



FA COURIER

14

a publication of the Fanconi Anemia Research Fund, Inc.

Welcome to the fourteenth issue of the *FA Courier*. We publish the *FA Courier*:

- To encourage families to contribute to the urgent need for research materials necessary for FA research;
- To keep families informed about current research projects and clinical trials; and
- To apprise researchers of the availability of research materials.

How can FA patients and families contribute?

To assist you in contributing research material, the Fund collaborates with the National Disease Research Interchange (NDRI) [*See article on page 2*].

This issue of the *FA Courier* contains requests from FA researchers for specific research materials. We urge you to read the articles in this newsletter carefully to determine if you can contribute materials to one or more projects.

What are research materials?

Research materials are blood, cord blood, bone marrow, skin (fibroblasts), and samples of tumors. Research materials also include the collection of data about the disease, acquired by the completion of questionnaires by FA patients or relatives.

When should you think of donating research materials?

Many FA patients undergo periodic complete blood counts and bone marrow aspirations. At that time, it is possible that the FA patient's physician can

draw a small additional amount to send to a research laboratory without any harm or additional discomfort to the FA patient. Whenever a tumor is biopsied or removed, it is possible to donate a small sample for research purposes. NDRI can be of assistance in obtaining samples so that they can be used for FA research.

Researchers don't need samples just from FA patients. Some studies request samples from **relatives** of FA patients, so please respond to these requests as well.

Thank you for helping researchers advance Fanconi anemia research at a rapid pace.

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Patients and Families: Help Build a Collection of Biomedical Research Materials

Biomedical Research Material Donations by FA Patients to the National Disease Research Interchange

Goal:

The Fund urgently wishes to expedite research into Fanconi anemia. To do that, we ask for your help in establishing a collection of biomedical research materials such as blood, bone marrow, skin (fibroblasts), samples of tumors, and related medical records so that FA researchers can conduct their research.

To facilitate collection of biomedical research materials for FA research, the Fund has entered into a partnership with the National Disease Research Interchange (NDRI). NDRI is a non-profit organization with over 25 years experience in obtaining, storing, and distributing human cells, tissues, and organs to researchers and scientists (www.ndriresource.org). NDRI receives funding for its Rare Disease Program from the National Institutes of Health and the Office of Rare Diseases.

Importance of project to FA families:

Biomedical research materials are needed for all aspects of FA research. As you know, FA is a very rare disease, resulting in difficulty in obtaining needed research material. Thus, we ask patients to consider donating research materials whenever they undergo a procedure such as a bone marrow aspiration or a periodic CBC.

The Fund particularly wishes to expedite research into the squamous cell cancers that affect so many patients. The number of FA patients who have biopsies of possible squamous cell tumors or have these tumors surgically removed is very small. Thus, we ask that each such patient consider donating tissue samples for FA research. Effective treatments and a cure for FA will be found through research.

Materials/Information needed:

The donation of research materials (such as biopsy material or tumor tissue from head and neck cancer) through NDRI

is designed to be simple and sensitive to donors and their families. Potential donors will receive a packet of information describing the donation process and consent forms. The NDRI will work with your surgeon or physician so that the tissue can be obtained at the time of the procedure.

NDRI follows strict governmental regulations and guidelines regarding donor consent and confidentiality; tissue samples are provided only to approved biomedical researchers who are specifically researching Fanconi anemia. NDRI matches tissue donations with appropriate requests and then sends the samples directly to that researcher. Personal details of the donor remain strictly confidential.

If a patient is diagnosed with squamous cell carcinoma or needs a biopsy, the natural focus is on that urgent medical need. NDRI therefore encourages prior enrollment months or even years in advance, so that a patient's information is on record and ready should the need for a biopsy or surgery arise. NDRI would then be able to contact your physician prior to the procedure and obtain your tissue donation without delay.

Cost of participating:

Donations of tumor biopsy material are made at no cost to the donor, except the cost of a blood draw if that is required for a particular research project.

