FA Family Newsletter

#35 A Semi-annual Publication of the Fanconi Anemia Research Fund, Inc. Spring 2004

Fanconi Anemia Scientific Symposium

A heightened sense of interest in FA science was in the air at the 15th Annual Fanconi Anemia Scientific Symposium in October. The discovery of the *FANCL* protein by the laboratories of Weidong Wang, PhD, Hans Joenje, PhD, and Maureen Hoatlin, PhD was the catalyst. Adding to the excitement were the lively discussions in the poster sessions, the FA genetic pathway proposed by Larry Thompson, PhD, Lawrence Livermore National Laboratory, and the excellent oral presentations, which were selected for the first time through submission of abstracts. The evaluations of the meeting documented that this symposium was, quite simply, exceptional.

Board Vice-president Dave Frohnmayer with the recipients of the Award of Appreciation for the discovery of FANCL.

One hundred fifty-three people attended the conference, which was held at the Renaissance Hotel in Houston, TX, from October 16-19, 2003. Participants came from 11 countries, 4 continents, and 54 research institutions and laboratories. Nine FA parents attended. The sessions included FA Gene Discovery and Molecular Diagnosis; DNA Damage and Repair;

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Recurring Clonal Chromosome Abnormalities are Associated with MDS/AML

Betsy Hirsch, PhD, University of Minnesota Medical School, has analyzed 93 FA patients for clonal abnormalities. Forty-three (or 46%) of these patients had abnormal clones. Seventy percent of these clones involved abnormalities of chromosomes 1, 3, and/or 7 (specifically, a gain of the long arm of chromosome 1, a gain of the long arm of chromosome 3, and loss of the long arm or all of chromosome 7). Other recurring clonal abnormalities that were each seen in greater than 5% of patients included losses of the short arms of chromosomes 7 and 17, losses of the long arms of chromosomes 5 and 11, and gains of chromosomes 8 and 21.

The gain of the long arm of chromosome 3 most frequently occurred as the only clonal abnormality, whereas the chromosome 1 and chromosome 7 abnormalities most frequently were seen in

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Highlights

MEDICAL NEWS

Abnormal Clones Can be Detected in Peripheral Blood

Researchers at Charité University Hospital, Berlin, have concluded that abnormal clones can be detected in peripheral blood as well as bone marrow. Researchers studied both blood and bone marrow samples from 91 FA patients. Using interphase fluorescence *in situ* hybridization (FISH), they were able to detect a strong correlation between chromosomal aberrations found in bone marrow cells and abnormal clones present in peripheral blood of FA patients. Using peripheral blood samples, they found that an aberration of chromosome 3q is usually the first abnormality to emerge.

Drawing peripheral blood is a far less invasive procedure than performing a bone marrow aspiration. If the Berlin results can be replicated elsewhere, this procedure would allow for easier, less expensive, and more frequent monitoring of a patient's clonal evolution into a dangerous pre-leukemic or leukemic condition. ◆

Two New Complementation Groups Identified

Marieke Levitus, MSc, of the Free University Medical Center, Amsterdam, described the identification of two new complementation groups: FA-I and FA-J, bringing to 11 the number of FA groups identified to date. So far, only four patients have been placed in each of these new groups. The specific genes for FA-I and FA-J have not yet been isolated. ◆

Marieke Levitus, MSc

An Abnormality on Chromosome 3 Predicts Evolution to MDS, AML

Heidemarie Neitzel, PhD, Charité University Hospital, Berlin, expanded on her earlier findings that a specific clonal abnormality, a gain of 3q (the long arm of chromosome 3) predicts evolution to myelodysplastic syndrome (MDS) and leukemia in FA patients. Her laboratory studied bone marrow aspirations from 80 patients, of whom 18 had the gain of chromosome 3. For most of these patients, this was the first abnormal clone discovered. Six of these patients subsequently developed a monosomy 7 (complete loss of one chromosome 7). These two abnormal clones are strongly associated with a poor prognosis, because of a rapid evolution of leukemia in the patient.

Dr. Neitzel noted that a clonal aberration can be associated with either rising or dropping blood counts, so the CBC may not predict evolution to MDS or AML.

Heidimarie Neitzel, PhD

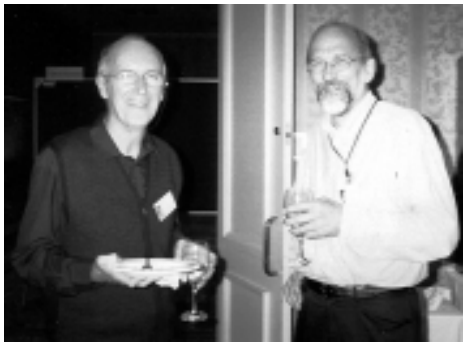
Cell lines with either 3q gains or monosomy 7 never disappear from the bone marrow, but rather persist and expand.

