prostate cancer have been difficult. In the United States, men stand a one-in-five chance of developing prostate cancer; the most common malignancy among men and the cause of more than 40,000 deaths annually. That indicates many different factors, genetic and environmental, may contribute to the disease. A high-fat diet, cigarette smoking, and multiple sexual partners are among the environmental suspects, but none has definitely been established as a risk factor. In addition, nearly all prostate cancer is diagnosed late in life, so an affected man's ancestors are rarely available for studies that might explain the part genes play in the disease.

Approximately 1 in every 500 men is believed to possess an altered version of the gene. The researchers estimate that alterations in the HPC-1 gene are responsible for at least a third of familial prostate cancer. Familial prostate cancer accounts for about 1 in 10 cases of the disease, while the numbers for the early onset form of the disease are somewhat higher.

"We know this gene seems to contribute to prostate cancer risk in a number of ethnic backgrounds," says Dr. Jeffrey Trent, scientific director of NCHGR's division of intramural research and head of the laboratory where the genotyping was conducted. "There's linkage in Swedish families as well as American families, including African-American families," adds Trent.

Development of a susceptibility test is still several steps away, requiring at a minimum the identification of the HPC-1 gene itself, according to NCHGR Director Dr. Francis Collins. "In the future," says Collins, "combining genetic susceptibility testing with testing for prostate-specific antigen and other early detection measures will be potentially of value in preventing deaths from this common disorder."

The study focused first on analyzing data and tissue samples from 66 high-risk American families collected by Johns Hopkins researchers. Most of the families were recruited through letters from urologists, and some were identified through media advertisements. At NCHGR, a genome-wide scan of DNA from these families indicated a gene on chromosome 1. The site was confirmed by analyzing DNA from an additional 13 high-risk American families and 12 high-risk families studied by scientists at Umea University.

The number of prostate cancer cases varies widely among different ethnic groups. African-American men suffer the highest incidence rate in the world, more than 180 cases annually per 100,000 population, and their death rate is also the highest, about 54 per 100,000. Both of the African-American families included in the study showed linkage to the site of HPC-1, suggesting that the gene may eventually help explain why African-American men are exceptionally vulnerable to the disease. In the U.S., incidence is quite high also (almost 135 cases per 100,000) among white men, lower (around 89 cases per 100,000) among Hispanic and Japanese men, and lowest of all in other groups whose ancestors came from Asia. It is estimated that 317,000 American men will be diagnosed with prostate cancer this year.

Hopkins researchers are asking individuals from families in which three or more close relatives have had prostate cancer and who wish to participate in a research study on the genetics of that disease to contact the study team at (410) 614-5434, or write to Dr. Patrick C. Walsh, Hereditary Prostate Cancer Study, Dept. W., Brady Urological Institute, Johns Hopkins University Hospital, Baltimore, MD 21287.

For more information about prostate cancer, call the Cancer Information Service at 1-800-4-CANCER.

Strep Vaccine, cont. from page 6

gator at Baylor College of Medicine in Houston, 100 women of child-bearing age received either the conjugate vaccine, the pure polysaccharide vaccine or a placebo injection. The conjugate vaccine stimulated the production of much higher levels of antibody than did the pure polysaccharide vaccine. In addition, linking the capsule to the tetanus toxoid protein did not affect the function of the resulting antibodies — in test tube experiments, antibodies produced by either vaccine neutralized Group B strep equally well.

Dr. Kasper, Dr. Baker and their colleagues then injected pregnant mice with antibodies isolated from women immunized with the conjugate vaccine. Upon exposure to Group B strep bacteria, nearly three-fourths of the offspring born to these mice were protected from infection. Offspring born to mice that had been injected during pregnancy with human serum lacking Group B strep antibodies died after exposure to the bacteria.

"These findings demonstrate that the antibodies produced by the conjugate vaccine are able to cross the placental membrane and could confer protection against Group B strep to the fetus," says Dr. Kasper.

The vaccine used in the current study was a monovalent product — designed to protect against just one of the various types of Group B strep that cause disease in infants. Ultimately, a multivalent vaccine, providing protection against all types, will be needed. Acknowledging that much more work remains before a Group B strep vaccine reaches the marketplace, Dr. Kasper says that the conjugate vaccine developed by his group provides a blueprint for subsequent vaccines.

"We're definitely headed in the right direction," he says. "This is a prototype of what Group B strep vaccines will look like."

"Reason is also choice."

John Milton