Contact:

If you are interested in donating research materials to NDRI, please contact the Private Donor Program by email at privatedonor@ndriresource.org or by phone at 1-800-222-6374. For more information or assistance in donating tissue, contact Teresa Kennedy, Family Support Coordinator, at 1-888-FANCONI or teresa@fanconi.org.

Requests for Research Materials

Principal Investigator:	Blanche Alter, MD, MPH Clinical Genetics Branch (CGB), National Cancer Institute (NCI), National Institutes of Health (NIH), Rockville, Maryland
Co-Investigators:	Neelam Giri, MD , CGB, NCI, NIH, Rockville, Maryland Sadie Hutson, RN, MSN, PhD , CGB, NCI, NIH, Rockville, Maryland
Title of research project:	Etiologic Investigation of Cancer Susceptibility in Inherited Bone Marrow Failure Syndromes
Funding source:	National Cancer Institute, Intramural Research Program

Needed:	Completion of questionnaires; bone marrow; tumor tissue; blood, serum, and plasma samples; mouth washings; skin biopsies [Accepting international patients]
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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 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). Gynecologic exams (females). All participants contribute personal medical and risk factor information and often samples of blood (bone marrow for those with FA) from their home community. Some families will visit the NIH Clinical Center for a more comprehensive clinical and laboratory evaluation. FA mutation testing will be performed in a CLIA-certified laboratory. Sibling interviews will be done at home or at the NIH.

Cost of participating:

All costs for participating, including transportation (from US and Canada), hotel, and meals for all family members, will be paid by the NCI.

Contact:

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Principal Investigators: **Arleen D. Auerbach, PhD**
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Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio
Margaret L. MacMillan, MD
University of Minnesota, Minneapolis, Minnesota

Co-Investigators: **David Kutler, MD**
Weill Medical College of Cornell University, New York, New York
Bhuvanesh Singh, MD
Memorial Sloan-Kettering Cancer Center, New York, New York

Title of research project: Entrance into the International Fanconi Anemia Registry

Funding Source: The Rockefeller University

Needed:	Completion of questionnaire; blood sample; skin fibroblasts; In patients with somatic mosaicism, cultured skin fibroblasts will be needed for complementation testing [Accepting international patients]
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Hypothesis:

The Rockefeller University Hospital is home to the International Fanconi Anemia Registry (IFAR), established in 1982 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. Information regarding genotype-phenotype correlation is being obtained, which may help to determine the physiologic roles of the cloned genes. We hypothesize that correlation between genotype and phenotype will define important regions within the FA genes that may shed light on their function in cell cycle control, programmed cell death, and DNA repair. This may lead to improvement in prediction of outcome for a given patient, based on genotype, and affect decision-making regarding timing of therapy options.

Importance of project to FA patients:

We aim to more fully define the variable clinical manifestations 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 ~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 as appropriate by law.

Eligibility criteria:

Any patient diagnosed as affected with FA, as well as parents.

Material/Information needed:

We need to receive a blood specimen from the patient to make a cell line. Mutation testing will be performed in a research laboratory. The IFAR form must be completed and can be downloaded at:
www.rockefeller.edu/labheads/auerbach/documents/IFAR_FORM.pdf.

Cost of participating:

The patient's blood and other specimens are usually shipped by clinician, as part of clinical testing.

Contact:

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Principal Investigator: Pamela S. Becker, MD, PhD
University of Washington, Seattle, Washington

Title of research project: Laboratory Studies of Gene Transfer for Fanconi Anemia

Funding Source: National Institutes of Health (National Heart Lung and Blood Institute)

Needed: Blood and bone marrow [Accepting international patients]
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Hypothesis:

The long-term goal of our research is to develop gene therapy as a treatment option for patients with Fanconi anemia. The first steps in this effort are to develop effective methods to deliver a normal gene to the blood stem cells of patients with Fanconi anemia. At this time, we are focusing on Fanconi anemia complementation group A (FANCA) and Fanconi anemia complementation group C (FANCC). We have developed a genetically modified, non-disease-causing virus that can deliver the FANCA or FANCC gene to blood cells in a laboratory dish. We have tested it in blood cells from people who do and do not have Fanconi anemia, and in blood cells from mice with 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 defect in the laboratory, we need a source of bone marrow and/or blood from patients with FANCA or C.