Dr. Neitzel believes it is crucial to identify these clonal aberrations accurately. Special techniques are needed, such as fluorescence *in situ* hybridization (FISH), interphase-FISH and micro-dissection. ◆

Screening for FA Disease Mutations

Gerard Pals, PhD, Free University Medical Center, Amsterdam, discussed the importance of screening for specific disease mutations in FA patients after the gene or complementation group of the patient is known. He also described the development of efficient screening techniques recently developed at his center. Pals noted that mutation analysis in FA is essential for: (1) reliable prenatal testing; (2) preimplantation genetic diagnosis; (3) gene therapy; and (4) in some cases it is extremely helpful in determining a specific patient's prognosis.

A major problem in FA mutation screening has been the high frequency of large deletions and duplications in the *FANCA* gene, which have been difficult to detect. Pals reported that researchers in Amsterdam have developed methods that can reliably detect both large and small sequence mutations in about 90% of FA patients with mutations in *FANCA, -C, -E, -F* and *-G*. Additional steps yield mutations in *FANCD1 (BRCA2)* and *FANCD2*. In the event mutation screening cannot assign a patient to one of the above groups, additional steps

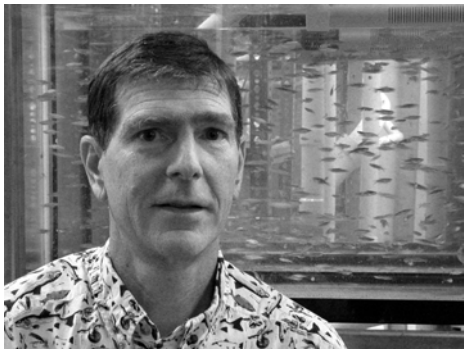


Gerard Pals, PhD (right) with Chris Mathew, PhD, Guy's Hospital, London

are taken to assign patients to complementation groups B, I, J, or a new group. Newly discovered FA genes, such as *FANCL*, are being added to the protocol. ◆

Zebrafish: A Possible Model for Understanding and Treating Fanconi Anemia

John Postlethwait, PhD, University of Oregon, is exploring the use of zebrafish as model organisms for understanding and possibly treating Fanconi anemia. His laboratory has isolated at least portions of all the known FA genes in zebrafish. Professor Postlethwait's hope is that the use of an inexpensive and accessible whole animal model for FA might be useful for screening compounds that might have therapeutic value.



John Postlethwait, PhD with the zebrafish

As animal models, zebrafish have certain advantages. They are vertebrates (they have a backbone), making them likely to be more similar to people than a more distantly related organism. They are easy to maintain, manipulate, observe and breed in the laboratory. Zebrafish eggs are produced in large numbers and fertilized externally. The embryos develop outside the mother's body, so scientists have ready access to them. The embryos are transparent so their growth and development can be observed constantly during development. Zebrafish with disease mutations can mimic human syndromes.

Postlethwait plans to develop zebrafish models for several of the FA genes. Once the models exist, he intends to screen a large number of small molecule compounds to identify compounds that might have therapeutic potential for FA patients. ◆

Second Edition of *FA: Standards for Clinical Care*

The second edition of *FA: Standards for Clinical Care* has now been published and is being sent to all recipients of this newsletter. If you have not yet received your copy or would like an additional copy for your physician or yourself, please contact us. Our thanks to Eva Guinan, MD, Dana-Farber Cancer Institute, for her role in moderating the consensus conference that led to the development of standards and the publication of the book. We extend our gratitude, also, to all the physicians who participated in developing these patient care guidelines. Special thanks to David G. Nathan, MD, Dana-Farber Cancer Institute, for writing the *Introduction*, and to Joyce Owen, PhD, Director Emeritus of the Fund, for editing the handbook. ◆

Patients in the FANC-D1 (BRCA2) Complementation Group at Extremely High Risk

Arleen Auerbach, PhD

In 2002, FA researchers discovered that one of the FA genes, *FANCD1*, is the breast cancer susceptibility gene *BRCA2*. At our recent Scientific Symposium, Arleen Auerbach of The Rockefeller University reported on 14 patients who are in this complementation group. She concluded that these patients are at very high risk for AML and solid tumors of the brain and kidney. These severe complications occur very early in the life of the patient.

