Greetings from PROGRESS, the Prostate Cancer Genetic Research Study. We hope you and your family had a pleasant summer. We apologize for the delay in this newsletter. We were waiting for our research results to be accepted for publication. We hope you find this brief summary of our results informative. If you have any questions about this newsletter or your participation in the study, please call us toll-free at 1-800-777-3035.

The Genome Scan Results Are In!

Results from the overall PROGRESS genetic analyses are ready for publication, eight years after the project first began. The goal from the beginning of PROGRESS was to complete a “genome scan” in all participating families. A genome scan is a search of different “addresses” or markers across all 23 pairs of chromosomes. This type of analysis uses the genetic results at each marker for each person to evaluate inheritance in each family. For example, we look to see if within a family the men with prostate cancer share the same marker more frequently than we would expect based on chance alone; if so, this may indicate an association between prostate cancer and a gene at the location of that particular marker. The results of a genome scan such as ours usually highlight one or more areas of the genome as sites that may harbor genes with mutations that could lead to prostate cancer. Our genome scan involved genotyping nearly 2,000 people at 441 markers (over 800,000 genotypes). We have now completed the genome scan for 254 PROGRESS families.

The PROGRESS genome scan highlights several areas on chromosomes 6, 7, 8 and 11 that could harbor hereditary prostate cancer genes. The strongest result was on the short arm of chromosome 6, which is the only region in which the results are statistically significant when taking into account the many markers evaluated. The results in the other regions are also very interesting because some of these areas have been previously suggested from other published genominc scans of families with prostate cancer. We paid close attention to regions previously identified as possible sites for prostate cancer genes. At these “hot spots” or regions of interest, we found modest support for some and little or no support for other areas reported by other prostate cancer researchers focusing on family studies. We also looked at our data under different assumptions about how the disease may be inherited such as using an autosomal dominant model (assumes that a carrier of a potential disease causing mutation only needs one copy of the faulty gene to develop cancer) or a recessive model (assumes that carriers of a potential disease causing mutation need to have inherited two copies of the mutated gene to get cancer). In addition, we evaluated sub-groups of families that met certain criteria: families with five or more affected men, families with men diagnosed at younger ages, families with other kinds of cancer in addition to prostate cancer (ovarian cancer, breast cancer, brain cancer), and other groupings. The reason for grouping families in these ways is to put together sets of “similar” families in which prostate cancer may be caused by the same genetic mutation. In other words, grouping families that share certain characteristics is like grouping “apples with apples” instead of “apples with oranges.” Looking carefully at subgroups of families that are more “alike” or “homogeneous” may help in searching for the address of genes that cause hereditary prostate cancer. This is particularly important because it appears that there are multiple genes involved. Even with all the groupings and other regions of interest, however, there was only one part of the genome (the short arm of chromosome 6 or 6p) that had a strong enough result to indicate where a disease-causing genetic mutation may exist.

The findings from the PROGRESS genome scan will be published in the November issue of the journal “Prostate.” Also in that same issue, several other prostate research groups from around the world will be publishing genome scan results from their own family studies. These results are an important milestone for prostate cancer genetics, as it will allow us to compare data across multiple different family studies to see if there are common regions identified by more than one group of investigators. If so, these areas may indicate the most promising regions to begin more definitive searches for the specific genes and mutations that may contribute to hereditary prostate cancer.
What Happens Now?

Now that we have published the major findings from our overall genetic study, some of you may be wondering what the future holds for the PROGRESS study. There is still much to be learned about prostate cancer that occurs in families and there is much work that remains to be done. Based on the results of the genomic scan, we will soon begin the process of searching for specific genes in the regions of interest highlighted in the scan data. In addition, there are several analyses that remain to be done. Specifically, we plan to utilize the detailed data on other cancers collected as part of the follow-up survey to identify subsets of “similar” families with prostate cancer and other cancers, for example kidney cancer, colon cancer or thyroid cancer. We will then complete an analysis to see if there is evidence in these defined subgroups of families for genes that may contribute to multiple cancer types within families. This same approach allowed us to identify the region on the short arm of chromosome 1 (CAPB), which appears to be important in families with both prostate cancer and primary brain cancer. A second approach for further analyses will incorporate the detailed clinical data such as Gleason score and stage of the prostate cancers that were abstracted from the medical records of PROGRESS participants. These analyses will allow us to search for any regions of the genome that may be associated with more aggressive prostate cancer. Lastly, we are just beginning to analyze other data collected as part of the recent PROGRESS follow-up survey. For example, we are evaluating what factors may be related to level of interest in undergoing a test to determine genetic risk.