Importance to FA patients:

Optimizing the gene delivery process is an essential step in developing gene therapy as a safe and effective treatment option for Fanconi anemia patients.

Eligibility criteria:

- Fanconi anemia complementation group A or C as determined by somatic cell hybrids, molecular characterization, Western blot analysis, or acquisition of mitomycin C resistance after *in vitro* transduction with a vector bearing the cDNA for Fanconi complementation group A or C
- Undergoing bone marrow aspiration and/or blood draw for clinical purposes

Material needed:

10 mL (2 teaspoons) of blood and/or 5 mL (1 teaspoon) of bone marrow

Cost of participating:

There is no cost for participating. Dr. Becker's laboratory will pay for shipment.

Contact:

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Principal Investigator: Christine Rini, PhD
Department of Oncological Sciences, Mount Sinai School of Medicine
New York, New York

Title of Project: Sharing our Strength: A Program for Bone Marrow or Stem Cell Transplant Survivors

Accepting: US patients only

What is the purpose of this study?

Hematopoietic stem cell transplantation (also known as *bone marrow transplant*) is an intensive medical treatment for Fanconi anemia, cancer such as leukemia, lymphoma, multiple myeloma, and other diseases. Because it is a physically and emotionally demanding treatment, many people report having ongoing physical and emotional difficulties after having a transplant. The *Sharing Our Strength* study is being conducted to help us understand people's transplant experiences and to test a new program designed to help them recover physically and emotionally after transplant.

What is involved?

Participants will be asked to complete a brief *screening interview* over the phone. Eligible participants who wish to continue in the study will complete an *initial interview* (about 60 minutes) that includes questions about background, how they feel emotionally and physically, personality, and relationships with others. They will also complete a questionnaire packet. Participants will then be randomly assigned to one of four writing groups that each write about a different topic. Four writing sessions will be completed at home (30 to 45 minutes each) - one a week for 4 weeks. The *follow-up interview* (about 60 minutes) will take place 3 months after the writing sessions, and participants will also complete a questionnaire packet. All study materials are completely confidential, and completed by mail and telephone so that participants won't need to travel to participate in the project.

Who can participate?

People may qualify to join the study if they are a transplant survivor who is 9 months to 3 years beyond transplant and not currently relapsed, they are at least 18 years old now (and at least 16 at the time of transplant), they speak English, and they have telephone service.

What are the benefits?

Although we cannot promise that participants will benefit from joining the study, transplant survivors have often said that discussing their experience with a supportive interviewer decreases their distress, and people who write often say that doing so is a positive experience.

What are the risks?

There is a chance that participants will feel some distress or discomfort as a result of answering some questions asked during the study or following writing. Past research has shown that such distress is usually minimal and transient. Participants will be assured that they can refuse to answer any questions or withdraw from the study at any time without penalty.

Will you be paid for participating in the study?

If participants complete the screening interview, they will be offered a choice of a \$20 Barnes and Noble gift certificate or a pair of movie tickets to reimburse them for their time. If they are eligible to complete the rest of the study, they will receive an additional \$20 in gift certificates (American Express gift checks) after completing the initial interview, all four writing exercises, and the follow-up interview. Therefore, participants will receive reimbursement worth a total of \$80.

Contact:

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Clinical Trials

Principal Investigator: Joseph Califano, MD
Johns Hopkins, Baltimore, Maryland

Title of Clinical Trial: Phase II Study of Single-Agent Cetuximab for Treatment of High-Risk Pre-Malignant Upper Aerodigestive (UAD) Lesions

Accepting: International patients

Rationale:

Over 45,000 new cases of Head and Neck Squamous Cell Carcinomas (HNSCC) are diagnosed in the United States yearly, and this disease affects over 600,000 people worldwide. The data identify a set of high-risk patients with oral pre-malignant lesions as a population with extraordinary risk for malignant progression and significant mortality, for whom there is no viable medical or surgical intervention. Cetuximab is an attractive therapeutic agent for these patients, in that it has a low risk toxicity profile and is effective in invasive head and neck cancer.

