National Cancer Institute

Clinical Genetics Branch (CGB)
Division of Cancer Epidemiology and Genetics (DCEG)

Summer 2007

Family Research Matters

Familial Testicular Cancer (FTC) Study Newsletter

Thank You for Taking Part in the Testicular Cancer Study

Our research team is truly grateful to you and your family members for taking part in our study as we search for the gene or genes related to testicular cancer.

In this issue of our participant newsletter, we would like to share some of the early results from the Familial Testicular Cancer (FTC) research project. Much work has been done since the study started four years ago, and our study is still going strong, with new families enrolling today.

As of January 31, 2007, 89 families have taken part, totaling 453 people, or 276 men and 177 women. This includes men with and without testicular cancer, their female family members, spouses, and other family members not related by bloodline. Of these families, 56 had more than one case of testicular cancer and 31 families had at least one man with cancer in both testicles. Two families had identical twins.

Most of the men and women (317 people) took part from their home communities by filling out questionnaires and giving blood samples. To date, 136 people also traveled to the Clinical Research Center at the National Institutes of Health (NIH) in Bethesda, Maryland for a two-day visit. During these visits, they received a detailed work-up to look at clinical, genetic, and laboratory factors that might be linked with FTC. We were able to meet with 55 men who had testicular cancer, 1 woman with a germ cell tumor, 69 male and female relatives, and 11 spouses.

Both groups have made vital contributions to this research. Our research simply could not be done without your willingness to take part in this study. Please accept our heartfelt "thank you" for all you have contributed to advancing our understanding of familial testicular cancer.

Larissa A. Korde, MD, MPH
Lead Investigator

Mark H. Greene MD

Mark H. Greene, MD
Principal Investigator

Contents

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Working Together Globally

The National Cancer Institute (NCI) belongs to a group of 21 research institutions that is worldwide in scope. This group is called the International Testicular Cancer Linkage Consortium (ITCLC). The scientists who are part of this group share our same goal – to find the gene or genes that cause men to be prone to testicular cancer. We have contributed DNA samples to the Consortium from the families who are taking part in our research effort.

Refining Our Gene-Hunting

As you may recall, our study started because of an ITCLC report published in 2000. Based on data from ***134 families***, the findings suggested that there might be a gene related to FTC located on the X-chromosome. We knew that a much larger set of families would need to be studied to see if this is true, and if so, to find the exact gene responsible. The NCI Clinical Genetics Branch joined the worldwide group in 2002 and gave 277 DNA samples from 41 FTC families. Many of you have already had your DNA analyzed as part of this project.

In March 2006, a second report came out from the ITCLC with results from another gene-hunting effort. This was based on a larger sample – ***237 families*** with two or more cases of testicular cancer. This is the largest set of families with more than one case of testicular cancer ever studied. Yet from this larger study, there was no proof to support the presence of an FTC gene on the X-chromosome. Even though this is disappointing, it's fairly common when trying to confirm a genetic finding that has been earlier reported by other scientists.

On a positive note, some data did suggest the presence of FTC genes on four additional chromosomes (numbers 2, 3, 12 and 18), although more study is needed to confirm these results.

So far, important progress has been made, but the genetics of FTC may be more complex than first thought – it may involve different genes acting together, rather than being caused by a single gene. Since a specific gene causing people to be more likely to develop testicular cancer has not been identified, a genetic test is not yet available. Developing such a test remains a major goal of this research project.

Future Steps

Along with other members of the ITCLC, we are still enrolling new families into this project. We are also using new, state-of-the-art gene-finding technology. The DNA samples and information you have given will continue to be used in our new analyses. A major goal of our project is to create a genetic test for FTC. This is especially important for families who have more than one case of testicular cancer, since this would help find out which specific family members are at greater genetic risk.

A Promising New Finding

Researchers have known that fertility is not quite normal in many men who develop testicular cancer. In fact, having low fertility seems to raise the risk of having testicular cancer. Recently, an area on the Y-chromosome (called *AZFc*) was found, and it contains several genes needed for normal sperm production. When a piece of this gene is missing or deleted, the man is infertile. This deletion is called "***gr/gr***." ITCLC researchers decided that this was a gene that made biological sense to study.

