Clinical Genetics Branch (CGB) • National Cancer Institute

Family Research Matters

A Newsletter for Family Members of the NCI Familial Breast-Ovarian Cancer Studies Registry

Fall 2003

New Information on Ways to Reduce the Risk of Breast and Ovarian Cancer

Women with *BRCA1* or *2* mutations face high risks of breast and ovarian cancer, and effective ways to reduce these risks are needed. In the last issue of *Family Research Matters* (Winter 2000/2001), we provided updates on research looking at preventive mastectomy, risk-reducing (also sometimes called 'prophylactic') salpingo-oophorectomy (removal of the ovaries and fallopian tubes), and the use of oral contraceptives (birth control pills) to protect against these cancers. Since then, new research has clarified even further the use of these approaches, and explored other ways to decrease cancer risks in women who carry mutations.

Surgery: Removal of Ovaries and Fallopian Tubes Decreases Cancer Risk

Surgical interventions, including risk-reducing salpingo-oophorectomy (RRSO), have been the mainstay of cancer prevention options offered to women with *BRCA1/2* mutations, but studies on the value of these procedures have been sparse. Now, two studies have provided new evidence that RRSO may reduce the risk of both breast and ovarian cancer, and another study suggests that simply tying off the fallopian tubes ("tubal ligation") may provide a protective effect as well. The first study found that women who carried a *BRCA1* or *2* mutation, and underwent RRSO, had a 95% decreased risk of ovarian cancer and a 50% decreased risk of breast cancer. A second study found very similar results – a decrease in risk of 85% for ovarian cancer and 68% for breast cancer. In both of these studies, there were rare women who developed an illness resembling ovarian cancer called "primary peritoneal carcinomatosis (PPC)," despite removal of their ovaries. A third study suggested that women with *BRCA1* mutations who had undergone tubal ligation were

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Nina and Judy's Story: An Ovarian Cancer Family's Twenty-Year Relationship with the NCI

We are "Nina" and "Judy," two sisters who have reached ages that we thought we'd never see. We hope that sharing our experiences as participants in the NCI Hereditary Breast and Ovarian Cancer study will encourage others to participate as well.

When we were younger, we thought our family was uniquely singled out by ovarian cancer — some sort of cosmic joke or curse that marked us as defective: we had lost both our maternal grandmother and mother to the disease. By the time our family was put in touch with the National Cancer Institute (NCI) in the early 1980s, we were in our 30s and our mother's two sisters had both developed ovarian cancer. Our aunts pleaded with us, as they were dying, to do everything that we could to find out why so many women in our family were developing ovarian cancer, and to take whatever preventive measures that best-informed medical professionals might advise, to avoid

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60% less likely to develop ovarian cancer. These studies support the belief that RRSO and tubal ligation markedly decrease the risk of ovarian cancer, and that RRSO also lowers the risk of breast cancer.

Tamoxifen: Evidence of Benefit in Some Women

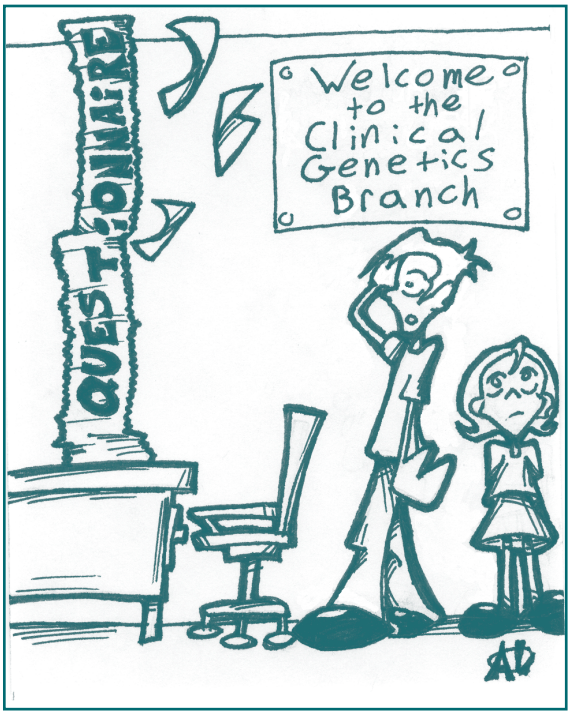
Researchers are also looking at non-surgical ways to reduce the risk of breast cancer. In 1998, a study found that tamoxifen, a drug used to treat breast cancer, also reduced the risk of breast cancer in healthy women. Two recent studies explored how tamoxifen may affect breast cancer risk in women with *BRCA1/2* mutations.

