

- ▣ cancer risk and quality of life) for high-risk women who elect surgery, and the utility of a novel ovarian cancer screening model ("ROCA"), which is based on longitudinal changes in CA-125.
- ▣ The screening portion of this project is already open to patient accrual through the CGN. The surgery arm of this trial is expected to open this summer, through GOG institutions nationwide.
- ▣ To be eligible, women must demonstrate a prior probability of carrying a BRCA1/2 mutation that is 20 percent or greater. We anticipate enrolling 1000 women in the surgery arm of the study, and 2400 women in the pilot study of ovarian screening. Women will be followed for 5 years.
- ▣ PI: **Dr. Mark H. Greene**

▣ **Clinical Genetics Branch Study of Familial Cancer of the Urinary Bladder**

Using the research strategy outlined under Familial Testicular Cancer, we are now in the planning stages of developing a similar high-risk family study (in collaboration with NCI's Urologic Oncology Branch) which will target cancer of the urinary bladder.

This will likely include a search for a clinical phenotype, including the risk of non-urinary cancers, aggressive cystoscopic screening for occult neoplastic and pre-neoplastic changes, and collection of DNA for linkage analysis and mapping of candidate major susceptibility genes.

We are actively seeking referral of new families having two or more affected members with cancer of the bladder, ureter or renal pelvis, in anticipation of the opening of this study (early 2003).

PI: **Dr. Ruthann Giusti**

CONTACT INFORMATION

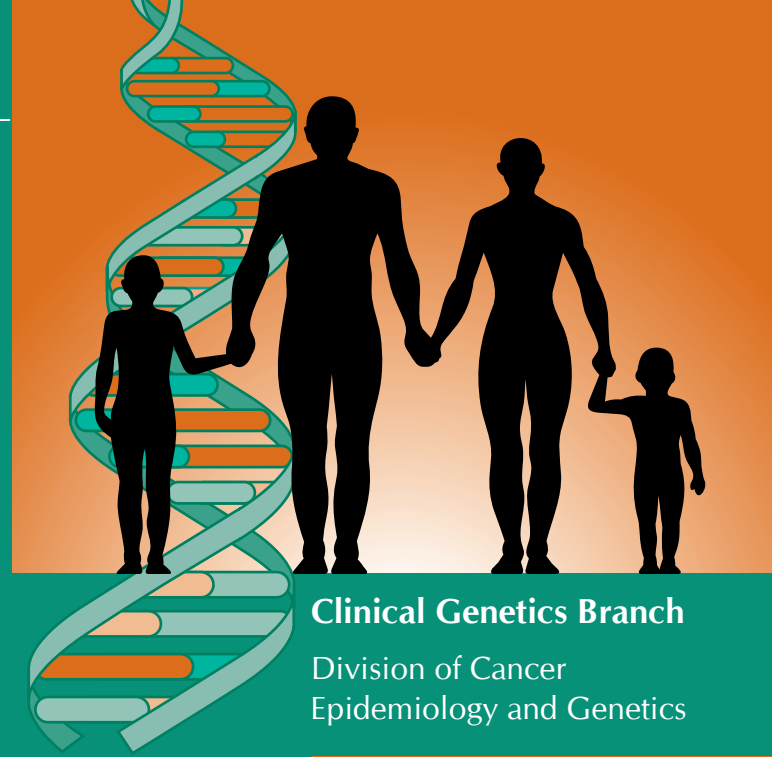
For further information regarding these projects, or other familial cancer susceptibility syndromes, visit the Clinical Genetics Branch Web site, at:

<http://dceg.cancer.gov/hgp/cgb/index.html>

To refer a new family, or to discuss one of these projects in greater detail:

Call our Cancer Genetics Referral Nurse, Stephanie Steinbart, at:
1-800-518-8474

Call one of our investigators (Mark H. Greene, MD; Blanche P. Alter, MD; Ruthann Giusti, MD; Joan L. Kramer, MD) at:
1-301-594-7642



Clinical Genetics Branch
Division of Cancer
Epidemiology and Genetics

**Family Studies
Research
Portfolio**



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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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"Saving Lives by Conquering Cancer Through Research in Clinical Cancer Genetics"

The Clinical Genetics Branch, the newest component of NCI's intramural Human Genetics Program, has as its mandate improving the quality of life and survival of persons at increased genetic risk of cancer. Our research paradigm, based upon the principles of epidemiology, employs a multidisciplinary approach to translating recent developments in the molecular biology of cancer susceptibility into evidence-based, patient management strategies.

