In the Laboratory

The laboratories at the Fred Hutchinson Cancer Research Center (FHCRC) and the University of Washington are continuing their work on the analyses of DNA samples which were submitted by PROGRESS study subjects. To update you on our progress, we offer you this brief and simplified explanation of how these samples are being used to find the genes for prostate cancer.

Each cell in the human body contains in its nucleus 23 pairs of chromosomes, which contain all the instructions to make and maintain our bodies. Each chromosome is made up of long strings of four different "bases" abbreviated A, T, C, and G that are arranged in pairs. These strings of "base pairs" are arranged in a certain order to form a code, like letters or words in a book. There are approximately three billion base pairs in the human genome. About 10% of this code contains "recipes" for the cell to produce certain proteins. These sections of the chromosome which contain instructions to make proteins are called genes.

To find the genes which may cause prostate cancer in the PROGRESS families, we are conducting a "genome screen." This process involves molecular examination of each of the cell's 23 pairs of chromosomes. Because there are billions of base pairs, it is not possible to look at every one. We look instead at "marker" regions located about every 10 million base pairs. The PROGRESS genome screen includes 400 different markers. We look at each family's DNA, with each marker, to see if men diagnosed with prostate cancer within a family have inherited the same particular regions of their genome either from their mother or father. This is particularly significant if the patients are diagnosed with prostate cancer early in life. We compare the data from all the families, looking to see if affected men in different families share common regions of their genome. If we find a region that looks significant, we look at the unaffected men to see if they lack such a region. For that reason, DNA samples from affected and unaffected men are equally valuable in our study. Some women in the family also provide helpful information on genes that occur in the family.

Once a suspicious area of a chromosome is identified, such regions become the target of intense study. These regions are most likely to contain genes which contribute to a man's susceptibility to prostate cancer. All families in the study are equally valued in this type of analysis, but larger families and families in which all invited family members have provided blood samples tend to provide more data.

In the labs at the Fred Hutchinson Cancer Research Center and the University of Washington, eight scientists are devoting 100% of their time to the genome screen of PROGRESS family DNA. Thus far, we've gotten some hints about regions of the genome that may contain prostate genes. Other researchers around the country are conducting similar studies on different groups of families. To date, we have screened the entire genome for 70 families, and have screened about one half of the genome in another 82 families. There are two regions of the genome that have been suggested by other studies to contain prostate cancer genes, both on chromosome 1. Detailed analysis of DNA from the PROGRESS families by Seattle scientists is expected to help find the exact genomic regions of interest and thus position researchers to begin closing in on the genes themselves.

--- Late Breaking Genetic News ---

A recent study by a group of French scientists has identified a second area of interest on chromosome 1 in prostate cancer families. The new report was published in the June 1998 issue of the American Journal of Human Genetics (vol.62: 1416-1424). The suspicious region (1q42.2-43) is on the same chromosome as the first prostate cancer region, which was identified by researchers at Johns Hopkins University in 1996. Our scientists are carefully reviewing the PROGRESS genome screen results in the new suspicious region to see if we find the same suspicious region in our group of families. Once our analyses are completed and published, we will share them with you.
The 1998 Prostate Cancer Facts

Each year the American Cancer Society (ACS) makes projections about the expected number of new cancer cases and cancer deaths due to each type of cancer. To obtain a copy of the 1998 Cancer Facts and Figures, you can call toll free 1-800-ACS-2345 or go to www.cancer.org on the Internet. For 1998, approximately 184,500 men in the United States will be newly diagnosed with prostate cancer and about 39,200 will die from this disease. For comparison, the ACS projections indicate that 178,700 women will be newly diagnosed with breast cancer and that 43,500 will die of breast cancer in 1998.

Prostate cancer is the most common cancer site in American men. The incidence (number of newly diagnosed prostate cancer cases per 100,000 men in the population) of prostate cancer increases with age. The incidence is higher in African Americans compared to Caucasian or Asian Americans, and is higher in men with a family history of the disease. Recent studies suggest that in the general population about 10% of prostate cancer is due to inherited susceptibility, but as much as 40% of the disease diagnosed in younger men may be due to inherited susceptibility. We anticipate that new discoveries in this area will be forthcoming over the next few years, based on PROGRESS and other similar studies currently underway.

The early detection of prostate cancer is based on the use of a blood test called prostate-specific antigen (PSA) and the digital rectal examination. PSA is an enzyme that is produced by prostate cells and its level is increased in most men with prostate cancer. Some increase in the level of PSA can also occur in men with benign prostatic hyperplasia (BPH), the over-growth of normal prostate tissue, and prostatitis or infection in the prostate gland. The American Cancer Society and the American Urology Association recommend that both the PSA and rectal examination be done each year beginning at age 50. Men considered to be at higher risk are those with a strong family history of prostate cancer (for example, prostate cancer in a father and/or brothers) and African American men. For these higher-risk groups, the ACS suggests that early detection of prostate cancer begin before age 50. The blood samples collected for PROGRESS are not tested for PSA. If you are interested in getting a PSA test, check with your doctor about how these guidelines may apply to you.

We have started analyzing information provided on the PROGRESS questionnaire, which is completed by men with and men without prostate cancer and selected women in these families. Based on a review of the questionnaire responses provided by the first 353 participating men who have not been diagnosed with prostate cancer, 66.7% report that they have had a PSA blood test done and 88.4% report that they have had a digital rectal examination for the early detection of prostate cancer. The average age of these 353 unaffected men (who have not been diagnosed with prostate cancer) is 54 years.

The PROGRESS questionnaire also collects information about family history of cancer. The distribution of prostate cancer in male relatives of the first 499 men with prostate cancer to complete and return the questionnaire is summarized in the table below. To be eligible for the PROGRESS study, a family must have three or more men diagnosed with prostate cancer. As shown, a third of the men with prostate cancer report that their father also had prostate cancer and almost 87% report one or more brothers diagnosed with the disease. These data and the other information collected in the PROGRESS questionnaire are incorporated into our ongoing analyses of the genotyping data described above. This information will be valuable in our search for specific genes that cause hereditary prostate cancer.

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Percentage Reporting</th>
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<tbody>
<tr>
<td>Father with prostate cancer</td>
<td>32.5%</td>
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<tr>
<td>Full brother(s) with prostate cancer</td>
<td>86.9%</td>
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<tr>
<td>Son(s) with prostate cancer</td>
<td>4.9%</td>
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<tr>
<td>Grandfather(s) with prostate cancer</td>
<td>6.0%</td>
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<tr>
<td>Paternal uncle(s) with prostate cancer</td>
<td>15.4%</td>
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<tr>
<td>Maternal uncle(s) with prostate cancer</td>
<td>9.6%</td>
</tr>
<tr>
<td>Nephew(s) with prostate cancer</td>
<td>11.6%</td>
</tr>
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Keep in Touch...

We are still collecting family information and blood samples from PROGRESS families, so if you have any outstanding study materials, it's not too late to send them in. If you have any family updates or wish to contact us for any reason, please feel free to call or write. We are always happy to hear from you!

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