Purpose:

This is a randomized trial of cetuximab treatment for patients with high-risk, premalignant UAD lesions. Three groups of patients (group 1: diffuse, group 2: recurrent, group 3: dysplastic) will receive Cetuximab 400 mg/m² on week one followed by 250 mg/m² on weeks 2-8. Patients in the control arm will have the option of moving into a treatment arm after completion of initial treatment. Patients will also be followed for development of HNSCC. Following the eight-week treatment with Cetuximab, groups 2 and 3 will undergo lesion resection based on the extent of initial disease. Safety of Cetuximab in this patient population will also be evaluated. The projected accrual goal is a total of 60 patients. 20 of the 60 patients are targeted to be enrolled at the Coordinating Center at Johns Hopkins, while enrollment of 40 patients is to be completed at 11 participating sites. IRB approval has been obtained and enrollment has started at Johns Hopkins, Medical University of South Carolina, and University of Illinois, Chicago, while other participating site are in the process of obtaining IRB approvals. To date, a total of 17 patients have been enrolled into the study, 6 have been treated, 2 are under treatment, and 2 patients are in screening.

The inclusion criteria for enrollment are:

Histologically confirmed, previously untreated high-risk UAD pre-malignant lesion consisting of one of the following groups:

- Unresectable, diffuse high grade dysplasia, defined as moderate or severe dysplasia whose anatomic extent cannot be assessed by physical examination and/or includes a large enough area or area of anatomic extent that cannot practicably be excised by standard surgical techniques
- Previously treated HNSCC with persistent or recurrent high grade dysplasia with no evidence of head and neck malignancy for three months prior to enrollment
- Dysplastic lesions with 3p or 9p loss of heterozygosity

Patients will undergo the following after enrollment into the study:

1. Informed consent.
2. Complete Head and Neck Exam.
3. Tolonium staining and Photodocumentation:
 - a. Tolonium Staining using vizlite Blue Oral Exam Kit - this is to be provided free of cost.
 - b. Photodocumentation
4. Biopsy (3mm punch) of lesion OR prior biopsy less than 3 months prior to enrollment.
5. Tumor specimen for LOH testing.
6. Pre-treatment evaluation which includes:
 - a. blood tests to confirm eligibility to receive study drug and
 - b. imaging studies to assess extent of disease as per the standard of care for the patient. Research blood samples to be sent to Coordinating Center.
7. Randomization to one of the two following groups:
 - a. Study Drug Group: Patient to receive weekly Cetuximab injections for 8 weeks on Days 1, 8, 15, 22, 29, 36, 43, and 50.

Califano (continued):

- b. Control Group: To undergo scheduled follow-up and observation on the same days mentioned above. Patients in this group may choose to receive the study drug after the 8 week period.
8. Post Treatment:
- a. Head and Neck Exam and blood draw
 - b. Tolonium Staining and Photodocumentation:
 - Tolonium Staining using Vizlite Blue Oral Exam Kit - this is to be provided free of cost.
 - Photodocumentation
 - c. Repeat biopsy of tumor for Group 1, and/or excision of lesion for patients in Groups 2 and 3.
 - d. Repeat biopsy specimen to go for LOH testing.

Contact

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Sharing Research Materials

The purpose of the *FA Courier* is to accelerate FA research by making research materials more readily available to scientists researching Fanconi anemia. The Fund requires that all investigators who publicize their need for research materials in the *FA Courier* share residual research materials received through the *Courier* and cooperate to the maximum feasible extent with other scientists who are studying Fanconi anemia. If you are a researcher who has developed FA antibodies and/or cell lines, and you are willing to share those antibodies or cell lines with other FA researchers, please contact Beverly Mayhew, Executive Director, at bev@fanconi.org.