Of the 14 patients, six had leukemia (five AML; one ALL). The median age for development of leukemia was 2.2 years, compared to 13.4 for the rest of the patients in the International Fanconi Anemia Registry (IFAR). All six patients had developed leukemia by the age of five. Four patients had brain cancer (medulloblastoma); two developed cancer of the kidney (Wilms tumor). The median age of the brain tumor patients was 3.5 years.

Auerbach noted that *BRCA2* carriers are also at high risk for the development of solid tumors. Four mothers had breast cancer. Auerbach recommends that carriers of *BRCA2* mutations who are planning children with a partner of Ashkenazi Jewish ancestry should consider undergoing genetic counseling, as *BRCA2* mutations are common in this group. ◆

Transplant Centers Report Protocols, Outcomes

Several transplanters who attended our August Family Meeting also updated attendees at the October Scientific Symposium. See *Newsletter #34* for a detailed description of the focus and results of stem cell transplants from these centers. A brief summary follows:

- The University of Minnesota has transplanted 11 FA patients with matched sibling donors, using a protocol that eliminates irradiation and uses T-cell depletion. All 11 patients survive with no GVHD.
- Memorial Sloan-Kettering has transplanted 12 FA patients with alternate (unrelated or mismatched related) donors; 11 of these patients were extremely high risk. Ten patients survive. Both non-survivors had a significant history of pulmonary disease and died post-transplant of pulmonary infection.
- The University of Minnesota has recently transplanted 39 patients with alternate donors. Of 18 patients considered "standard risk," 74% survive. Of 19 patients deemed "high risk," 25% survive. Going to transplant before age 18, prior to development of myelodysplasia or leukemia, prior to developing a gram-negative infection or fungal infection, and with a 6/6 donor, improves survival outcomes.
- Charité Hospital, Berlin, has performed 14 matched unrelated donor transplants, using busulfan and eliminating irradiation from the protocol. Nine of 14 patients survive. The greatest risk factor was progression to AML before the transplant. ◆

Transplant physicians Wolfram Ebell, Farid Boulad, Ingrid Kuehnle, Ricardo Pasquini, John Wagner, Margaret MacMillan, and Eliane Gluckman at the Scientific Symposium.

Laboratories Disagree on Characterization of FA Head & Neck Tumors

David Kutler, MD, New York University, and Ruud Brakenhoff, PhD, Free University Medical Center, Amsterdam, have reported very different findings concerning the nature of head and neck squamous cell carcinomas found in FA patients. Kutler examined head and neck tumors from 18 FA patients. In 15 of the 18 tumors, he found evidence of human papilloma virus (HPV). This finding raises the hope that vaccination against HPV may prevent development of head and neck tumors in some FA patients. However, Brakenhoff has studied cell lines from 4 FA tumors, and all are negative for HPV. In addition, all 4 of these tumors had mutations in the tumor suppressor gene p53, whereas none of the 18 tumors studied by Kutler had these mutations. Additional work needs to be done before these different findings can be reconciled. ◆

David Kutler, MD

Rudd Brakenhoff, PhD

Gelinas Receives *Distinguished Service Award*

Richard Gelinas, PhD, a member of the Scientific Advisory Board of the Fanconi Anemia Research Fund and a Senior Scientist at Celltech Group, received the Fund's *Distinguished Service Award* at the Presenters' Dinner during the Scientific Symposium in Houston in October.

In bestowing the award on behalf of the Board of Directors, Dave Frohnmayer, co-founder of the Fund, noted that Gelinas has been a full partner with the Fund since its inception. He was one of the attendees at the Fund's first Symposium, and he has served on the Scientific Advisory Board with dedication and distinction. Dave observed that Gelinas has been tireless and exceptionally valuable

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New Efforts to Reduce Toxicity in Sibling Transplants

Ricardo Pasquini, MD, Hospital de Clinicas, Curitiba, Brazil, reported on efforts to eliminate radiation and reduce the dose of cyclophosphamide in 120 FA patients transplanted between November 1983 and June 2003. Transplanters used four decreasing doses of cyclophosphamide, from 120 mg/kg to 60 mg/kg. Only patients with aplastic anemia (not myelodysplastic syndrome or leukemia) were selected, and all had matched sibling donors (except for two who had matched related but not sibling donors).