We looked for the *gr/gr* deletion in the DNA of 431 men with testicular cancer who came from families with more than one case. We found that they were **three times more likely** to have this genetic defect than 2,599 men in the control group without testicular cancer.

We then tested 1,376 men with testicular cancer who did **not** have a family history of cancer. We found that they were **twice as likely** to have the *gr/gr* deletion as the men in the control group (without cancer).

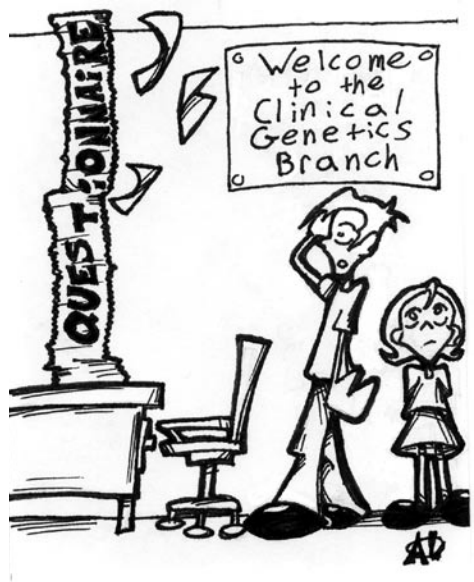
Both of these findings were highly significant, and the linkage was strongest for men with seminoma (rather than non-seminoma) cancers. The fact that the *gr/gr* deletion appeared both in patients with and without a family history suggests that it may not be specific for FTC, but might be a more general genetic indicator (modifier) of risk.

This important new finding is shedding more light on how testicular cancer develops. It has also led to intense study of genes in the *AZFc* region. Unfortunately, the defect is very uncommon in FTC patients (only 3% of whom actually have the deletion), so clinical testing with regard to a man's risk is not yet practical. The DNA samples from our study families were an important part of this analysis and the new information we found.

What Did We Learn About Study Families?

From the forms that families completed, it was clear that many of you would be interested in having a genetic test within 6 months, if one were to become available. In general, we found:

- People who were worried about insurance discrimination were not as interested in getting a test, even though most had health insurance.
- Younger people, those who were more worried about cancer, and those with supportive families were more likely to be interested in genetic testing.



- Other factors that influence a person's decision for testing include a doctor's advice and a need for information to help make health decisions for their children.

This study is the first to describe social and relationship factors that influence people who are thinking about using new genetic tests in the context of testicular cancer. It shows how important it is to address concerns about genetic discrimination which, with very rare exceptions, has not proven to be a problem. We hope that this information will help show the need for legislation aimed at making genetic discrimination illegal. Congress is currently considering a bill on this issue called the Genetic Information Nondiscrimination Act (GINA), and its chances of passing this year appear to be good.

How will our research help? Families will benefit if they feel comfortable with the new tests, have the support of their doctors, and access to genetic counseling, and if the genetic testing is done using a family-centered approach.

Where Do We Go From Here?

We have some exciting analyses planned using the data we have already gathered, such as:

Testicular Ultrasound Findings

These may show whether certain family members are at higher testicular cancer risk than others.

Testicular Self-Exam (TSE)

Some health groups suggest that men in families with a history of testicular cancer should do monthly TSE. We are studying the TSE practices of men *without* cancer in high-risk families. We will identify the medical and psychological factors associated with their willingness to perform TSE. Early findings suggest that health care providers need to be specific in encouraging high-risk men to perform TSE and to teach them how to do this simple exam. See page 9 for steps on how to do a TSE.

Genetic Knowledge

We are preparing a report of what people entering the study did and did not know about genetics in general, and the genetics of FTC. This will help us focus our educational efforts so that members of high-risk families can make informed choices about their health care.

ITCLC Cancer Analysis

We are combining data with ITCLC centers in England and Norway to look at cancers ***other than testicular cancer*** that have occurred in our families. The goal is to see if other cancers occur more often in the families of men with testicular cancer. Even though there are currently no data to suggest that other cancers are part of FTC, this issue needs more study.

Genetic Analyses

We continue to study genes of biological interest (sometimes called the "candidate gene approach," see page 11 glossary). We are analyzing DNA from affected men in our study for changes in a gene called *PDE11A*. This gene is associated with familial tumors in the adrenal gland, and also appears to be important in normal testicular function.