Principal Investigator: Colin Sieff, MB.BCh.
Children's Hospital Boston, Boston, Massachusetts

Title of clinical trial: Phase I/II Dose Escalation Trial of Danazol in Patients with Fanconi Anemia or Dyskeratosis Congenita

Accepting: International patients

Hypothesis:

Fanconi anemia (FA) and Dyskeratosis congenita (DC) are inherited bone marrow failure syndromes for which anabolic steroids are often used, but in which specific androgens have never been studied. Masculinizing side effects from the usual androgen (oxymetholone) present major problems, leading to a need for another agent. Danazol is an attenuated androgen, and thus may have fewer side effects; however, its hematologic efficacy in the setting of FA and DC has never been investigated.

The purpose of this Phase I/II dose escalation trial is to determine the minimum effective dose of danazol and to evaluate adverse side effects. An additional goal is to investigate gene expression signatures of patient progenitor cells after exposure to danazol, both *in vitro* and *in vivo*, to correlate gene expression with responsiveness to treatment and to identify new treatments.

Importance of project to FA patients:

If danazol does not have serious masculinizing or other side effects and is efficacious in stimulating blood cell production, it could prove very useful in the management of bone marrow failure, particularly among patients who do not have a matched sibling donor.

Eligibility:

Inclusion criteria:

- Patients must be diagnosed with FA that is documented by a positive chromosomal breakage test
- Patients must have at least one of the following peripheral blood cytopenias: Absolute neutrophil count <500 μ L; platelet count <30,000/ μ L; hemoglobin <8.0 gm/dL
- Patients must have a negative pregnancy test and agree to use medically approved birth control
- Patients must be either 3 years of age or \geq 14 kg (30 lbs)

Exclusion criteria:

- Concurrent use of anticoagulants
- Use of androgen therapy within past 3 months
- Patients with liver disease (SGOT, SGPT or bilirubin greater than the upper limit of normal)
- Patients with renal disease (serum creatinine greater than the upper limit of normal for age)
- Patients who have HLA matched sibling donors

Study Procedures:

Screening:

Informed consent, physical exam and blood work, bone marrow aspiration and biopsy, left wrist radiograph, liver ultrasound, post oral glucose test

Treatment weeks 2, 5, 8:

Physical exam and blood work

Treatment week 12:

Physical exam and blood work, post oral glucose

Treatment week 14 (only if dose increase):

Physical exam and blood work

Treatment week 18:

Physical exam and blood work

Treatment week 20 (only if dose increase):

Physical exam and blood work

Treatment week 24:

Physical exam and blood work, liver ultrasound, post oral glucose

Follow-up weeks 38 and 52:

Physical exam and blood work, left wrist radiograph (week 52 only), liver ultrasound (week 52 only), post oral glucose

Contact:

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Principal Investigator: **Monica Thakar, MD**
Fred Hutchinson Cancer Research Center, Seattle, Washington

Title of clinical trial: Nonmyeloablative Hematopoietic Cell Transplantation for Patients with Fanconi Anemia Using Alternative Marrow Donors: A Phase I/II Dose-Finding Study

Accepting: US and Brazil patients only

What is the purpose of this study?

Many people with Fanconi anemia develop bone marrow failure or leukemia. Both of these conditions may be cured by stem cell transplantation, but it is sometimes difficult to find an appropriately matched donor to use. The purpose of this study is to test whether it is possible to use an alternative bone marrow donor who is “half-matched,” or haploidentical, to the patient’s tissue type. The haploidentical donor is related to the patient and is usually the parent or sibling. We can also use matched unrelated donors on this protocol. We will test whether using lower doses of radiation and a novel immunosuppressive regimen will allow the patient to accept the new donor cells with fewer side effects. This is a dose-finding study. Different doses of radiation will be tested.

Who can participate?