The best results were in the group of 30 patients who received only 60 mg/kg of cyclophosphamide. Survival was 100%. All had mucositis, which resolved in all cases. Fifteen percent suffered from acute graft-versus-host disease (GVHD); 14% from chronic GVHD. One patient lost his graft 600 days post-transplant. He is alive but transfusion dependent. Pasquini concluded that 60 mg/kg is the appropriate dosage for this patient population and that radiation can be safely eliminated. ◆


Ricardo Pasquini, MD

Recurring Clonal Chromosome Abnormalities

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Betsy Hirsch, PhD

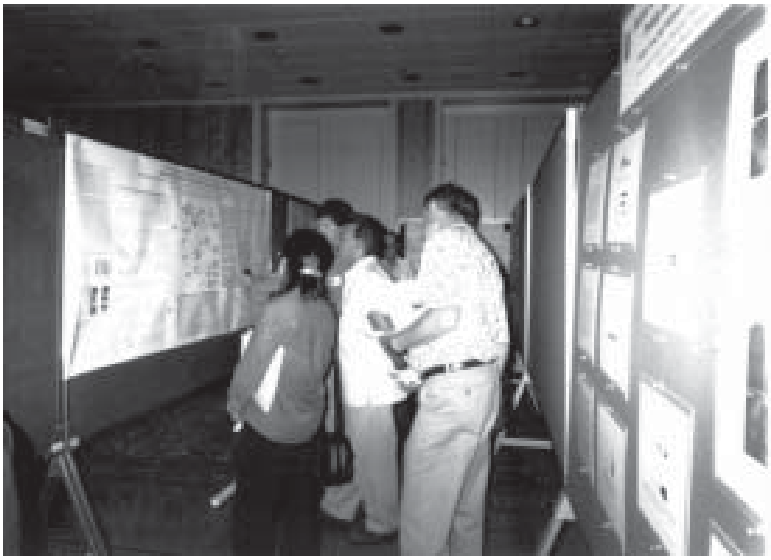
combination with other recurring chromosome abnormalities. With increasing age, there is an increase in the likelihood of developing an abnormal clone (the average age of those without a clone is 10.3 yrs; of those with an abnormal clone, the average age is 16.5 yrs.).

A significant correlation was also found between the presence of clonal abnormalities and the disease status of the patients. Of 26 patients with myelodysplastic syndrome (MDS), 24 (92%) had one or more clonal chromosome abnormalities. Of four patients with AML, three had complex clones with multiple clonal chromosome abnormalities. In contrast, among 49 patients with aplastic anemia but no evidence of MDS or AML, 40 (82%) had normal cytogenetics. These studies suggest a very strong clinical care precaution: the finding of any of the designated recurring chromosomal abnormalities, with the possible exception of the loss of short arm material from chromosome 7, and especially the abnormalities of chromosomes 1, 3 and 7, warrant very close clinical follow-up, as they may signal the development of MDS or AML. ◆

From the Poster Sessions at the Scientific Symposium

Forty-five researchers presented posters at the October Scientific Symposium. Several described case studies of individual FA patients whose experiences were unique or unexpected. A few short summaries:

- Jean-Hugues Dalle, MD, Sainte-Justine Hospital, Montreal, Canada, described an FA patient's successful pregnancies following transplantation. This 17-year-old was transplanted from her HLA-matched sibling. She received 500 cGy of irradiation. Thirty months post-transplant she had no menstrual periods, consistent with ovarian failure. However, 52 months after transplantation she delivered a baby boy and 66 months post-transplant she delivered a female baby. Although unusual, Dalle concludes that a normal pregnancy is possible after stem cell transplantation in some FA patients.
- Farid Boulad, MD, Memorial Sloan-Kettering Cancer Center, described a patient transplanted at age 9, using a protocol that included total body irradiation (TBI). This patient relapsed 7 1/2 months post-transplant with her own host cells and pancytopenia. She progressed to AML with 45% blasts in her marrow. She was transplanted a second time with high dose busulfan, fludarabine and no radiation. At 8 months post-transplant she had a fully reconstituted bone marrow with normal counts. Boulad concludes that high dose busulfan plus fludarabine can be well tolerated and should be considered for secondary transplants if TBI was first used, and possibly for primary transplants to avoid the use of TBI.
- Dr. Boulad also reported on an FA patient diagnosed at age 8 with low counts, who was put on androgens, then lost to follow-up. At age 34 she presented with numerous skin nodules, which responded to steroids. She was diagnosed with a significant B- and T-cell immunodeficiency. She received a bone marrow transplant from her HLA-identical sibling and had normal counts and no nodules 6 months post-transplant. ◆



Symposium participants discussing posters

Gelinas

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Richard Gelinas, PhD

in keeping abreast of the research relating to FA, reviewing grant applications, and assisting the Fund in setting its course regarding research funding directions. Dave expressed the gratitude of the Board of Directors for Gelinas' ongoing commitment to finding a cure and making life better for FA youngsters. ◆

Editors' Note and Disclaimer

Statements and opinions expressed in this newsletter are those of the authors and not necessarily those of the editors or the Fanconi Anemia Research Fund. Information provided in this newsletter about medications, treatments or products should not be construed as medical instruction or scientific endorsement. Always consult your physician before taking any action based on this information.

