Welcome to the 17th issue of the FA Courier. This is a summary of current requests for materials and clinical trials. Please click on the embedded links for complete information about each request or clinical trial, including eligibility and protocol descriptions. Please call us at 1-888-FANCONI if you need assistance.

For FA Patients and Families:

Etiologic Investigation of Cancer Susceptibility in Inherited Bone Marrow Failure Syndromes

This project will identify cancer-prone families with underlying Fanconi anemia prior to the appearance of cancer.

Principal Investigator: Blanche Alter, MD, MPH
Clinical Genetics Branch, National Cancer Institute, National Institutes of Health, Rockville, Md.
Contact: Lisa Leathwood, Research Nurse
Telephone: 800-518-8474 or 301-881-7593; Email: lisaleathwood@westat.com

Hypothesis:
This project will identify cancer-prone families with underlying Fanconi anemia (FA) prior to the appearance of cancer. The goal is to learn more about FA, in order to improve the quality of life for persons from affected families. Hypotheses: 1) A prospective cohort will provide new information regarding cancer risk. 2) Mutation in FA genes are relevant to cancer pathways in non-hereditary forms of cancers. 3) Patients with FA who develop cancer differ from patients with FA who do not develop cancer. 4) Carriers of FA mutations are at an increased risk of cancer. 5) A substudy will explore the experiences of healthy siblings of FA patients, in order to determine how we can help families manage FA.

Importance of project to FA patients:
FA patients have a remarkably high risk of leukemia and solid tumors. A large epidemiologic study will determine actual cancer risks, identify individually predictive features and define management. The prognostic significance of specific FA mutations and non-FA genes will be identified. The role of viruses in FA solid tumors will be examined. Features of the bone marrow that are associated with progression to leukemia will be defined. FA patients are at high risk of HPV-associated head and neck and gynecologic cancer.

Eligibility criteria:
1) Any patient with FA. Bone marrow failure is NOT required. 2) Patients with suspected FA despite negative chromosome breakage tests. 3) First-degree relatives: siblings (half or full), biologic parents, biologic grandparents and children. 4) Non-FA patients with tumors of the types seen in FA (head and neck, esophageal and gynecological), without the usual risk factors (e.g., age, smoking, drinking).

Material/Information needed:
Questionnaires: Family History Questionnaire (in-depth family medical history); Individual Information Questionnaire (in-depth personal medical history for the patients and their immediate family members); Follow-up Form (every 2 years). Bone marrow: 2-5 ml of marrow, marrow aspirate and biopsy slide. Tumor tissue: fresh, reports, slides, blocks. Blood, serum and plasma samples. Mouth washings for oral cavity cells. Skin biopsies for chromosome breakage or DNA (in some patients). Results of gynecologic exams (females). All participants contribute personal medical and risk factor information and often samples of blood (bone

continued on next page
Gene Function in Bone Marrow Cells from Patients with Fanconi Anemia and from Healthy Participants

Patients and healthy volunteers undergo bone marrow aspiration and/or peripheral blood sampling. Blood and bone marrow samples are tested in biological and molecular genetic assays. For more information, view the full text description of this study on ClinicalTrials.gov by clicking this link.

Principal Investigator: Grover C. Bagby, MD, OHSU Knight Cancer Institute, Portland, Ore.
Telephone: 503-273-5133; Email: trials@ohsu.edu
Alternate Contact: R. Keaney Rathbun; Telephone: 503-273-5133

Gene Transfer for Patients with Fanconi Anemia Complementation Group A (FANCA)

This is a Phase I study designed to develop gene transfer as a treatment for Fanconi anemia complementation group A patients. The objective of this study is to transfer a functional copy of the Fanconi anemia gene for complementation group A by lentiviral vector into bone marrow stem cells from Fanconi anemia patients and then re-infuse these cells with the ultimate goal of improving the patient blood counts. For more information, view the full text description of this study on ClinicalTrials.gov by clicking this link.