The first study analyzed women who carried either a *BRCA1* or *BRCA2* mutation and who had already been diagnosed with breast cancer. Women who took tamoxifen were less likely to develop a second cancer in the opposite breast than women who did not take this medication. This protective effect appeared to be stronger in women with *BRCA1* than in women with *BRCA2* mutations (60% versus 30%). In a separate and much smaller study, researchers observed the opposite effect: tamoxifen reduced breast cancer by 60% in women with *BRCA2* mutations, but did not appear to have an effect on women with *BRCA1* mutations. At the present time, it is still uncertain as to whether tamoxifen can be counted on to reduce breast cancer risk among *BRCA1/2* mutation carriers. This is a complicated decision that needs to be discussed with your physician.

Oral Contraceptives: A Balance of Risk and Benefit

Oral contraceptive pills (OCPs) represent a balance of risk and benefit among women who carry BRCA mutations. It has long been known that OCPs reduce the risk of ovarian cancer by as much as 50% among women in the general population. In 1998, research suggested that OCPs could decrease the risk of ovarian cancer by a similar amount in women who carried BRCA mutations. However, a second study found no evidence of a protective effect among carriers. These contradictory findings leave us uncertain about the effectiveness of OCPs in the prevention of ovarian cancer among *BRCA1/2* mutation carriers.

Data from the general population suggesting that OCPs may cause a small increase in breast cancer risk among young, long-term users adds to the difficulties in deciding whether to use OCPs to reduce the risk of hereditary ovarian cancer. However, there is little information on the effect of OCPs on breast cancer development in high-risk women. A recent study examined this question and found no evidence of harm among women who carried *BRCA2* mutations. However, among women with *BRCA1* mutations, there was a modest (20%) increased risk of breast cancer. This risk seemed greatest among women who had either used OCPs for at least five years, before the age of 30, or before the year 1975. This is the first evidence to support the concern that the potential benefits related to OCP use to reduce the risk of ovarian cancer may need to be weighed against a possible increase in the risk of breast cancer.



Where to Go from Here?

Reducing the risk of breast and ovarian cancer for women who carry BRCA mutations remains a critical goal. While mounting evidence suggests that surgery may be the most effective means so far to reduce this risk, there is still a need to study other approaches that either improve on surgery, provide an option for women who cannot or do not wish to have surgery, or offer a less invasive option. Tamoxifen shows promise in reducing the breast cancer risk among women in the general population, but more studies are needed to determine if this same benefit is seen in women with BRCA mutations. [*See Exemestane Trial story for further chemoprevention options.*] Similarly, the information related to OCP use in mutation carriers is contradictory. The possible increase in breast cancer risk associated with OCP use in mutation carriers sounds a further note of caution. In the meantime, if you carry a BRCA mutation, you should discuss your cancer prevention options with your health care provider. These are complicated, difficult decisions that must be made on an individual basis. We are working hard to clear up the confusion in this important area, so that these decisions will be easier for women and their physicians.

CGB Opens GOG 0199

The Clinical Genetics Branch is currently coordinating a national study in collaboration with the Gynecologic Oncology Group (GOG), known as GOG 0199, to examine the effectiveness of risk-reducing surgery (RRSO) and ovarian screening in women who are at increased genetic risk of developing ovarian cancer. One group of women will undergo RRSO, and the tissue removed at surgery will also be investigated to see whether a new way of examining the ovaries after they are removed provides better information about cancer-related tissue changes. A second group of subjects will be women who choose not to have preventive surgery. These women will be followed closely to see if screening with multiple CA-125 blood tests over time can detect ovarian or tubal cancers in their early stages. Members of CGB's HBOC families are invited to enroll in this study here at NCI, or through a GOG center nearer to their homes. [See the following Web site for more information about this study: **http://dceg.nci.nih.gov/clinical-activeprotocols.html.**

CGB Finds Evidence of Prostate Cancer Excess in Hereditary Breast/ Ovarian Cancer Families

In our first newsletter, we reported that Dr. Ruthann Giusti was conducting a study to evaluate whether men with BRCA1 or BRCA2 mutations might be at increased risk of prostate cancer. Several prior studies had suggested that this might be true, but other scientific reports had failed to find this association, leaving considerable uncertainty regarding whether prostate cancer really is one of the cancers that is part of the HBOC syndrome.

