Genomewide Scan

The goal of PROGRESS is to understand why prostate cancer runs in some families by uncovering the genes that cause this disease. The way we search for genes is called a genomewide scan. A genome scan is the process of looking at many different signposts or “markers” in the DNA to see if there are certain sections of the genome that are associated with prostate cancer. For example, if men with prostate cancer always inherit the same sequence of DNA and men in the same family without prostate cancer have not inherited that sequence of DNA, we would look more closely to see if there is something about that sequence that may explain why the men developed prostate cancer. We are looking at nearly 400 markers in more than 2,000 people to find patterns of DNA that may be associated with the disease. We published our first genome scan findings in July 2000, based on the first 94 completed families. A total of 253 families will be included in our second genome scan analysis, to be completed during 2001. We hope to have sufficient information in this larger data set to identify additional regions that may contain hereditary prostate cancer genes.

Stratified Analyses

In addition to our ongoing work on the genome scan, we are using the data you provided in the PROGRESS questionnaire to help us search for prostate cancer genes. This is another way of finding genes by attempting to study subsets of families that share similar characteristics. Because hereditary prostate cancer probably involves several genes, it is common to group or “stratify” families that may be more likely to share the same gene. For example, in breast cancer research, this approach was used to identify the gene called BRCA2. In a large group of families with breast cancer, the researchers noticed that a few families also had relatives diagnosed with ovarian cancer. By studying the genetics of the smaller group of families with both breast and ovarian cancer, the breast cancer researchers were able to identify a gene that increases the risk of breast cancer in some families. We hope that by using the same technique and studying groups of similar families, we will find the location of additional genes for prostate cancer.

One way to group the PROGRESS families is by using medical information collected when the prostate cancer was diagnosed. In addition to completing the PROGRESS survey, men with prostate cancer were asked to provide consent to allow us to access their prostate-related medical records. We have collected copies of medical records for those men who provided consent, and have been working to summarize or “abstract” the data from the records. When a man is diagnosed with prostate cancer, the local pathologist studies the prostate tissue from a biopsy or surgery using a microscope to assign a grade to the cancer. Tumor grade reflects how abnormal the cancer cells look compared to normal cells. The doctor also determines the stage of disease, which reflects the spread of the cancer – that is, whether it is only in the prostate gland or has spread to other areas of the body. Both the stage and the grade are used to indicate how advanced the cancer is at diagnosis. Though the stage and grade are not always a predictor of how quickly the cancer will progress, it is one way to measure the severity of the disease. We plan to divide the PROGRESS families into groups with more advanced and less advanced cancer to see if there are genetic differences between the groups. We hope this will give us new insights into the genes involved in the cancer process.
Another way to stratify families is by the presence of other cancers in family members. You may recall that in 1999 we identified a region or "locus" on chromosome one called CAPB that was associated with prostate cancer in families who also had relatives with breast cancer. This strategy of grouping families by using other cancers has great potential to help us find prostate cancer genes. We are currently using the family information provided in your questionnaires to find out which of the PROGRESS families also have a relative(s) with breast cancer. The families with both prostate cancer and breast cancer will be grouped together and compared with families with prostate cancer who have no relatives with breast cancer.

Ongoing Follow-Up

One problem we have encountered when creating these groups of families is that the information we collected from you is several years old. PROGRESS began collecting data in 1995, more than five years ago! We know that in the last five years some of you have had additional treatments for cancer and in some cases other family members have been diagnosed with prostate cancer or another type of cancer. Many of you have been kind enough to call us with updated information. To systematically update our information about you and your family, we are preparing a follow-up survey. We will be mailing the follow-up surveys during 2001 and 2002. The follow-up questionnaire will include questions about your health and your family’s health in the last several years as well as other topics. As always, your continued participation in PROGRESS is entirely voluntary. We greatly appreciate the vast amount of information you have already provided about your family. We hope that by continuing our study and updating our information, we can eventually find the genes that cause hereditary prostate cancer.

Prostate Cancer News Update

Since our last newsletter, the Mayo Clinic, located in Rochester, MN, announced a fifth genetic region associated with prostate cancer in families. The locus is called HPC20, because it is located on chromosome 20. The four other previously identified loci are HPC1, PCAP, and CAPB, which are all located on chromosome 1, and HPCX, which is located on the X chromosome. As with the other four, the HPC20 locus has not yet been cloned. This means that a small part of chromosome 20 appears to be associated with prostate cancer in some families, but it is not clear whether a prostate cancer gene is present at that location. Another recent development was reported by the University of Utah. There is a newly cloned gene called HPC2, which appears to be associated with prostate cancer in some people. These results are preliminary and have not been confirmed in family studies such as PROGRESS. Groups of researchers around the country are investigating the recently reported genetic regions. We will keep you updated as new information is available for all the reported genetic regions associated with prostate cancer in families.

Thank You for Your Help!

In the last volume of our newsletter, we asked for information from selected participants to be used to collect death certificates for deceased men with prostate cancer. Of the 128 people contacted, we have received 83% of the forms back. If you did not get a form with your last newsletter, we did not need your help. If you did receive a form and have not yet returned it, it is not too late to send it back. We have been sending out requests to each state or province for copies of the death certificates. On the death certificate, we hope to receive documentation of prostate cancer for certain deceased relatives. This information is very valuable for our analysis and we couldn’t have done this without your help.