Principal Investigator: Pamela S. Becker, MD, PhD, University of Washington, Seattle, Wash.
Contact: Jennifer E. Adair, PhD, Clinical Research Associate (Kiem group), Fred Hutchinson Cancer Research Center, Seattle, Wash.; Telephone: 206-667-7110; Email: jadair@fhcrc.org

Laboratory Studies of Gene Transfer for Fanconi Anemia

In order to optimize the delivery of a normal FANCA or FANCC gene to abnormal cells, and to test its ability to correct the Fanconi anemia defect in the laboratory, researchers need a source of bone marrow and/or blood from patients with FANCA or FANCC.

Principal Investigator: Pamela S. Becker, MD, PhD, University of Washington, Seattle, Wash.
Telephone: 206-616-1589; Email: pbecker@u.washington.edu

Molecular Surveillance for Squamous Cell Carcinoma of the Upper Aerodigestive Tract

Development of a screening test for cancer of the mouth and throat (head and neck cancer): cancers of the mouth and throat may go undetected in their earliest and most treatable stages. A new test that analyzes the DNA from cells released when an individual gargles is being developed at Johns Hopkins.

Principal Investigator: Wayne Koch, MD, Johns Hopkins, Baltimore, Md.; Telephone: 410-955-4906
Alternate Contact: Zubair Khan, MD, MPH, Study Coordinator
Telephone: 410-955-3157; Email: zkhan@jhmi.edu
The International Fanconi Anemia Registry (IFAR)
The IFAR is investigating the genetics of FA, the various symptoms of FA, and the correlation between the two, otherwise known as the genotype-phenotype correlation. This should help define important regions within the FA genes that may shed light on their function in DNA repair, cell cycle control, and programmed cell death. These concepts are important to understand in detail the problems in Fanconi anemia, but also could help our understanding of cancer development in general.

Principal Investigators: Agata Smogorzewska, MD, PhD, The Rockefeller University, New York, N.Y. Farid Boulad, MD, Memorial Sloan-Kettering Cancer Center, New York, N.Y. Stella Davies, MBBS, PhD, MRCP, Cincinnati Children’s Hospital Medical Ctr, Cincinnati, Ohio Margaret L. MacMillan, MD, University of Minnesota, Minneapolis, Minn.

Co-Investigators: Arleen D. Auerbach, PhD, The Rockefeller University, New York, N.Y. David Kutler, MD, Weill Medical College of Cornell University, New York, N.Y. Bhuvanesh Singh, MD, Memorial Sloan-Kettering Cancer Center, New York, N.Y. John E. Wagner, Jr., MD, University of Minnesota, Minneapolis, Minn.

Contact: Agata Smogorzewska, MD, PhD or Erica Sanborn, MS, CGC The Rockefeller University, New York, N.Y. Telephone: 212-327-7850 (Dr. Smogorzewska) or 212-327-8613 (Erica Sanborn) Email: asmogorzewska@mail.rockefeller.edu or esanborn@rockefeller.edu Website: http://lab.rockefeller.edu/smogorzewska/ifar/

Funding sources: The Rockefeller University, NIH, Starr Foundation, Burroughs Wellcome Fund, Rita Allen Foundation

Accepting: All patients with Fanconi anemia or Fanconi-like symptoms

Hypothesis:
The Rockefeller University Hospital is home to the International Fanconi Anemia Registry (IFAR) which was established in 1982. The purpose of the Registry is to study a large number of patients exhibiting the full spectrum of diverse features of FA. Questions relating to diagnosis, natural history of the disease, prognosis, treatment and cancer incidence in FA are being addressed by the IFAR studies. In addition, through numerous collaborations, we are using the most current technologies available to try to identify the genetic changes (mutations) causing Fanconi anemia in each participating family, as well as identify new FA genes. Information regarding the relationship between the genetics and severity of presentation (called genotype-phenotype correlation) is being assessed, which may help to determine the normal roles of the FA genes, hopefully shedding light on their function in cell cycle control, programmed cell death and DNA repair. This may lead to improvement in prediction of outcome and affect decision-making regarding timing of therapy options.