Dr. Giusti studied nearly 1000 Ashkenazi Jewish men diagnosed in Israel with prostate cancer. All these

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New NCI Breast Cancer Chemoprevention Study

Exciting new medications that may be useful as breast cancer prevention agents are being tested at the NCI. **Exemestane**, a drug which decreases the amount of circulating estrogen in the body, and **celecoxib**, a drug commonly used for arthritis pain, have both shown promise as medications that may be useful in reducing the risk of breast cancer. As a member of a family at increased genetic risk of breast cancer, you may be eligible to participate in this new study. Participants will undergo a bone density (DEXA) scan first, to make sure their bones are strong. Then, they will be assigned to receive either exemestane alone, or exemestane plus celecoxib, for five years. Both medications are pills, each taken one time per day. Participants will be evaluated at the NIH Clinical Center at the beginning of the study, and then once a year for five years, with mammograms, bone mineral density tests, blood tests, tissue tests and questionnaires. We are interested in studying the effect of these medicines on tissue markers of breast cancer risk, such as the density of breast tissue on mammograms, and hormone levels in the blood. Please contact Stephanie Steinbart, RN at 800-518-8474, for more information, if you might be interested in joining this study. This project is being run by our clinical colleagues and collaborators at the NCI Center for Cancer Research, Drs. JoAnne Zujewski and Jennifer Eng-Wong.

Nina and Judy's Story...

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becoming another family cancer statistic.

At Nina's request, a doctor friend suggested that we consider joining a familial cancer study being led by NCI researchers. We hoped that by enrolling in this project, we might gain some sense of control over our futures. At a minimum, we thought that we'd have access to better information about what leading medical researchers could tell us about this insidious killer.

Both of us discussed the study openly with immediate and extended family members. It undoubtedly helped that our family has a tradition of sharing information, emotions and advice relatively freely – solicited or not! Every family member in a direct line of descent from our maternal grandmother was encouraged to participate. Motivated by the belief that their involvement might help their own children make informed health care decisions, all agreed. In addition, all of us hoped our participation might benefit other families with similar cancer histories, for by then we knew our family was far from unique.

NCI doctors advised that women at risk wait until finished with childbearing, and then have preventive surgery to remove the ovaries. Even with our family history, this seemed drastic. After all, we weren't sick (that we knew of), and the thought of plunging into early menopause was uniformly unappealing. Who would volunteer to subject themselves to hot flashes, night sweats, insomnia, and ricocheting emotions? After months of discussions, reading research papers, and consulting with doctors, family, and friends, Nina made the decision to have prophylactic surgery. Several years later, in September 1984, Judy made the same decision. Ovarian tissues samples sent to NCI showed no cancer in either of

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us. And then we waited for medical science to catch up.

And medical science has made progress. In the mid-1990s, the BRCA1 and BRCA2 genes were identified, and we later learned that at least one of our family members tested positive for a specific BRCA1 mutation. Family members were invited to NIH for genetic counseling, and then, if they wished, for individual testing to determine if they carried the mutation that would greatly increase their chances of developing breast or ovarian cancer.

We sisters had become fatalists, assuming that we were both mutation carriers living under what we were sure was a premature death sentence. We decided to go to NIH together along with our spouses, who had lived this with us and been so supportive. NCI paid for all of us to travel to Bethesda for counseling and testing. (The Clinical Center even has a travel agency in the building that can make your travel arrangements.)

From the moment we arrived at the NIH center, in the spring of 2002, we were treated not just as case histories, but as an integral part of the research team. The entire day was devoted to us. After an explanation of human subject participation and informed consent, a genetic counselor provided general information on breast and ovarian cancers, and what had been learned about inherited cancers. Questionnaires covered not only our physical status but any psychological, emotional, and familial issues we might have. There was never any pressure, overt or implied, to undergo genetic testing. The study team even explained issues of privacy and the implications of sharing information with our primary healthcare providers or our health insurers. The decision to do so was left entirely to us.

We had very thorough breast and pelvic exams— and not the usual cursory 5-minute annuals we women are so often subjected to by our regular physicians! They took complete medical histories, and shared current thinking on topics such as cancer screening and hormone replacement therapy. There were many opportunities to ask questions.