Medical History

We are starting to analyze data from the study's medical history form. The same form has been used to collect information from ITCLC study participants in England. By combining the information from both groups of patients, we hope to find features that are common in FTC patients. We continue to work with scientists around the world to learn as much as we can about FTC.

Chromosome Analysis

We have analyzed the chromosomes of 30 men with testicular cancer from our families. We were looking for any abnormal chromosomes that might give a clue to the location of an FTC gene. We used very complex methods of analysis and did not find any defects. However, no one has ever done a chromosome study like this in FTC families, so our negative finding still represents important scientific information. We will soon publish the results in hopes of preventing other scientists from using funds to repeat similar studies.

Possible New Syndrome

One of our main goals is to define the clinical features of the FTC syndrome. We collect very detailed information about all people in the study and stay alert to unusual events that could lead to a new finding. One of the families in our study included a man with a personal and family history of testicular cancer. He also had a surprising number of other abnormalities including a tumor of the pituitary gland, a new cancer of the kidney, multiple colon polyps, many skin moles and benign fatty tumors. None of the other FTC participants had this unusual combination of problems. This patient was studied intensively for mutations in other genes which were known to be linked with one or more of his findings. We were not able to find any abnormality to explain his condition. This led us to theorize that he may have a new syndrome not previously recognized. A report describing this patient and his family has recently been published to alert the medical community to be on the lookout for similar cases.

This wide array of research (and more is planned) is made possible by our systematic gathering of information and samples, such as blood, DNA, serum, plasma and semen. By doing this, we can continue our research for many years, based on the data collected from your one evaluation.

How Do We Protect Your Rights and Confidentiality?

We have pioneered cancer research methods, including collecting and storing personal data and samples (blood, DNA, serum, plasma and tumor tissue) from people who take part in our studies. We are part of a research program (NCI's Division of Cancer Epidemiology and Genetics) that has been using this design for more than 30 years. We can keep the samples frozen for many years, so that as tests, tools, and knowledge improve, we can continue our research using these samples, rather than collecting new ones.

Protecting your privacy is our utmost concern, so we want to share with you more details of how the Clinical Genetics Branch (CGB) handles your samples:

- When we first design a study (called a protocol), we make every effort to list the specific uses we intend for the samples and to give scientific reasons why lab studies are necessary. Having NCI's Institutional Review Board (IRB) review our study plans gives you another layer of protection. The IRB has the right to deny research if it believes the risk to the participant is too high or the scientific reasons are not sound.
- At the beginning of a study, each participant signs an informed consent form. This form describes the study and outlines possible uses of samples in the future. Those who take part in the study can allow or decline use of their samples for these purposes. In general, you can refuse to give samples and still take part in the study. The consent form also makes it clear that you have the right, at any time, to request that your samples be taken out of storage and destroyed.

- We collect samples and store them in a special laboratory that keeps them in a stable condition. These are closely-guarded, highly-secure facilities. Special safeguards are in place to protect your samples. We use a custom-designed computer system to track the location of samples, whether they are in our facility or are in the labs of other researchers we are working with. **All samples are given a code number and do not carry your name or other identifying information.**
- We use samples only for the purposes outlined in the IRB-approved protocol and informed consent form. If we find new uses for your samples beyond those listed in the study design or consent form, then we must bring new proposals to the IRB for review and approval. The IRB has the right to approve the plan, refuse the plan, or require that we come back to you and ask for your consent to use your samples in the manner we propose.
- Lab investigators who are either part of NCI or the National Institutes of Health or are in labs in the U.S. or overseas that have formal agreements with us can study your samples. If we send samples to them, the samples are coded so that it is impossible for the lab researcher to identify you personally.
- The data we obtain from lab studies can help us learn more about the disease we are studying. Often, these data give us clues for more research, but usually they are not useful to patients as they make decisions about their ongoing health care. If we unexpectedly learn something new that we believe is important for you to know, we will contact you and share the information with you and your health care providers.
- All samples are labeled with coded specimen numbers. Your name or other personal data are not on the label. Personal data is not shared with lab collaborators. The only people who can make the connection between the code and your personal data are those CGB staff who are directly involved in this specific study. The number of CGB staff with access to this sensitive information is kept to a minimum.
- All information is kept in password-protected computer files, or in secure, locked file cabinets. Access to this information is strictly limited and controlled.
- A Certificate of Confidentiality given to CGB by the U.S. Department of Health and Human Services also protects your research data. This certificate strictly limits outside parties from gaining access to your information.
- Our research staff has formal training on protection of your data, with yearly update trainings. We take the duty of protecting your information very seriously.

