

THE *PROGRESS* REPORT



Volume 14

Spring/Summer 2005

Welcome to the 14th edition of The Progress Report, a newsletter for participants enrolled in PROGRESS, the Prostate Cancer Genetic Research Study. We are continuing our work to try to discover and understand the genes associated with hereditary prostate cancer in families. The goal of the newsletter is to keep you updated on our latest research findings and other related news concerning prostate cancer, and we hope you find it both informative and helpful. We really appreciate your ongoing help with the study. If you have any questions about this newsletter or your participation, please call us toll-free at 1-800-777-3035.

Changes to the PROGRESS Team

In December 2004, we welcomed our new study manager, Laura McIntosh, who hails all the way from Scotland. She replaces Suzanne Kolb, who has been involved with PROGRESS from its earliest days and is fortunately still available to provide her invaluable support and advice. We wish her well in her new position. Before moving to the US, Laura completed her PhD in London, where she worked on a large family study, so she brings relevant experience to her new role.

We also hired a new program assistant, Jack Kindred, in September to help out with our follow-up. Jack has many years of experience as a telephone interviewer within FHCRC and we are very pleased to have him onboard. We thought it might be nice to show you what our new team members look like:



Jack Kindred, Program Assistant (left)
and Laura McIntosh, Study Manager (right)

Follow-Up Survey Update

Since July 2002 we have mailed out 1,640 follow-up surveys to PROGRESS participants. These surveys provide valuable updates regarding new diagnoses of prostate cancer in participants and their relatives. They also collect a more detailed account of any history of other cancers in family members, and obtain additional information concerning personal medical history.



Some participants were also asked for their general opinions regarding prostate cancer and genetic testing. Many of you included your own comments in the final section, which were of great interest and often very inspiring. To date, we have received 1,399 completed surveys (85%), which are now data entered, and ready to undergo preliminary analyses.

The information you provided will allow us to extend family pedigrees and carry out analyses on subsets of PROGRESS families that share a history of other cancers, including pancreatic, gastric, and colon. We will also be evaluating your opinions regarding level of risk for prostate cancer, and your general level of interest in genetic testing.

We would like to thank everyone who contributed to this extremely valuable and important phase of the study by completing and returning their survey, and to encourage anyone who has not yet done so, to respond as soon as possible.

Past and Present Analyses

In 2003, we reported the findings from our genome-wide scan of 254 PROGRESS families, which highlighted several areas on chromosomes 6, 7, 8, and 11 as potential “hotspots” in which to look for hereditary prostate cancer genes. Several other family studies published genome-wide scan results in the same edition of the journal “The Prostate” (December, 2003). However, this group of genome scans produced inconsistent results. Only one research group reported a lod score greater than 3 (at chromosome 20), the cut-off for strong evidence of linkage. Similarly, although several regions were reported with lod scores greater than 2, no single chromosome was reported at this level by more than one group.

In fact, no single chromosomal region has emerged as a candidate for harboring the gene for an inherited predisposition to prostate cancer. Rather, hereditary prostate cancer appears to involve multiple genes, which influence the development of the disease in different families. One strategy to narrow down the regions, or loci, containing these genes is to group families according to certain shared characteristics that may make them more genetically similar or “homogeneous”. The characteristics commonly applied include: age at diagnosis, number of prostate cancer cases in the family, presence of other types of cancer in relatives, ethnicity and country of origin, and family history of cancer on the mother’s side, the father’s side, or both sides of the family. Some successful examples of this approach are our previously reported findings in families with a shared history of prostate cancer and brain cancer (at chromosome 1p36), and in families with an Ashkenazi Jewish heritage (at chromosome 7).

Ongoing analyses are being conducted in a larger sample of Ashkenazi Jewish families, and we will soon be looking at families with a history of pancreatic cancer, gastric cancer, and colon cancer. We may be contacting some of you to clarify details of these other cancers reported in family members. Another method for grouping families is to look at clinical variables, such as stage and grade of prostate tumors (Gleason score). We are currently analyzing PROGRESS families according to clinical features of the prostate cancer. In addition to analyzing groups of similar families, another solution to the genetic complexity of prostate cancer is to analyze even larger sets of families.

GLOSSARY OF 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).

Genetic marker: A particular sequence (piece) of DNA, for which the location on the genome is known, that can be used as a “landmark” to tell where and on which chromosome a disease-related gene may be located

Genome-wide 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

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

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

Linkage threshold: A LOD score greater than or equal to 3.30 is the cutoff for “strong” or “significant” evidence of linkage (expected to occur 0.05 times by chance in a genome scan), and a LOD score greater than or equal to 1.86 is the cutoff for “suggestive” evidence of linkage (expected to occur once by chance in a genome scan)

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

For a single study, PROGRESS has the largest number of hereditary prostate cancer families in the world. However, combined analyses using data from several family studies, have even greater statistical power to find the genes causing the disease in different subgroups of affected families. So, the PROGRESS team has joined together with a large group of research teams from all over the world to form the International Consortium for Prostate Cancer Genetics (ICPCG).

Certain family-level data from all the participating groups were sent to a centralized Data Coordinating Center (no personal identifiers or individual-level data were shared). The first combined genome-wide scan of this pooled dataset - the largest of its kind to date involving 1,233 families - has now been completed and accepted for publication in the American Journal of Human Genetics.