We both agreed to undergo genetic testing, convinced that at least one of us would test positive for the mutation. Blood was (painlessly) drawn in the Clinical Center's laboratory that same afternoon. We were each asked how we would feel if we were the one to be mutation positive and the other negative. Amazingly, we gave the same answer: each would be happy for the other!

The team asked whether we wanted to have the test results disclosed to us separately or together, and if we had discussed how and with whom we would share the results. We were both impressed with the sensitivity, thoughtfulness and care with which we were treated. The team often shared their own experiences and perspectives with us, and the day was filled with camaraderie and laughter.

When the results were ready for disclosure, we again traveled to NCI with our spouses. Results were disclosed individually, and we were also offered the opportunity to discuss them together. As anticipated, one of us tested mutation-positive. Our reactions were a mix of predictable and unexpected emotions. Judy, mutation-positive, was as concerned about how Nina, the non-carrier, would take the news, as the reverse. Judy felt comforted knowing that she had done what was medically prudent to increase her chances of survival, and felt that she would be better able to help her children (who she now knew were at risk of inheriting the family's BRCA1 mutation) make informed decisions about their own medical care. Nina was unexpectedly faced with the prospect of a normal lifespan, and took comfort in the knowledge that she helped Judy make a life-extending decision to have elective surgery.

Even after our NCI visit, the study team continued their support with follow-up calls to see how we were doing. They offered reassurance that they were available to help address any further concerns we or our children might have. As a result of the disclosure, Judy has enrolled in the NCI Breast Cancer Imaging Study.

We both strongly believe that our 20 year experience as NIH research subjects has enabled us to receive the best and most up-to-date medical care, and we hope that both men and women in at-risk families who are faced with making these decisions will take the opportunity to consult with the NCI study staff. Because we feel so positive about our experience at NCI, we have agreed to make ourselves available to discuss any aspect of it with those facing the same issues. If you wish to talk to either of us, please contact Nancy Weissman at (301) 594-7642, or weissman@mail.nih.gov.

["Nina" and "Judy" are pseudonyms used to protect the privacy of the two women who so kindly agreed to share their thoughts with us.]

Behavioral and Psychosocial Studies Play Key Roles in CGB Research

You may be interested to learn that CGB's research program also focuses on understanding the psychological, behavioral and social impact of an increased genetic risk of cancer on individuals who are both mutation carriers and non-carriers, and their family members. We hope that the information we obtain in these studies will help us to improve the quality of life for persons who must cope with the consequences of their strong family history of cancer.

In order to conduct the highest quality studies of this kind, CGB has assembled a team of physicians, nurses, genetic counselors, social workers, and research assistants who have a special interest in the behavioral and psychological aspects of familial cancer. Behavioral and social scientists from NCI and other academic institutions are partnering with us to bring their special experience and expertise to our studies.

The Breast Imaging Study, in which many of you are now participating (Protocol 01-C-0009, see **http://dceg.nci.nih.gov/clinical-activeprotocols.html**) is the first CGB project to include emotional, behavioral and social research. Those of you who completed questionnaires for the Breast Imaging study know that we are studying such issues as:

- your cancer screening practices,
- how you perceive and understand your risks of developing cancer,
- how you make decisions about whether and with whom you will share your genetic information,
- your use of complementary/alternative health care practices,
- what you expected from participating in the study, and
- what it was like to undergo the various study-related breast imaging procedures.

In addition, participants have the opportunity to speak with Nancy Weissman, our Licensed Clinical Social Worker, about how living at high risk of cancer has affected their lives. June Peters, our Genetic Counselor, also meets with participants to test a new method of mapping an individual's social support systems *(see box on the CEGRM pilot study)*.

These studies are in their early stages; we will update you when we have results to share. We are grateful to each of you for permitting us to ask about these very personal and sometimes difficult issues. We hope that this information will help us to understand the needs of families like yours, and provide suggestions to assist your health care providers in meeting these needs.

