Greetings

Welcome to the 21st edition of The Progress Report, a newsletter for participants in the Prostate Cancer Genetic Research Study or PROGRESS. We really appreciate your ongoing participation and help with the study. The goal of the newsletter is to keep in touch with you and to provide updates on our research. We hope you will find it both informative and helpful. If you have any questions about this newsletter or your participation, please call us toll-free at 1-800-777-3035. We are always pleased to hear from you.

Family Study Updates

Whole-exome Sequencing Project

As we outlined in the last edition of The Progress Report, our whole-exome sequencing (WES) and follow-up genotyping projects identified two genetic variants which are associated with an increased risk of prostate cancer in hereditary prostate cancer (HPC) families as well as in the general population. The two variants are located in the BTNL2 gene on the short arm of chromosome 6. These findings have now been published and if you would like a paper copy please let us know (Fitzgerald et al., Cancer Epidemiology Biomarkers and Prevention 2013; 22: 1520-8). Earlier studies have shown that variants in the BTNL2 gene are associated with inflammatory autoimmune disorders including sarcoidosis and rheumatoid arthritis, as well as inflammatory bowel disease and ulcerative colitis. These results support the possibility that the BTNL2 gene may contribute to the development of prostate cancer via the inflammation pathway.
ICPCG Project Updates

The PROGRESS study has been a member of the International Consortium for Prostate Cancer Genetics (ICPCG) since it was formed in 1996. The consortium consists of research groups from over 20 institutions in North America, Europe, and Australia. The strength of the ICPCG lies in its ability to perform large meta-analyses combining data from over 2,500 HPC families, to try to identify the genes with mutations that contribute to the inherited susceptibility to prostate cancer found in some families. The ICPCG is currently conducting a whole-exome sequencing project that includes 366 families with at least 3 men diagnosed with prostate cancer. A total of 539 men with prostate cancer were sequenced, including 76 individuals from 56 PROGRESS families. Analyses of the sequencing data are underway and we will update you as soon as the results are available.

The ICPCG is also conducting a genome-wide association study. This approach is used to look for associations between common genetic variants (present in 5% or more of the general population) and particular diseases to see if the variants are observed significantly more or less frequently in people who have the disease (cases) compared to people who do not have the disease (controls). The ICPCG is using this approach to study prostate cancer cases from HPC families compared to controls taken from existing studies that included mainly men with no family history of prostate cancer. DNA samples for 132 men with prostate cancer from PROGRESS families and 122 controls from one of Dr. Stanford's case-control studies were sent for genotyping. Across the combined ICPCG groups a total of 3,990 DNA samples, from 2,468 cases and 1,422 controls, were genotyped. The genotyping has been completed and analyses are underway. As always, we will update you when the results are available.

SNPs Associated With Risk of Prostate Cancer Recurrence or Progression

There is a range of possible clinical outcomes related to prostate cancer, as some tumors are very slow-growing while others are fast-growing, more aggressive and potentially life-threatening. Currently, most men diagnosed with prostate cancer are initially treated with radiation therapy or surgery, although a growing number of men with low-risk disease are opting for active surveillance (see following discussion). Of those men who initially undergo active treatment for prostate cancer, approximately a third will experience disease recurrence or progression. For the subset of patients with more aggressive disease, their prostate cancer recurrence may prove to be life-threatening over time. New biomarkers are needed to improve on the ability of conventional clinical and pathology measures evaluated at diagnosis such as PSA level, Gleason score and tumor stage, to identify individual patients who are more likely to develop disease recurrence that could reduce survival.

Genetic factors are known to play a role in the development of prostate cancer, and recent studies have identified several genetic variants called single nucleotide polymorphisms (SNPs) associated with more aggressive prostate cancer. We genotyped 937 SNPs in biological pathways of interest for prostate cancer progression including steroid hormones, inflammation, growth factors and DNA repair, in over 1,000 men with prostate cancer to see if they were associated with prostate cancer survival. Twenty-two of the SNPs were associated with a significantly greater risk of dying from prostate cancer, five of which were confirmed to be associated with prostate cancer mortality in a cohort of over 2,800 patients from a large population-based study conducted in Sweden.
We recently evaluated the same set of 22 SNPs in 957 men with prostate cancer from the PROGRESS study. Three of the original 22 SNPs were associated with prostate cancer survival. With further confirmation the hope is that these results can be translated into a tool that could be used at the time of diagnosis to identify men who are at greater risk for having a potentially lethal form of prostate cancer. These high-risk individuals could then be treated earlier with more aggressive forms of therapy, hopefully leading to improved survival outcomes. Further validation is underway to establish the subset of the most informative SNPs in collaboration with investigators in Finland, Australia and the UK. We will update you when findings are available.

Other Prostate Cancer Research Updates

Chemotherapy for Metastatic Prostate Cancer

Findings from a large clinical trial involving 790 patients were presented at the annual meeting of the American Society of Clinical Oncology (ASCO) in June. The results showed that men with hormone-sensitive metastatic prostate cancer who received the chemotherapy drug Docetaxel at the start of androgen deprivation therapy (ADT) lived more than a year longer than patients who received ADT alone. Approximately two-thirds of patients had extensive metastatic disease, defined as cancer that had spread to major organs such as the liver, or had spread to four or more bone sites, or both. This group of cases experienced the greatest benefit from the combined therapy (Docetaxel plus ADT) with the longest increase in overall survival (49.2 months versus 32.2 months for those who received ADT alone). Further follow-up studies are ongoing, but this is a significant breakthrough in the treatment of later-stage, metastatic prostate cancer.

Active Surveillance for Prostate Cancer

Increasingly, men with newly diagnosed, low-risk prostate cancer are opting for active surveillance, which involves regular monitoring with PSA blood tests, digital rectal exams and periodic repeat prostate biopsies, rather than immediate active treatment. In this way, men who are least likely to experience morbidity from prostate cancer can avoid or delay more invasive treatments that often have adverse side-effects that may reduce quality of life. Men who initially choose active surveillance but then show evidence of an increased amount of cancer in the biopsy or more aggressive features of prostate cancer such as an increase in Gleason score are then offered treatment with curative intent, such as radical prostatectomy or radiation therapy. Our colleague, Dr. Daniel Lin, is leading a program called the Canary Prostate Cancer Active Surveillance Study (PASS). PASS has collected blood, urine, prostate tissue, and quality of life surveys on over 1,000 men who chose active surveillance with the goal of identifying biomarkers to predict disease progression among these men. Results from the study could eventually help patients and their physicians make more informed decisions on how to manage newly diagnosed prostate cancer.

Health Status Updates

In order to keep family and clinical records up to date and to maximize the accuracy and power of ongoing study analyses, it is very important that you keep us informed about any changes in your current health status. We would particularly like to know of any new diagnosis of prostate cancer or any other type of cancer in you or your family. You can reach us via any of the methods listed in the “Contact Information” section on the next page. Your help is always very much appreciated and we would like to thank you for your ongoing participation in the PROGRESS study.
If you would like copies of our earlier newsletters or additional information regarding the study, including a list of published study-related articles, please visit our website:

If you would like a copy of any of our published papers, or if you have any questions, or would like to report any family updates or changes in your current address or phone information, please feel free to contact us.