This study is open to FA patients who have bone marrow involving 2 of the following 3 lineages:

- granulocyte count <0.5 x 10⁹/L
- platelet count <20 x 10⁹/L
- hemoglobin <8 g/dL

or to FA patients with 1 of the above and a life-threatening event or to FA patients requiring red blood cell or platelet transfusions because of bone marrow failure.

If being treated for leukemia, the patient must be considered in remission.

What is involved?

Patients will undergo a bone marrow transplant using a novel, dose-finding conditioning and immunosuppressive regimen. Treatment will last 3½ months or more, with follow-up every year thereafter.

What are the benefits?

For FA patients who must undergo stem cell transplant for bone marrow failure or leukemia but do not have a fully matched donor, this will allow the opportunity for a potentially life-saving treatment. This will also allow the opportunity to use lower-doses of radiation therapy to lower the risks of long-term side effects.

What are the risks?

Risks associated with bone marrow transplant are extensive and include infections, graft-versus-host disease, rejection, secondary cancers, and even death. Using a half-matched donor or unrelated donor (instead of fully matched sibling donor) may increase these risks. The risks of this study will be explained in detail to you.

Will you be paid to participate in this study?

No.

Contact:

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Clinical Trials Nurse, Nonmyeloablative Transplants
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To FA Families: If you need assistance researching a clinical trial or with the costs associated with participating in a clinical trial, please contact Teresa Kennedy, Family Support Coordinator. Call toll-free at 1-888-FANCONI or email teresa@fanconi.org

FA Researchers: Available Research Materials

National Disease Research Interchange: Biomedical Research Materials for Research into Fanconi Anemia

Background:

To facilitate collection of biomedical research materials for FA research, the Fanconi Anemia Research Fund has entered into a partnership with the National Disease Research Interchange (NDRI). NDRI is a 501(c)3 not-for-profit organization with over 25 years experience distributing human cells, tissues, and organs to researchers and scientists (www.ndriresource.org). In conjunction with the NIH Office of Rare Diseases, in 2002 NDRI began to develop a program focused on the unmet needs of the rare disease research community for human organs and tissues. NDRI receives funding for its Rare Disease Program from the National Institutes of Health and the Office of Rare Diseases.

Available Research Materials:

Biomedical samples of Fanconi anemia are available to researchers. Given the rarity of FA, the supply of some biomedical research materials is occasionally limited. Samples are provided only to those researchers who are specifically studying FA.

In general, NDRI places around 20,000 biospecimens annually with researchers in academic and government

laboratories, as well as those in biomedical and pharmaceutical industries. To that end, the organization works with organ procurement organizations, eye banks, tissue banks, and major medical centers in the United States. NDRI has also developed unique programs to serve researchers studying rare diseases, such as Fanconi anemia. Importantly, NDRI has developed mechanisms to aseptically obtain tissues with a very short death to preservation interval, making them ideal for cell culture, genomic, and proteomic research. NDRI also serves the cancer research community with tumor and normal adjacent tissues specimens preserved at 4°C, frozen, snap-frozen, or formalin-fixed/paraffin embedded.

NDRI will strive to meet your exact needs for FA research. Please visit www.ndriresource.org to learn how NDRI can be a valuable resource for your research. To receive an application, contact a Rare Disease Coordinator at raredisease@ndriresource.org or by phone at 1-800-222-6374. The application is also available on NDRI's website under the Quick Links section.

FA Antibody Project: Antisera Now Available against Fanconi Complementation Group Proteins

Background:

To facilitate research into Fanconi anemia, the Fund has sponsored the development of affinity-purified rabbit polyclonal antisera against the Fanconi complementation group proteins. Ray Monnat, Jr., MD, University of Washington School of Medicine and a member of the Fund's Scientific Advisory Board, spearheads this effort.

The rabbit antisera were developed with a commercial partner, Open Biosystems in Huntsville, Alabama, using peptide epitopes, and were validated by a combination of peptide ELISA assays and Western blot analyses with and without peptide blocking using cell lysates from different FANC protein-positive and negative human cell lines. All positive antisera were then affinity-purified and again titered by ELISA assay to determine sensitivity of detection. Antisera against most of these proteins and USP1 are now available for distribution to all qualified investigators to further our understanding of Fanconi anemia biology.