Pilot Study of CEGRM Tool Successfully Completed

During the past year, twenty women who were participating in our Breast Imaging Study also took part in a pilot test of the Colored Eco-Genetic Relationship Map (abbreviated as CEGRM; pronounced "See-Gram"). This new tool, developed by our lead genetic counselor, June Peters, and her sociology colleague Dr. Regina Kenen, provides a quick and easy way to collect and display information about women's social interactions related to exchanges of health information and emotional support from family, friends, colleagues and other acquaintances. To transform their genetic pedigree into a CEGRM, participants apply colored, adhesive symbols, each representing a different type of important social interaction.

The pilot study has been completed, and the preliminary results were presented in March 2003 at the annual meeting of the American Society of Preventive Oncology, in Philadelphia, PA. A manuscript summarizing the results is being written, and will be submitted for publication in the medical literature.

We found that the process of constructing the CEGRM was easily learned, comfortable, fun, and informative. Most participants felt free, under conditions of confidentiality, to share stories about their friends and families that facilitated the counselor's understanding of the ways in which close relationships helped them to cope with their family history of cancer. The process of doing the CEGRM also provided insights to some participants themselves about how they find support in their relationships.

Further studies of the CEGRM are being planned to help refine, customize, and extend its use in persons who have an increased genetic risk of cancer. As is the case with all our studies, this project could not have been completed without the participation of volunteers from families like yours. **We send out a special thanks to the women who made this study possible.**

Variations in Breast Cancer Risk: "Why Do Some People with BRCA1/2 Mutations Get Cancer While Others with the Same Mutation Don't?"

Women who carry a mutation in the *BRCA1* or *BRCA2* genes have a much greater chance of developing breast and ovarian cancer than other women. The exact risk with the same mutation varies a lot from woman to woman. Women in families with many cases of breast and ovarian cancer, like yours, may have an 80 or 90% chance of developing one of these cancers by age 70, but when averaged over all mutation carriers, including the many who don't have a strong family history, the risk is around 50%. In other words, when we consider **all** carriers of *BRCA1* or *BRCA2* mutations, the chance of developing breast cancer by age 70 is roughly 50:50, or one out of every two mutation carriers.

However, even in families with multiple cases of breast and ovarian cancer, it appears that not all women who are carriers of the family mutation (and who have not been diagnosed with cancer) have a uniformly high risk of cancer. In any given family, some mutation carriers may live to a ripe old age and never get cancer, while other women get breast cancer, and still others get ovarian cancer. Yet all of the at-risk women in any one family carry exactly the same mutation! What accounts for this variation in the effects of *BRCA1/2* mutations?

Observations like this make us think that there may be "protective" and "triggering" factors that influence an individual *BRCA1/2* mutation carrier's risk of cancer. These additional factors may tip the balance one way or the other, and influence what the final effect of the gene mutation will be. We call these factors "modifiers," and they may be environmental exposures (like a hormonal medication), reproductive variations (such as whether or not you have had a baby), or even other genes. At present, the modifiers that influence what happens to persons with *BRCA1/2* mutations are unknown, but this is a subject of active research, both within CGB and by investigators around the world. If we could identify these triggering or protective factors, we could provide more precise estimates of cancer risk to individual mutation carriers, and we would better understand exactly how cancers develop or don't develop. This would allow us to take better care of folks who have a *BRCA1/2* mutation.

Clinical Genetics Branch investigators are searching for other genes which might influence how a *BRCA1/2* mutation affects a carrier's health. We do this by analyzing the DNA samples that you have provided to us as part of your participation in our studies, including those *from individuals who do **not** carry the mutation* (as a comparison group), These samples are essential to our laboratory work aimed at finding genetic modifiers. So even though we may not have seen you in a long time, you continue to make important contributions to our ongoing research. And, as is always the case, if we identify information that we can use to provide you with better medical advice, we will notify you of our findings and give you an opportunity to learn how that information could be applied to your care.

Herbal Remedies – "What's in That Bottle?"

In 1997 Americans spent $5.1 billion on herbal "medicine." Yet, because most herbal products in the United States are considered **dietary supplements,** they are *not* regulated as medicines, and are *not* required to meet Federal drug quality standards. The manufacturer of an herbal preparation is responsible for the truthfulness of claims made on the label, and must be able to support those claims with evidence, but the Dietary Supplement and Health Education Act (which sets the standard for herbal medicines) neither provides a standard for the evidence needed, nor does it require submission of that evidence to the FDA. In 2001, poison-control centers around the country received nearly 20,000 reports related to dietary supplements. Since 1993, 7,000 bad reactions to dietary supplements have been reported to the FDA. Many of these are related to:

- Mis-labeling or adulteration of the product
- Dietary supplements that interfere with the action of approved drugs used to treat cancer or HIV-AIDS
- Dietary supplements that contain much larger amounts of the herb than is listed on the label, doses which may be harmful
- Dietary supplements that contain less ingredients than listed on the label
- The wrong ingredient is in the bottle
- The product is contaminated with other drugs, bacteria, pesticides, glass, lead or other foreign material
- Improper packaging

Recently, the FDA proposed a rule to establish new standards or "current good manufacturing practices," which is intended to reduce the risks associated with adulterated or misbranded dietary supplements. This rule has not yet taken effect.

Clearly, the American public uses herbal medicines widely, and some do produce beneficial effects. However,

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others do not, and some may cause serious harm or illness. The American consumer has the right to expect that what is claimed to be in the bottle is what is actually in the bottle, and that the product really does what the manufacturer claims it will do. At the present time, that is often not the case. We therefore urge caution in the use of herbal preparations. Just because a product is called "natural," or an "herb," does not insure that it is safe. Users of such products take them because they expect these herbs to have a beneficial effect. In order for herbal products to have a beneficial effect, they must be biologically active, or be able to affect how cells function. If they are biologically active, there is potential for harmful as well as beneficial effects. Let the buyer beware! Ask your health care provider if the herbal preparations that you are taking are safe.

CGB Finds Evidence ...

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men were tested for the presence of the three BRCA mutations (the so-called "founder mutations") which account for nearly 90% of all BRCA mutations in persons of Ashkenazi Jewish heritage. We found that Israeli Ashkenazi men with prostate cancer were twice as likely to have one of these mutations than were men in the comparison groups. Interestingly, although earlier-than-usual age at cancer diagnosis is a feature of many hereditary cancers, the mutation-positive men in our study were not younger than the mutation-negative cases.

We concluded that the risk of prostate cancer is modestly elevated among Ashkenazi Jewish men with a BRCA mutation, and that these risks appeared to be somewhat lower than those which had been reported previously in non-Jewish populations. This information supports the conclusion that men with BRCA mutations do have a somewhat higher risk of prostate cancer than men without such mutations. Formal prostate cancer screening recommendations for men with BRCA mutations have not yet been developed. Men who have a mutation in BRCA1 or BRCA2 should discuss the risks and benefits of various screening options with their health care provider. This report will be published soon in the Journal of Medical Genetics.

Staff Changes within CGB

We are very sorry to announce the departure from NCI of Dr. Ruthann Giusti, who has been leading our Breast Imaging Study. Ruthann has accepted a position in the Biologics Program at the Food and Drug Administration (FDA). She has been a key member of the CGB staff since its inception in September 1999, and has made great contributions to helping us to launch this new research program. Fortunately, Ruthann will continue to participate in the Breast Imaging Study as an Adjunct Investigator, by attending research clinics on a regular basis.

We are extremely fortunate to have found a remarkably capable clinical investigator to take over as the Principal Investigator for the Breast Imaging Study. **Dr. Sheila Prindiville** has degrees in both medicine and public health. She is board-certified in Medical Oncology, and has special fellowship training in Cancer Prevention. She has come to NCI from the University of Colorado, where she conducted research in cancer epidemiology and prevention. Sheila is based in the NCI Genetics Branch, at the National Naval Medical Center, and has joined CGB as an Adjunct Investigator to run the Breast Imaging Study. We are very pleased to welcome her to the CGB team.

Dr. **Joan Kramer** is another key member of our hereditary breast/ovarian cancer research group. Joan did her specialty training at the University of Texas in San Antonio, is board-certified in medical oncology and hematology, and is now doing post-doctoral research with us in clinical cancer genetics. She is the lead investigator on our Familial Testicular Cancer Study, and also provides critical support to the HBOC project as well.

Finally, **Dr. Michael Martin** has joined CGB as our newest post-doctoral fellow. Michael is in the United States under the auspices of an exchange program between the U.S. and Ireland. He, too, is board-certified in Medical Oncology, and he also has a PhD in genetics. He will spend two years with us, and a significant portion of his time will be devoted to the Hereditary Breast/Ovarian Cancer Project. Michael is a valuable addition to the CGB team, and we extend a hearty welcome to him as well.