An initial analysis of the combined group of families identified five regions with ‘suggestive’ evidence for linkage (at chromosomes 5q12, 8p21, 15q11, 17q21, and 22q12). When families were grouped according to the number of affected family members, the finding on chromosome 22q12 increased from “suggestive” to “significant” in a subset of 269 families with ≥ 5 affected members. This region may therefore be a strong candidate for harboring a gene causing the disease in this subgroup of families.

All of the regions highlighted in the genome-wide scan are still quite large and contain many genes, so they will be investigated in greater detail to try and pinpoint the actual gene(s) responsible for causing hereditary prostate cancer. As usual, we will continue to send you updates on our findings as soon as they are available.



Prostate Cancer and Diet

Many of you who have not been diagnosed with prostate cancer, have been kind enough to complete a Food Frequency Questionnaire, telling us about your intake of a wide range of foods, along with a Dietary Supplement Survey on use of vitamins and mineral supplements. There is a lot of research being conducted into the possible role of dietary factors in relation to the development and prevention of cancers of all types, and we hope to evaluate similar variables in relation to prostate cancer within PROGRESS. An example of current research is SELECT (Selenium and Vitamin E Prostate Cancer Prevention Trial), which is examining the effects of selenium and vitamin E on the incidence, or number of new diagnoses, of prostate cancer over a 7-year period. Details can be found on the FHCRC web-site at: <http://www.fhcrc.org/science/programs.html>

Closer to home, our own Principal Investigator, Dr. Janet Stanford, conducted a study into the relationship between alcohol consumption and risk of prostate cancer in a large case-control study of 1,456 men in King County, WA (International Journal of Cancer 2005; 113: 133-140). Participants provided information on their lifetime consumption of beer, liquor, and wine. Weekly red wine consumption, at a level of 4 or more 4 oz (1/2 cup) glasses, was associated with almost a 50% reduction in relative risk, especially in men with more aggressive forms of the disease. Red wine is rich in chemical compounds known as polyphenols, which are thought to have high anti-oxidant and anti-inflammatory properties.



Using the same group of study participants, Dr. Stanford and her colleagues previously looked for any relationships between fruit and vegetable intake and risk of prostate cancer (J Natl Cancer Inst 2000; 92: 61-68). They found that total vegetable consumption reduced the relative risk of prostate cancer significantly (men eating 28 or more servings per week showed a 35% decreased risk compared to men eating 14 servings per week or less). In addition, a person’s weekly intake of cruciferous vegetables such as, broccoli, cabbage, cauliflower, and Brussel sprouts, was associated with an even higher protective effect against prostate cancer (men eating 3 or more servings per week had a 41% decreased risk compared with men eating less than 1 serving per week).

Some studies have also suggested that intake of tomatoes or tomato products, which contain lycopene, may be associated with a lower risk of developing prostate cancer. Cruciferous vegetables and tomato products may act as anti-oxidants and thereby alter cancer risk. Ongoing research is being done on anti-oxidants and their potential role in cancer prevention.

In acknowledgement of our “home-grown” findings, we have included 2 tasty recipes based on cruciferous vegetables. There are also several cookbooks on the market, which may be of interest. One in particular,

“The Taste for Living Cookbook”, is published by the Prostate Cancer Foundation (PCF), and contains recipes created specially for the chairman, Michael Milken, a prostate cancer survivor. “The New American Plate Cookbook” was published by the American Institute for Cancer Research, and is full of recipes promoting a diet rich in plant foods, which may help to guard against cancer. If you would like further details on current prevention guidelines, the Cancer Information Service (1-800-422-6237) and the American Cancer Society (1-800-227-2345) both provide extensive and up-to-date resources.

Crunchy Asian Salad

1 cup broccoli florets
1 cup cauliflowerets
1 cup cherry tomatoes
1/2 cup fresh snow peas
1 green onions, chopped
1/2 cup water chestnuts, sliced and drained



In a large bowl, combine the broccoli, cauliflower, tomatoes, snow peas and green onions. Stir in water chestnuts.

Dressing:

4 1/2 teaspoons reduced sodium soy sauce
1 tablespoon apple cider vinegar
1 tablespoon sesame oil
3/4 teaspoon sugar
1/2 teaspoon sesame seeds, toasted
1/2 teaspoon olive oil
Dash of pepper



Combine all ingredients in a jar or container with a tight-fitting lid and shake well. Pour over vegetables and coat thoroughly. Refrigerate for at least three hours for best flavor.

RECIPES

Penne Pasta with Broccoli Rabe

1 lb penne pasta
2-3 pounds broccoli rabe (available in most supermarkets)
4 or more cloves garlic, roughly chopped (not put through a press)
4 Tbs olive oil
1 tsp red pepper flakes (or to taste)
1/2 cup grated Parmesan cheese (Reggiano if available)



Cut stems of broccoli rabe into 1-1/2 pieces. Cut off flower tops and set aside. Cook stems in salted, boiling water until nearly cooked through. Drain and plunge into ice water to stop cooking.

Heat oil in large skillet. Add garlic and cook over low heat until browned, about 2-3 minutes. Add broccoli rabe flowers and red pepper and cook for 1-2 minutes. Add cooked stems and heat through. At the same time, cook pasta in boiling water until al dente (about 10 minutes).

Contact Information

If you would like additional information regarding the study, or a copy of any of our papers, please let us know.

Also if you have any questions or would like to report any family updates, please contact us.

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