The Sixteenth Annual

International Fanconi Anemia Scientific Symposium

October 14 - 17, 2004

Hyatt Regency Hotel
Cambridge, Massachusetts

Scientific Symposium

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Signal Transduction; Bone Marrow Transplantation; Novel Therapies; Carcinogenesis; and Leukemogenesis.

At the Presenters' Dinner, Master of Ceremonies Dave Frohnmayer honored the discovery of the *FANCL* protein by presenting an Award of Appreciation to the following researchers: Ruhikanta Meetei, PhD, Zhijiang Yan, PhD, Chen Ling, MS, and Weidong Wang, National Institute on Aging; Johan de Winter, PhD, Annette Medhurst, PhD, Quinten Waisfisz, PhD, Henri van de Vrugt, PhD, Anneke Oostra, and Hans Joenje, PhD, Free University, Amsterdam; Colin Bishop, PhD, Baylor College of Medicine; and Michael Wallisch, PhD, and Maureen Hoatlin, PhD, Oregon Health & Science University.

Included as an insert in this newsletter is a listing of the Symposium oral and poster presentations. If you would like a copy of one or more of these abstracts, indicate your request on the enclosed form and return it to the FA Research Fund office or you may download the abstracts from the FA Research Fund website, www.fanconi.org. ◆

FAMILY NEWS

Repetition

by Kim Williams

There are five stages in the grieving process: denial, anger, bargaining, depression, and acceptance.

Most people accept that they will follow these stages after the loss of a loved one, the end of a marriage, or the diagnosis of an illness. Unfortunately, as a parent of a child with Fanconi anemia, our grieving process does not stop with these five stages. Instead, our grieving repeats these five stages over and over and over again.

My child is not dead or critically ill yet. But that does not stop me from grieving. I cannot forget that her thumb was not there when she was born. I cannot forget that she has to be monitored for blood counts, bone marrow, kidney, and thyroid function. Every time those tests are done, I go through the stages. As each test approaches, I deny that there is the possibility that this test will come back with a negative result.

I sit quietly listening as my colleagues complain about trivial issues that I wish I could have. I am angry that their lives seem so much easier and that they get to tuck their healthy kids into bed tonight, many not even aware of the terrible disease, Fanconi anemia.

I pray and plead and tell God that I will do anything if He can just make the doctor call back with good news. I feel a weight on my heart as I wait for the results. I suffer for my child, wanting a perfect, normal life for her, but knowing that all I can do is provide what is available. Hers is a life full of love, but also full of doctors, needles, tests, stress, pain, and crying. There is nothing I can think of that I would not do to make it better for her. Sometimes the sorrow is so overwhelming that I can think of nothing else. But as quickly as I am taken over by it, I am reminded of the beauty she has brought to my life, and I am again whole.

Kim and Abby Williams

Then, as always, I accept that I am her mother. I provide her with the support and love she needs. I remind myself that I have three months of reprieve because this month's counts are normal. I can then set the appointment for three months from now— and try to put it out of my mind again until then. But, of course, it does not go away; it just seems dulled for a few weeks.

The most amazing part is that this isn't just my family—I am part of a community of mothers. When another child is lost to this disease, the rest of us mourn right along with the mother and family. It is a reminder to me that I may be there one day. Their suffering brings back my five stages. Again I go through the process, wondering "why my baby"? Yet, I know that I would not wish Fanconi anemia on anyone else and that I am so blessed to have my child, with FA or not.

To all those mothers who grieve with me, may God bless you with short stages of grief and help you through when they seem to repeat too often. ◆

Use of Logo

This is just a reminder to our FA families: please use our logo or letterhead only after you have consulted the staff of the FA Research Fund and received their approval. This is necessary to be sure our messages are accurate and consistent. It also helps to avoid legal complications. We are happy to collaborate on fundraisers and mailings.

Our Transplant Experience

by Pat Gleason

"Ominous" is the smallest word to describe facing a bone marrow transplant. "WOW" is the biggest word to describe looking back at it. Amanda Gleason is 16 now. Eight years ago when she was diagnosed, FA children had little more than a prayer to get past transplant without a matched sibling donor. Survival was <25%. That was the reality.

When the reality of the diagnosis finally hit, I was at a loss. I could not function at work or home. I wallowed in self-pity. It was as if I was told my child died. What relieved me of my angst were prayers, friends, and fund-raising. Fundraising took much effort, focus, and time. We hosted "Beef and Beers," which were gala events and much fun. From 150 to 500 people showed up each year.