Resources and Information

The **Clinical Genetics Branch** offers information about our clinical research studies on the Web at: **http://dceg.nci.nih.gov/clinical-activeprotocols.html** For example, if you click on "01-C-0009 - Breast Imaging Studies of Women at High Genetic Risk of Cancer" you will be able to read the main protocol for that study. The site also links you to the other interesting information about our Branch, and about other branches in the Division of Cancer Epidemiology and Genetics, of which we are a part.

The **American Society of Clinical Oncologists** (**ASCO**) now offers patient information to the public on its new Web site "People Living with Cancer." The site can be located at: **http://www.plwc.org.** ASCO is composed of physicians and other professionals involved in the treatment of people with cancer. Its site offers information on breast, ovarian and 50 other types of cancer. It also provides information on patient support organizations, clinical trials, and a medical dictionary.

F.O.R.C.E. or *Facing Our Risk of Cancer Empowered* is a nonprofit organization for women at high risk of cancer due to their genetic status or family history, and for men living in families where a BRCA mutation may be present. Its Web site at: **http://www.facingourrisk.org** includes a comprehensive guide to financial and other important resources, message boards, and chat rooms.

The **National Cancer Institute** (**NCI**) provides cancer information about different types of cancer, to the public at no charge. Call **1-800-4-CANCER** to speak to an information specialist about any cancer related question, or to order such free booklets as ***What You Need to Know About Ovarian Cancer*** and ***Understanding Breast Cancer***. You can also view these booklets online and get other useful information on cancer, resources and clinical trials at NCI's educational Web site: **http://cancer.gov**

The mission of the **Vital Options® International TeleSupport®** Cancer Network is to use modern communications technology to reach people dealing with cancer. Vital Options holds a weekly syndicated call-in cancer radio talk show called "The Group Room®," which provides a forum for patients, long-term survivors, family members, physicians, and therapists to discuss cancer issues. Listeners can participate in the show during its broadcast every Sunday from 4PM to 6PM (Eastern Time) by calling the toll-free telephone number, 1-800-477-7666. A live Web simulcast of "The Group Room" can be heard by logging onto the Vital Options Web site at: **http://vitaloptions.org/**.

Glossary of Terms

BRCA1 and BRCA2 (**BR**east **CA**ncer genes numbers 1 and 2) are two normal genes involved in cell growth. When altered or mutated, they increase the risk of developing breast, ovarian and perhaps other cancers.

Chemoprevention: The use of drugs, medicines, vitamins, or other agents to try to reduce the risk of, or delay the development of, cancer.

Celecoxib: A medicine that reduces pain. Celecoxib belongs to the family of drugs called non-steroidal anti-inflammatory agents. It is being studied as a medication which might reduce the risk of cancer.

Exemestane: An anticancer drug used to decrease estrogen production and to suppress the growth of estrogen-dependent tumors.

Genetic Modifier: This term is applied to a gene which controls, regulates, alters or somehow modifies the effect of another gene, or a person's response to an environmental exposure. Modifier genes make proteins which influence how other genes function or which influence how cells respond to a specific exposure.

Mutations are changes or alterations in genes that prevent the gene from working properly. Some mutations, called "germline," are inherited from parents and may be transmitted from one generation to the next, while others, called "somatic," occur only in one organ, and are not passed on to children.

Oral Contraceptive Pills (**OCP**): Also known commonly as "birth control pills." These medications contain various combinations of the female hormones estrogen and progesterone, and are used primarily to prevent pregnancy.

Primary Peritoneal Carcinomatosis (**PPC**) is a cancer that looks and behaves like ovarian cancer in women whose ovaries seem to be normal. It is thought to arise from the lining of the abdominal cavity, where the ovaries, uterus, kidneys, liver and other organs are located.

Prophylactic Mastectomy (**PM**) is the removal of one or both breasts prior to any signs of cancer, for the purpose of preventing breast cancer.

Risk-Reducing Salpingo-oophorectomy (**RRSO**) is the removal of both ovaries and the fallopian tubes, for the purpose of preventing ovarian and fallopian tube cancer.

Tamoxifen: An anticancer medicine that belongs to the family of drugs called anti-estrogens. Tamoxifen blocks the effects of the hormone estrogen in the body. It is used to prevent or delay the return of breast cancer or to control its spread. It has been shown to lower the risk of breast cancer among women at increased breast cancer risk.