We are very pleased to report that we have recently received notice of continued funding of the PROGRESS study from the National Institutes of Health, National Cancer Institute to maintain our contact with you and to continue to try to find the genes that cause prostate cancer to occur in families. The blood samples and surveys collected from you and your family will continue to be a valuable research tool to help understand why prostate cancer runs in some families. We appreciate your ongoing willingness to contribute to this major research effort and want to acknowledge that none of this would be possible without the cooperation of study participants. If at any time you wish to ask questions or provide comments about the study, please call us toll-free at 1-800-777-3035. Also, please let us know if you would like to receive a copy of the genomic scan paper when reprints become available this fall.

Follow-Up Survey Update

Between July 2002 and January 2003, we mailed more than 1,600 follow-up surveys to PROGRESS participants. The follow-up surveys provide valuable updates to the information we already collected about you and your family, especially information about new diagnoses of cancer in yourself or your relatives.

To date, we have received more than 1,200 responses and are entering the data into a computer file for analysis. Many of you who responded took the time to write your thoughts in the comments section at the back of the survey. Our research team has been pleased to see so many good wishes from you. In addition, your comments written in the back of the surveys were informative and some were very touching.

It's not too late to reply! We are still waiting to hear from 364 of you. If you are one of those who have been slow to respond, please take a moment to send back your survey. We will be sending a reminder to those who haven't replied, but you can save us the cost of postage if you mail your survey back today. We really appreciate your ongoing help and cooperation.
International Group Plans Cooperative Meta-Analyses

The PROGRESS scientists are part of a collaborative research group called the ICPCG, International Consortium for Prostate Cancer Genetics. The ICPCG is a group of scientists from around the world who are all working with separate groups of families to identify the genes that cause prostate cancer. The institutions represented by the ICPCG members are listed in the column to the right. Currently, the ICPCG is planning a meta-analysis, in which data from these study groups would be analyzed together to look for prostate cancer genes. This approach is important because of the large number of families (over 2000) from which data are available. The large sample will improve our ability to confirm regions of interest and find new regions. The first meta-analyses planned are for the HPCX and HPC20 regions, two locations in the genome previously implicated in hereditary prostate cancer. It is hoped that by combining the information we will be more successful in narrowing the regions where prostate cancer genes may be found. The ICPCG group is funded by the National Cancer Institute, which recognizes the significant opportunity afforded by this international team of researchers working toward a common goal of preventing prostate cancer in future generations.

Our participation in the combined ICPCG analyses is important because PROGRESS is one of the largest and most comprehensive of the prostate cancer family studies. For those who may be concerned about how these analyses will be done, we want to assure you that they will not involve release of any personal or identifiable data. All data contributed to the ICPCG data coordinating center for meta-analyses will have all identifiers removed. Only grouped data without identifiers are required for pooling of family data that will allow us to assess regions of interest in this large collaborative effort.

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Johns Hopkins University, Baltimore, Maryland
Mayo Clinic, Rochester, Minnesota
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Stanford University, Stanford, California
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University of Southern California, Los Angeles, California
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University of Paris VII, France
University of Tampere, Finland
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AUSTRALIA
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GLOSSARY OF GENETIC TERMS

Chromosomes: Structures found in every cell nucleus that store and transmit genetic information. Chromosomes come in pairs. The human genome consists of 22 pairs of autosomes, numbered 1 through 22, and one pair of sex chromosomes (XX for females, XY for males).

DNA: The substance of heredity. A molecule that carries the genetic information or code that cells need to replicate and to produce proteins.

Gene: A segment of DNA which contains instructions for a cell to produce a protein. Each person inherits two copies of each gene, one from their mother and one from their father.

Human genome: All of the genetic material (genes) in the 23 pairs of human chromosomes.

Genome scan: A technique to find disease-causing genes by looking for patterns of inheritance at many different genetic markers (or sign-posts) across the entire genome.

Linkage analysis: A statistical technique to identify markers which trace patterns of heredity (genes) in families with several people affected with the disease.

Locus: (plural: loci) The position or location on a chromosome of a particular gene or marker.

LOD Score: (abbreviation for “logarithm of the odds ratio”) A statistical result that measures the strength of an association between a genetic marker and a potential disease gene within a family.

Marker: A particular sequence (piece) of DNA (for which the location is known), that can be used as an established “landmark” within the genome to tell where and on which chromosome a gene may be located.

Mutation: A permanent change in the DNA sequence of a gene; can be inherited or acquired during one’s lifetime.

Susceptibility gene: An inherited (present at birth) segment of DNA which may contain mutations or important changes in its code that make an individual more likely to develop a disease or condition.

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Word Find

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