At Amanda's diagnosis, transplant was out of the question and androgens were the only real option. They gave us the time needed for transplants to improve enough to allow her a chance at survival. We attended the FA meetings and listened to the doctors.

Over the years, to avoid problems associated with androgens, the bugle call changed from androgens to transplant. Amanda developed a problem associated with androgens, hepatic adenoma. We expected this and were prepared. We started transfusions and other androgens that did not damage the liver as much. When the hematologist recommended that Amanda continue transfusions, I remembered Dr. MacMillan from Minnesota talking about "quality of life." I looked at Amanda and saw a vivacious 13-year-old reduced to receiving frequent transfusions. By having her life revolve around day hospital, her mind and spirit were not doing well. We had to go to transplant, and we had to go now.

We knew the FA transplant physicians and facilities, but which one to choose? We looked at protocols, facilities, and outcomes. We looked at experience, graft-versus-host disease and infection statistics. We even considered going overseas and would have gone, if it had been the right decision for us. In the end, we chose Dr. Farid Boulad at Memorial Sloan-Kettering in New York. This decision was hard but, with the benefit of hindsight, the right decision.

As we approached transplant, we expressed to Dr. Boulad our concern about the possibility of Amanda having a liver bleed from her adenoma, leading to her possible death. Dr. Boulad consulted with liver experts and with interventional radiologists. They recommended a procedure by which they would go into her liver through her femoral artery to block the blood flow to one rather large adenoma, causing it to shrivel up and die. This embolization, as it was called, would be less invasive than surgery and have less risk of infection.

Amanda's liver embolization was done, and the outcome was good. That changed three weeks later when an MRI revealed that the adenoma had returned. Another embolization was scheduled, which caused us to lose our 9½ out of 10 matched unrelated donor for the eventual transplant. Fortunately, there was another available, an even better 10/10 matched unrelated donor. The second embolization was more successful, and the adenoma was much reduced in size. It was time for transplant.

Amanda Gleason with Paul Butrico, New Jersey State Police Sergeant, her 10/10 Matched Unrelated Donor

December 12, 2002 was day zero. The worst day for me was 6 days earlier, total body irradiation. That was the day that I put my daughter at death's door and prayed that God would return her. But I knew that everything that was being done for her from that day forward was giving her a chance at a new life.

In terms of transplants, Amanda's was very "uneventful." No GVHD. No infection. No liver bleeding. Amanda is now 13 months post transplant. She is newly diagnosed with Type 1 Diabetes. We are not thoroughly convinced that this diagnosis will prove true, although it is being addressed. We don't know what this means in the long run, but a "long run" is something that Amanda never had a chance at before transplant. Now she does.

In no uncertain terms, transplant is horrible. To try to describe the process would do it injustice. Carole Siniawski's work on her son Jake's web page was of great assistance to us. I would

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Life After a Bone Marrow Transplant

by Matthew Abramov

This past February was the 21st year since my bone marrow transplant. My older brother Michael was my donor; he is my one and only sibling. When you think about the odds of a sibling bone marrow match, it truly was a miracle.

These days I live in Vermont with my parents; we have been here coming up on seven years. Originally we were from Long Island, New York, and I had my transplant at Memorial Sloan-Kettering in Manhattan. Even with a successful BMT I have had, and continue to have, difficulties due to graft-vs- host disease. Chronic dry eyes and avascular necrosis of both hips are my most troublesome conditions. [Editor's note: Avascular necrosis is death of bone tissue due to impaired blood supply, marked by severe pain in the affected region.] After seeking out doctors for relief of these conditions with little to no help, I have learned to live with this.

As for working and health insurance, that also has been a

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The Abramovs: Michael (brother), Peter (father), Matthew, and Donna (mother)

Transplant Experience

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recommend that everyone read through all of the pages. It helped us to prepare for transplant.

I know that Amanda is not cured. Her bone marrow is working great, and her biggest problem to date has been resolved for now. I know that cancer is on the horizon. I can see that the horizon is a long way off for Amanda, and that gives me joy.

I've been bubbly with joy ever since the FA Family Meeting last summer. Every year we went to the Family Meeting, looking for information. Every year we would cry individually and as a group as we remembered who had died during the year. This year was so different from all those past, in that we remembered those who died, but also saw those who made it past transplant. Even the recent diagnosis of diabetes has not diminished the good that I feel inside.