Our goal is to learn as much as we can about familial testicular cancer as quickly as possible, without placing you or your privacy at risk. We hope you will be reassured that the system we have in place will safely allow us to do both.

Your samples are an incredibly valuable gift to science and the community at large. It is, without a doubt, the gift that keeps on giving! Thank you again for your remarkable generosity.

The Latest on Treatment

Testicular germ cell cancer (found in cells that give rise to sperm) is a highly treatable, often curable disease. The cure rate approaches 100% for tumors found in the early stages. Widespread disease is also curable, as in the inspiring story of Lance Armstrong. Treatments after surgery depend on things like the type of cancer (seminoma or non-seminoma) and its extent. Treatment for this type of cancer is well-established; no dramatic new changes in therapy have occurred in recent years.

A recent study in Europe found that a chemotherapy drug named carboplatin (Paraplatin®) is a safe and effective option when seminoma is found in a very early stage (Stage I), instead of the current choice between close monitoring or radiation therapy. For men at high risk of having the cancer come back or spread elsewhere in the body, or for those whose cancer has returned, studies are now evaluating using higher doses of chemotherapy followed by an infusion of the patient's own bone marrow.

The goals of treatment vary, based on the patient's prognosis. For men with early-stage disease, research focuses on finding the least amount of treatment that can lead to excellent survival, while lowering the long-term side effects of therapy.

Intensive chemotherapy, new drugs and aggressive surgery are being evaluated for advanced or recurrent cancer. A new report indicates that high-dose chemotherapy plus stem-cell rescue may cure some patients with recurrent cancer after platinum therapy.

Several newer chemotherapy drugs appear promising in the treatment of patients whose cancer has returned, such as paclitaxel, gemcitabine, and oxaliplatin. Two- and three-drug combinations of these agents are under active study. So, even though most men with testicular cancer have very successful treatment, active research is ongoing to improve survival and quality of life even more.

Resources

For more information on diagnosis, treatment, monitoring, and survivorship, contact:

- **The National Cancer Institute**
  http://www.cancer.gov/cancertopics/types/testicular
- **The Testicular Cancer Resource Center**
  http://tcrc.acor.org
- **The Lance Armstrong Foundation**
  http://www.livestrong.org
- **The American Society of Clinical Oncology's People Living With Cancer**
  http://www.plwc.org/testicular
- **The American Cancer Society**
  http://www.cancer.org

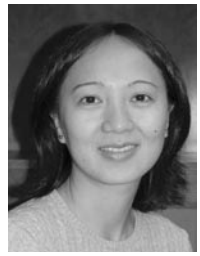
Information regarding testicular cancer, treatment, clinical (treatment) trials, support/survivorship, and the genetics of cancer is available at many Web sites. Only a few are listed. Many other sites can be reached through electronic links at the ones listed here. The following Web sites are from reputable organizations, which update information regularly. However, our listing of these sites does not constitute an endorsement of their services by either the NCI or the NIH.

About Our Staff

Dr. Joan Kramer, who was instrumental in the initial design and activation of the FTC study, left the NCI to join a full-time, clinically-focused academic oncology practice. **Susan Pfeiffer**, the primary research nurse with whom most of you have interacted at one time or another has also moved on. She is currently doing medical consulting for a law firm in Washington, D.C.

We will miss them both, and we know that you join us in wishing them the best of luck in their future endeavors. We are enormously grateful to them for their critical roles in getting the FTC study up and running. The analyses we are doing today are possible due to their hard work over the past four years.