IMPORTANT: An essential part of this project is the use and sharing of experience with these antisera with the Fanconi community. Thus, it is essential that all end users of specific antisera for immunofluorescence, immunoprecipitation, Western blot or other analysis to help all users of these antisera. This feedback can be entered on the Antibody website, where it will be archived and made available to all users. **We will not honor additional requests for reagents from users who do not provide feedback on their experience using antisera.**

Availability and Distribution:

The Fanconi Anemia Research Fund has contracted with Oregon Health & Science University through the laboratory of Markus Grompe, MD, Department of Medical and Molecular Genetics, to manage the FA Antibody Project in conjunction with the FA Cell Repository already housed at

OHSU. Xioman Zhu, MD, is in charge of this project. Rabbit polyclonal affinity-purified antisera prepared against either peptide epitopes or fusion protein antigens are available now to most of the Fanconi complementation group proteins and for the deubiquitinating enzyme USP1.

The antisera listed are available to all qualified non-commercial Fanconi anemia investigators via the FA Antibody Project website at <http://www.ohsu.edu/fa>. There is no charge for the antisera. Requesting investigators must complete a Use Agreement and Materials Transfer Form and provide a valid shipping account number to cover the cost of shipping. Commercial users may arrange to purchase the antisera via a distribution agreement with Open Biosystems.

As noted, an important aspect of this open source/end user project is to share useful information. This is an essential aspect of this effort and a requirement for receiving antisera.

Direct general inquiries regarding FANC antibodies to:

Ray Monnat, MD
Departments of Pathology and of Genome Sciences
University of Washington
Telephone: 206-616-7392
Fax: 206-543-3967
Email: monnat@u.washington.edu

Direct antibody distribution questions to:

Xioman Zhu, MD
Oregon Stem Cell Center
Oregon Health & Science University
Telephone: 503-494-6889
Fax: 503-494-6886
Email: zhuxi@ohsu.edu

Pilot Study Awards Funding Available for Research

The Fanconi Anemia Research Fund, Inc., seeks applications for basic or applied research into the mechanisms, pathogenesis, and/or treatment of Fanconi anemia. These awards are usually for one year of support and are intended to fund pilot studies designed to test new ideas and to provide initial data to support applications for further funding by other (and larger) agencies that support biomedical research.

Fanconi anemia is an autosomal recessive disease characterized by bone marrow failure, variable congenital anomalies, and a predisposition to leukemia. Cells from FA patients exhibit hypersensitivity to alkylating agents such as mitomycin C (MMC) and diepoxybutane (DEB). Indeed, the hypersensitivity to cytotoxic effects of DNA cross-linking agents is currently used as the basis for the diagnostic tests for FA. It is known that FA is genetically heterogeneous, with at least thirteen complementation groups and thirteen cloned genes [A, B, C, D1 (BRCA2), D2, E, F, G, I, J, L, M, and N] identified thus far.

Better understanding of Fanconi anemia that can lead to effective treatment of the various phases of the disease is so urgently needed. Studies of Fanconi anemia may also have important implications for solid tumor malignancies such as head and neck, gastrointestinal, and gynecological cancers.

Application Process:

An abbreviated NIH-style application is used. Under emergency circumstances researchers whom we are currently supporting or who have an established track record in FA research can apply for small supplementary grants on an accelerated basis. Selection for a research award is based upon scientific merit and relevance, as determined by the Fund's peer review procedure.

Apply to:

Fanconi Anemia Research Fund
1801 Willamette Street, Suite 200
Eugene, OR 97401
Telephone: 1-541-687-4658
Fax: 1-541-687-0548
Email: info@fanconi.org

Applications due:

Applications are reviewed on an ongoing basis.



Fanconi Anemia
RESEARCH FUND, INC.

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