As a final note, I want to point out that Amanda was not the only one who went through transplant. Our whole family did. We are all different for the experience. As a family, we survived what is a horrible process. We did it with help and prayers from many and, by the grace of God, are here to talk about it. ◆

In Loving Memory

Amanda Chandler
10/16/79 - 10/24/03

Amy Gray
1/24/77 - 1/5/04

Audrey Hettinga
2/2/69 - 12/1/03

Tom Konikowski
5/31/87 - 2/17/04

Jake Shearer
11/8/81 - 10/24/03

Robert Sherman
6/9/93 - 1/16/04

Cade Smith
3/8/03 - 2/18/04

FUNDRAISING

Working for a Cure

by Kim and John Connelly

Evan Connelly and his sister, Claire

When the words Fanconi anemia first entered our lives about two years ago, we had all we could do to educate ourselves about FA and find Evan the best health care available. Gradually, we began to feel comfortable with our knowledge of FA, and Evan's initial baseline screenings developed into routine visits. We decided to make the trip to our first FA Regional Meeting in Minneapolis last May. On the 5-hour drive home, we discussed the experience and all the information that was presented to us. The one thing that we realized from that meeting is that research is progressing at an incredible rate and that it seems like we are so close to a cure. Still, the harsh reality is that the only way this research is going to continue to progress is with continued financial support.

We realized that we could not attempt fundraising alone. Our lives are hectic with Evan's FA, jobs, schools, classes for the kids, friends, and so on. So, we compiled a list of 20 of our closest friends and family members. When we asked them for help, not one wavered in the least to say they were one hundred percent on board! Since then, we have met once a month, and we are now five weeks away from our first "Evan's Enchanted Evening." It will be an elegant dinner dance with a live/silent auction.

Our families have published a cookbook that sold 500 copies in 4 weeks; we are now waiting for our second printing of the book. John's employer has sent a letter to every one of the company's suppliers, and the company is matching every dollar that is raised.

Our family members who live out of town are beginning efforts for another fundraising activity later in the year. When asked, our family and friends welcomed our request for help and were relieved that they no longer felt helpless. For us, we have grown closer to each one of them, and even some strangers, along the way.

One of the biggest obstacles that we have faced is keeping people interested and motivated after the initial impact of getting started. You cannot judge one person for devoting a lot of time to our efforts and another for only making it to one meeting. People have their own lives and families and, of course, that is their first priority. One of the things that we have done to keep everyone involved is to keep everyone informed. If there is something interesting in a newsletter or e-mail, we make a copy for everyone. We are sure to keep everyone abreast of successes and struggles. And, most importantly, we start each monthly meeting with a meal so that we can socialize before we get to work!

One of our biggest fears regarding fundraising was that we didn't want friends and family to feel as though we always had our hand out for donations. We constantly stress to anyone who will listen that thoughts and prayers are so appreciated and a means of effective support to us as well. There is a time and place for requesting a donation, and it should be done professionally and with appreciation.

Our decision to fundraise was not one we took lightly. We are learning as we go and that seems to be accepted by everyone. Fundraising has been a good deal of work, but also a great deal of fun. We have strengthened friendships and had many laughs. But one thing is for certain: we could not be more proud that our financial efforts are going to such a wonderful cause, saving Evan's life. ◆

A Very Successful Fundraising Letter

by Brian Horrigan and Amy Levine

Levine-Horrigan Family: from left to right, Lee Levine, Colin Levine-Horigan, Amy Levine, Delia Levine-Horrigan, Brian Horrigan, and Bob Levine

Many of you may have read our family's fundraising letter, which was posted to the FA Family E-group a few weeks ago. Here's the history of the letter:

We had been promising ourselves that we would do a fundraising project at least since 2000, the year after our daughter, Delia, age 16, was diagnosed with FA. A big fundraising event, as other families have been able to do, did not seem possible, but we thought we could at least pull together a letter to send to everyone we knew.

That, too, proved easier to imagine than to actually do. In the immediate wake of Delia's diagnosis, we did send out a broadcast e-mail, explaining what was going on and referring readers to the FARF website, but few contributions resulted. Then, in January 2002, we sent out one of our periodic New Year's letters, this one being the first real letter since the diagnosis. It was your basic "Christmas" letter, with general news, holiday greetings, a paragraph about Delia and FA, and an appeal for donations. Again, not many responses.

Like a lot of families, we were hesitant to make a direct appeal: asking for money is never easy, Delia leads a pretty normal life and does not appear sick, so why draw attention to it? But we decided we could mount a small campaign around our 25th wedding anniversary in 2003—perhaps pitch the idea of donating $25 to FARF as a commemoration and having a big barbecue at our house in St. Paul. We began to collect addresses of everyone who had been at our wedding so many years ago, adding them to our existing database. But, Amy and I are in the familiar "sandwich" generation, dealing with aging and ailing parents as well as rebellious and demanding teenagers. We learned that Amy's parents would need some major attention in the summer, so the party was suddenly out.