Importance of project to FA patients:
We aim to more fully define the variable clinical features associated with FA, particularly the congenital malformations and malignancies, and to determine to what extent the clinical findings in FA patients and carrier family members correlates with the specific mutation/region of mutation, i.e. genotype. The recent identification of the genes responsible for more than 90% of the cases of FA make it possible to evaluate patients and family members by mutation group, comparing phenotype with genotype. We will conduct a thorough clinical and molecular genetic analysis with the objectives of learning about the extent, the causes and the optimal treatment for FA-associated medical problems. As part of the project, we are developing more rapid methods for mutation screening. Genetic information will be made available to patients’ physicians after they are confirmed in a clinical laboratory.

Eligibility criteria:
Any patient diagnosed as affected with FA (or FA-like symptoms), as well as parents and sometimes siblings.

Material/Information needed:
We need to receive a blood specimen from the patient and his/her parents to make cell lines. Mutation testing will be performed in a research laboratory. Further information about the IFAR study, including how to enroll, can be found at http://lab.rockefeller.edu/smogorzewska/ifar/families. If there are questions about enrollment or the study in general please contact the study coordinator, Erica Sanborn at 212-327-8613 or esanborn@rockefeller.edu.

Cost of participating:
There are no costs associated with participation in the IFAR.
Salivary Biomarkers in Oral Cancer
Researchers have identified biomarkers in the saliva to detect oral cancer. They hypothesize that, in the future, these oral cancer saliva biomarkers may be used to help detect early cases of oral cancer in FA patients. Dr. Wong is collecting saliva samples from FA patients with newly diagnosed oral cancer—after the biopsy and before medical treatment begins.

Principal Investigator: David Wong, DMD, DMSc, UCLA School of Dentistry, Los Angeles, Calif.
Contact: Teresa Kennedy, Fanconi Anemia Research Fund
Telephone: 541-687-4658 (toll-free in the US at 888-326-2664); Email: teresa@fanconi.org

Clinical Trial:
Pioglitazone
This trial is available at a number of sites throughout the U.S. and at a facility in Italy

Pioglitazone for Oral Premalignant Lesions
The goal of this clinical research study is to learn how Actos® (pioglitazone) may affect oral premalignant lesions (OPLs) and/or the risk of mouth cancer. The safety of this drug will also be studied. Neither you nor the study doctor will know if you are receiving the study drug or the placebo. However, if necessary for your safety, the study doctor will be able to determine which one you are receiving. For more information, view the full text description of this study on ClinicalTrials.gov by clicking this link.

Principal Investigators: Jay Boyle, MD, Memorial Sloan-Kettering Cancer Center, New York, N.Y.
Telephone: 212-639-7654; Email: boylej@mskcc.org
Frank Ondrey, MD, PhD, FACS, University of Minnesota, Minneapolis, Minn.
Telephone: 612-624-5900; Email: ondre002@umn.edu

Clinical Trial:
Viral therapy
Patients with AML/ALL/MDS are not eligible to participate in the initial trial

Viral Therapy in Treating Young Patients with Relapsed or Refractory Solid Tumors
This phase I trial is studying the side effects and the best dose of viral therapy in treating young patients with relapsed or refractory solid tumors. This is one of the first trials using live human viruses for the treatment of pediatric cancers. For more information, view the full text description of this study on ClinicalTrials.gov by clicking this link.

Principal Investigator: E. Anders Kolb, MD, Alfred I. duPont Hospital for Children, Wilmington, Del.
Telephone: 302-651-5567; Email: eakolb@nemours.org

Clinical Trial:
Danazol
Phase I/II Dose Escalation Trial of Danazol in Patients with Fanconi Anemia or Dyskeratosis Congenita
The purpose of this Phase I/II dose escalation trial is to determine the minimum effective dose of danazol, an attenuated androgen, when used for Fanconi anemia and Dyskeratosis congenita and to evaluate adverse side effects. For more information, view the full text description of this study on ClinicalTrials.gov by clicking this link.