Dr. Larissa Korde has taken over from Dr. Kramer as the study's Lead Investigator. Dr. Korde received a B.A. from the College of William and Mary in 1992, an M.D. from New York Medical College in 1998, and a Masters degree in Public Health from George Washington University in 2003. Dr. Korde completed her residency in Internal Medicine at Georgetown University Medical Center, followed by a Medical Oncology fellowship and a Cancer Prevention fellowship at the NCI. She is board certified in both Internal Medicine and Medical Oncology. Dr. Korde joined the Clinical Genetics Branch in October 2005. Her research interests include lifestyle factors and their effect on cancer risk, the identification of intermediate endpoints for cancer prevention and treatment trials, and designing intervention trials for populations at increased risk of certain cancers.



Dr. Phuong Mai has also recently joined our clinical research team. Dr. Mai received her M.D. degree in 1997. She completed her residency in Internal Medicine at Tulane University Medical Center in 2000 and her Medical Oncology fellowship at the University of Texas Health Science Center at San Antonio in 2004. During that fellowship, she simultaneously earned a Master of Science degree in Clinical Investigation. Most recently, Dr. Mai has completed a special post-doctoral training program in Clinical Cancer Genetics at the City of Hope National Medical Center in Duarte, CA. She is board-certified in Internal Medicine and Medical Oncology. Dr. Mai joined the Clinical Genetics Branch in October 2006. Her research interests include the effects of behavioral factors on cancer risks, early detection and intervention in populations at increased risk of specific cancers, and genetic modifiers of cancer risk.

We are also pleased to welcome **Claudia Soho** to the FTC Research Team. She has replaced Susan Pfeiffer as the primary research nurse for the study. Claudia received her Bachelors degree in Nursing from George Mason University in 1995 and has been an oncology nurse since that time. She is the primary research nurse in CGB's Familial Testicular Cancer study. Previously, she held positions related to oncology research, as a clinical trial specialist for the American Society of Clinical Oncology (ASCO) and as a research nurse in solid tumor and hematologic malignancies at the Georgetown University Lombardi Comprehensive Cancer Center. She is an Oncology Certified Nurse (OCN) and a Certified Clinical Research Professional (CCRP).

Testicular Self-Examination (TSE)

If you have a family history of testicular cancer

Monthly self-exams of the testicles can help you become familiar with this area of the body and may help in finding cancer at an early – and very curable – stage. TSE is not suggested for men who have no known risk factors, but it is often recommended for those who are at higher risk of the disease, such as those with a family history.

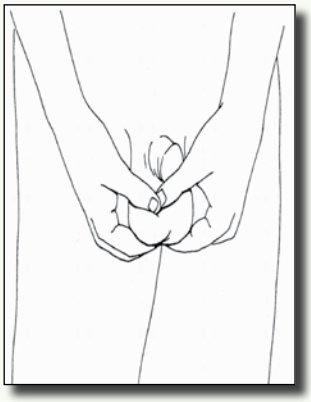
Monthly check

Set aside time after a warm bath or shower (heat relaxes the scrotum, making it easier to spot anything abnormal). Keep in mind that the point is not to find something wrong, it is to learn what everything feels like normally, so that you will know if something changes.

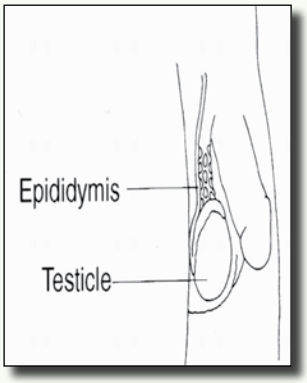
Follow these simple steps

1 Stand in front of a mirror. Check for any swelling on the scrotal skin.

2 Feel each testicle with both hands. Place the index and middle fingers under the testicle with the thumbs placed on top. Roll the testicle gently between the thumbs and fingers – you should not feel any pain when doing the exam. Don't be alarmed if one testicle seems slightly larger than the other as that is normal.



3 **Find the epididymis**, the soft, tube-like structure behind the testicle that collects and carries sperm. If you are familiar with this structure, you won't mistake it for a suspicious lump. Cancerous lumps usually are found on the sides of the testicle but can also show up on the front. Lumps on the epididymis are not cancerous. Also, please note that free-floating lumps in the scrotum that are not attached in any way to a testicle are not likely to be testicular cancer.



4 If you find a lump on your testicle, see a doctor, preferably an urologist, right away. The abnormality may not be cancer, but if it is, early diagnosis and treatment are key. **When in doubt, check it out** - if only for peace of mind!