One major component of this research program is the study of persons from cancer-prone families. Families eligible for one of our protocols are invited to travel to the NIH Clinical Center, at the Government's expense, where they undergo an etiologically-focused clinical evaluation, genetic risk assessment, imaging studies, psychosocial/behavioral evaluation, collection of biological specimens, genetic counseling and mutation testing (where appropriate), and are given recommendations regarding cancer surveillance and risk reduction.

□

□ CURRENT STUDIES

Pilot Study of Breast Imaging in Premenopausal Women at High Genetic Risk of Breast Cancer

This study is designed to assess the roles of mammography, MRI and PET imaging in premenopausal women at high genetic risk of breast cancer. Study participants also undergo breast duct lavage, for standard cytology assessment and research molecular studies on the duct epithelium cells so obtained. Participants undergo a baseline examination, and annual follow-up examinations for four years. Evaluation also includes transvaginal ultrasound and CA125 testing for women with intact ovaries.

PI: **Dr. Ruthann Giusti**

□ **Etiologic Investigation of Cancer Susceptibility in Inherited Bone Marrow Failure Syndromes**

Members of families affected by one of a series of inherited bone marrow failure syndromes (including Fanconi's anemia, dyskeratosis congenita, Diamond-Blackfan anemia, Shwachman-Diamond syndrome, severe congenital neutropenia, thrombocytopenia absent radii syndrome, etc.) are eligible for this protocol. It is well-known that these disorders are characterized by a predisposition to aplastic anemia and acute leukemia in childhood.

It is less well appreciated that they also convey a high risk of developing selected solid tumors, particularly of the upper aerodigestive and genital tracts.

Study participants provide personal medical, family history and risk factor information, contribute DNA for gene-finding studies, and are eligible to visit the NIH for a detailed evaluation of the type described above.

□ Specific studies are tailored to the individual syndromes. Patients will have access to the full

- range of medical specialists required for comprehensive assessment of these
- complex, multi-system disorders, including mutation testing for those disorders in which a causative gene is known. See our study-specific Web site at:

<http://marrowfailure.cancer.gov/>

□ PI: **Dr. Blanche Alter**

□ **Multidisciplinary Study of Familial Testicular Cancer**

With the recent mapping of an hereditary testicular cancer susceptibility gene to chromosome Xq27, there has been a renewal of interest in this relatively uncommon familial cancer syndrome. The Clinical Genetics Branch has joined forces with the International Testicular Cancer Linkage Consortium to intensify susceptibility gene mapping and cloning efforts. In addition, we will soon open (Summer 2002) an interdisciplinary study at the NIH Clinical Center aimed at more accurately defining the clinical phenotype of familial testicular cancer, including a search for genitourinary anomalies and other cancers which might be part of this syndrome, and an evaluation of the role of testicular intraepithelial neoplasia ("TIN") in this setting. Refer to:

<http://familial-testicular-cancer.cancer.gov/>

PI: **Dr. Mark H. Greene**

□ **National Prospective Cohort Study of Prophylactic Salpingo-oophorectomy and Ovarian Screening in Women at Increased Genetic Risk of Ovarian Cancer**

In collaboration with the Gynecologic Oncology Group (GOG) and the Cancer Genetics Network (CGN), the Clinical Genetics Branch is launching a nationwide study designed to assess the natural history of the post-prophylactic salpingo-oophorectomy state (including prospective