Principal Investigator: Colin Sieff, MB BCh, Children’s Hospital Boston, Boston, Mass.
Telephone: 617-919-4241; Email: colin.sieff@childrens.harvard.edu

Clinical Trial:
Cetuximab and/or IMC-A12
Phase II Study of Cetuximab and/or IMC-A12 in Squamous Cell Carcinomas of the Head and Neck
In this program, patients with head and neck cancer who are candidates for surgical resection receive therapy with cetuximab, cixutumumab (IMC-A12), or both, during a period of two to three weeks leading up to surgery. These drugs have demonstrated promising activity against head and neck cancers in previous clinical and/or laboratory studies. The post-treatment surgical specimen is then collected and the tumor is analyzed for changes in cancer cell molecules in response to therapy. For more information, view the full text description of this study on ClinicalTrials.gov by clicking this link.

Principal Investigator: William N. William Jr., MD, The University of Texas MD Anderson Cancer Center, Houston, Texas
Telephone: 713-792-6363; Email: wnwilla@mdanderson.org
Alternate Contact: Cynthia Trainer, RN
Telephone: 713-792-6363

Needed: Saliva samples from FA patients with newly diagnosed oral cancer, given after the biopsy and before medical treatment begins
For FA Patients and Families continued

Testing Services for FA Patients: Molecular Testing

The Knight Diagnostic Laboratories at Oregon Health & Science University have made available molecular tumor tissue tests that are designed to identify potential treatment targets in cancer and to predict the likelihood of benefit for patients treated with the latest therapeutics. The Fund will cover the cost of the test, discounted to $300 through an agreement with Knight Diagnostic Laboratories. This testing is available at NO CHARGE to FA patients.

For more information, contact:
Teresa Kennedy
Director of Family Support Services
Fanconi Anemia Research Fund, Inc.,
Eugene, OR
Telephone: 541-687-4658 or 1-888-FANCONI (888-326-2664)
Email: teresa@fanconi.org

Send tumor tissue samples to:
Christopher Corless, MD, PhD, Medical Director
OHSU Dept. of Pathology (mailcode L113)
3181 SW Sam Jackson Park Road, Portland, OR 97239
Telephone: 503-494-6834
Email: corlessc@ohsu.edu

For FA Researchers:

FA Antibody Project: Antisera Now Available Against Fanconi Anemia Complementation Group Proteins

Fanconi Anemia Research Fund has sponsored the development of high-titer, affinity-purified rabbit polyclonal antisera against the Fanconi anemia complementation group proteins in order to facilitate research on Fanconi anemia.

Affinity-purified antisera are currently available against the following 14 FANC proteins: FANCA, B, C, D2, E, F, G, I, J, M and N, and the deubiquitinating enzyme USP1 protein. Antibodies are being developed to the two most recently identified FANC proteins, FANCO/RAD51C and FANCP/SLX4 proteins, and should be available in the second quarter 2012, together with new antisera generated using previously successful epitopes to FANCC, FANCD1/BRCA2 and FANCG. We still have very limited stocks of FANCL antisera kindly provided to us for redistribution.

In addition to affinity-purified antisera, unpurified sera are available for many FANC protein antibody projects listed above for investigators who would like to try alternative purification approaches or uses.

Investigators requesting antisera must complete a request via the website www.ohsu.edu/fa and be willing to meet the FARF’s use agreement. We depend critically on user feedback on these antisera, so will require this as well from all end-users.

General inquiries contact: Ray Monnat, MD
University of Washington, Seattle, Wash.
Telephone: 206-616-7392; Email: monnat@u.washington.edu

Antibody distribution contact: Laura Marquez
Oregon Health & Science University, Portland, Ore.
Telephone: 503-494-6889; Email: marquezl@ohsu.edu

Availability of Tumor Samples for FA Research

The FA researchers listed below may make FA SCC cell lines available upon request to qualified colleagues. Please note material transfer standards, policies and costs may differ between laboratories.

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<th>Cell line type</th>
<th>Cell line #</th>
<th>Contact</th>
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<td>SCC (FA-A)</td>
<td>OHSU974</td>
<td>Grover Bagby, MD (<a href="mailto:grover@ohsu.edu">grover@ohsu.edu</a>)</td>
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<tr>
<td>SCC (FA-C)</td>
<td>VU-SCC-1131</td>
<td>Johan de Winter, PhD (<a href="mailto:j.dewinter@vumc.nl">j.dewinter@vumc.nl</a>)</td>
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<td>SCC (FA-A)</td>
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