Most doctors agree that checking a man's testicles should be part of a general physical exam. The American Cancer Society (ACS) recommends a testicular exam by your doctor as part of a routine cancer-related checkup.

Symptoms to keep in mind

- Any enlargement of a testicle
- A major decrease in the size in one of the testicles
- A feeling of heaviness in the scrotum
- A dull ache in the lower abdomen or in the groin
- A sudden collection of fluid in the scrotum
- Pain or discomfort in a testicle or in the scrotum
- Enlargement or tenderness of the breasts

Symptoms that are not normally signs of testicular cancer

- A pimple, ingrown hair or rash on the scrotal skin
- A free-floating lump in the scrotum, seemingly not attached to anything
- A lump on the epididymis or tubes coming from the testicle that kind of feels like a third testicle
- Pain or burning during urination
- Blood in the urine or semen

Remember, only a physician can make a cancer diagnosis. For that matter, only a physician can determine if the testicle is normal.

If you think something feels different than normal, see the doctor!

Words to Know – Cancer Genetics Research Terms

affected – An individual in a pedigree or family who has the condition that is being studied (in this case, testicular cancer).

allele – One of the variant forms of a gene at a particular location on a chromosome. Different alleles produce variation in inherited characteristics such as hair color or blood type. In an individual, one form of the allele (the dominant one) may be expressed more than another form (the recessive one).

autosomal – Refers to any of the chromosomes numbered 1-22 or the genes on chromosomes 1-22. This term excludes the sex-determining chromosomes, X and Y.

cancer screening – Clinical testing designed to identify the presence of a specific cancer in an individual who is thought to be at risk of developing that specific cancer, and who has no symptoms to suggest the presence of cancer. The intent is to find cancers at the earliest possible stage in their development to improve the chances for disease cure.

candidate genes – These are known genes which are considered as possible contributors to a person's genetic predisposition to cancer, based on what is known about the normal function of those genes and their role in other medical conditions. This contrasts with the linkage analysis approach (see below), which does not require knowing ahead of time which specific genes might be important.

chromosome – Physical structure consisting of a large DNA molecule organized into genes and supported by special proteins called chromatin. Each human has 46 chromosomes: 2 pairs of each of the 22 autosomes, plus either two X chromosomes (women) or an X and a Y chromosome (men).

congenital – A condition or trait present at birth, whether the result of a genetic or non-genetic factors.

cytogenetics – The study of the structure, function, and abnormalities of human chromosomes.

disease-causing mutation – A gene change or alteration that causes or predisposes an individual to developing a specific disease.

familial – A characteristic or trait that occurs with greater frequency in a given family than in the general population. These may have either a genetic or a non-genetic cause.

family history – The genetic relationships within a family combined with the medical history of individual family members. When represented in diagram form using standardized symbols and terminology, it is usually referred to as a **pedigree** or a **family tree.**

first-degree relative – A parent, sibling or child of an individual.

gene – The basic unit of heredity; every gene occupies a specific location on a chromosome. Each gene is made of chemicals called nucleotides which are arranged like beads on a string, in sets of three, each of which instructs the cell to use a specific amino acid as it manufactures the protein controlled by that gene. Most genes code for a specific protein or segment of protein, and it is the proteins that are responsible for specific characteristics or functions within a cell.

genetic counseling – A communication process that helps affected or at-risk individuals and families to understand the natural history, disease risks and mode of transmission of a genetic disorder, to facilitate informed consent for genetic testing when appropriate, to discuss options for risk management and family planning, and to provide or refer individuals for psychosocial support as needed.

genetic marker – An identifiable segment of DNA (e.g., Single Nucleotide Polymorphism [SNP], Restriction Fragment Length Polymorphism [RFLP], Variable Number of Tandem Repeats [VNTR], microsatellite) with enough variation between individuals that its inheritance and co-inheritance with alleles of a given gene can be traced; used in linkage analysis.

genetic predisposition – Increased likelihood or chance of developing a particular disease due to the presence of one or more gene mutations and/or a family history that indicates an increased risk of the disease. Also called **genetic susceptibility**.

genetic screening – Laboratory testing of a specific gene for disease-related changes or mutations; it is designed to identify specific individuals in a given population who are at higher risk of having or developing a particular disorder, as a result of carrying an altered gene for that disorder.

germline – Body tissues that carry genetic information which can be passed from parent to child, that is, eggs and sperm.

kindred – An extended family.

linkage – The tendency for genes or segments of DNA that are located very close to one another along a chromosome to be inherited together.

linkage analysis – A gene hunting technique that traces patterns of disease in high-risk families by identifying genetic markers of known chromosomal location that are inherited along with the trait or disease of interest. In contrast to the candidate gene approach (see above), linkage analysis does not require knowing ahead of time which specific genes might be important.

mode of inheritance – The manner in which a genetic trait or disorder is passed from one generation to the next. Autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive, multifactorial, and mitochondrial inheritance are examples. Each mode of inheritance results in a characteristic pattern of affected and unaffected family members.

mutation – A change in the usual DNA sequence within a particular gene. Mutations can be harmful (that is, they may increase the risk of disease), beneficial (they may protect against developing disease), or neutral (they have no effect one way or the other on disease risk).

non-seminoma – One of two main tissue subtypes of testicular cancer. Non-seminoma cell types include: embryonal carcinoma, teratoma, yolk sac carcinoma, choriocarcinoma and various combinations of these cell types. For non-seminoma cancer, teratoma presents the lowest the risk of spread and choriocarcinoma presents the highest risk of spread, with the other cell types being intermediate.

phenotype – The observable physical or laboratory characteristics in an individual that result from the expression of a gene or set of genes; the clinical presentation of an individual with a particular genetic background. In FTC, the phenotype of greatest interest is testicular cancer.

predisposing (disease-related) mutation – A germline mutation that increases an individual's susceptibility or predisposition to a certain disease or disorder. When such a mutation is inherited, development of the illness is more likely, but not 100% certain. Also called a **susceptibility gene**.

presymptomatic testing – Genetic analysis of an individual who is at risk of a specific genetic disorder, but shows no current symptoms.

risk assessment – The quantitative or qualitative assessment of an individual's risk of carrying a certain gene mutation, or developing a particular disorder, or of having a child with a certain disorder; this is sometimes done by using mathematical or statistical models including such factors as personal health history, family medical history and ethnic background.

second-degree relative – An aunt, uncle, grandparent, grandchild, niece, nephew, or half-sibling of an individual.

seminoma – One of two main tissue subtypes of testicular cancer. It has a distinctive appearance under the microscope, and is of importance clinically because this form of testicular cancer is much more effectively treated with radiation therapy.

unaffected – An individual who does not have the condition or disease occurring in his or her family.

For definitions of genetic terms that do not appear on this list, please refer to the online glossary of terms provided for patients by the NCI:

www.cancer.gov/cancertopics/genetics-terms-alphalist

Medical Articles

The following published articles give more detail on the studies described in this newsletter:

Page 2
Genome-wide linkage screen for testicular germ cell tumour susceptibility loci. *Human Molecular Genetics,* 2006, Volume 15, pages 443-451

Page 3
The Y deletion gr/gr and susceptibility to testicular germ cell tumor. *American Journal of Human Genetics*, 2005, Volume 77, pages 1034-1043

Page 3
Familial testicular cancer (FTC): interest in genetic testing among high-risk family members. *Genetics in Medicine*, 2006, Volume 8, page 760-770

Page 4
Possible new syndrome with pituitary adenoma, colonic polyposis, lipomatosis, lentigines and renal carcinoma in association with familial testicular germ cell malignancy: a case report. *BMC J Medical Case Reports,* 2007; 1:9 (**www.jmedicalcasereports.com/content/1/1/9**)

Page 7
High-dose chemotherapy plus stem-cell rescue may cure some patients with recurrent cancer after platinum therapy. *New England Journal of Medicine,* 2007; Volume 357, pages 340-348

Want to Learn More?

If you would like more information on anything you have read in this newsletter, or on any aspect of the Familial Testicular Cancer Study, please contact Claudia Soho at (301) 881-3847 or toll-free at 1-800-518-8474, or by email at claudiasoho@westat.com

NIH Publication No. 07-6268
August 2007