Our summertime campaign got moved to the end of the year. We beefed up our address database, adding neighbors (to whom we had never before felt a need to send newsy letters), co-workers (with home addresses, so we would not have to use workplace addresses), every family member we could find, and, of course, all of those wedding guests, many of whom we had not heard from in 25 years. It's hard to imagine doing this without the Internet and "people-search" features. We compiled a list of nearly 500 households. Our goal was to get a letter out in early to mid-November and—with the extraordinary help of the FARF office (laying out the letter, adding the photographs, dealing with our cumbersome database, stuffing and mailing all of the envelopes)—we succeeded. People got their letters just after Thanksgiving and right before the first wave of Christmas cards and year-end fundraising appeals.

The letter itself was not as hard to write as we thought. That old advice to budding writers—"write about what you know"—certainly applies here. FARF's guide to fundraising, with its sample letters, certainly helped. The message is clear: be direct, personal, and honest. Tell your readers that their donations can really make a difference—and can do so almost immediately. FARF's record of getting the money to where it can do the most good speaks for itself; you just have to get the word out. A picture of your FA child or your whole family (we added both) is always appealing. Our daughter

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Donations

Donations may be made to the Fanconi Anemia Research Fund, a 501(c)(3) organization, as follows:

- Online: Look for the Donations link on our home page (www.fanconi.org).
- Telephone: Call us at (541) 687-4658 or toll free (800) 828-4891.
- Mail: 1801 Willamette Street, Suite 200, Eugene, OR 97401

Family Fundraising Efforts

From January 1 through December 31, 2003, FA families raised $890,086 for Fanconi anemia research. Of that, the Frohnmayer family raised an astonishing $430,970. The Fanconi Anemia Research Fund simply could not exist without their total commitment to this effort and the unwavering support of their friends in Oregon and across the country.

We were encouraged this year that 114 other FA families stepped up to the plate and raised $459,116. Sixty-five of these families raised $500 or over. **This is the first time that all other families combined exceeded the efforts of Dave and Lynn**. We're delighted by this result and look forward to a continuation of the momentum! My heartfelt thanks to every single one of the FA families who joined with the Frohnmayers in writing a fundraising letter, making a personal donation, or holding a fundraising event in 2003.

The challenge, of course, remains because of the crucial work yet to be done and the cost of this very important research. If you did not raise funds in 2003 or would like to find a way to raise more, we very much need your help and would be pleased to assist you with fundraising in 2004.

$75,000 and up
Dave & Lynn Frohnmayer

$50,000 - $75,000
Audrey & John Barrow
Alan & Rachel Grossman
Kevin & Lorraine McQueen

$20,000 - $50,000
Christopher Scaff

$10,000 - $19,999
Laurie Strongin & Allan Goldberg
Brian Horrigan & Amy Levine
Charles & Katy Hull
Christie & Randy Kelley
Deane Marchbein & Stuart Cohen
Mark & Diane Pearl
Jeff & Arianne Pederson
Bob & Andrea Sacks
Erik & Lori Salo

$5,000 - $9,999
Randy & Nancy Bloxom
Joseph Chou
Andrew & Jennifer Gough
Beth & Jeff Janock
Tony & Lina Nahas
Jack & Lisa Nash
Fred & Nancy Nunes

$1,000 - $4,999
Vicki & Andrew Athens
Ken & Jeanne Atkinson
Mark & Linda Baumiller
Darryl Blecher & Diana Fitch
Donald & Danielle Burkin
Susan & Chris Collins
Brian & Margaret Curtis
Pat & Mary DiMarino
Antonino & Marie DiMercurio
Ed & Janice Duffy
Gene & Lynn Eddy
Stephen & Doreen Flynn
John & Martina Hartmann
Jeff Hoffman & Judy Hoffman
John & Karilyn Kelson
Robert & Jennifer Kiesel
Ayala Laufer
Eugene & Renee Lemmon
Eric & Beth Losekamp
Lynnette & Gregory Lowrimore
Peggy McDaniel
Sheila Muhlen
Robert & Mary Nori
Peter & Janice Pless
Dianne & John Ploetz
Jack & Tannis Redekop
Lynn & Rick Sablosky
Mike & Catherine Sanders
Bill & Connie Schenone
Brenda Seiford
Glen & Peggy Shearer
Karen Steingarten
Greg & Brandi Stuart
Mark & Susan Trager
Mike & Beth Vangel
Marc & Sandi Weiner
Kim & Michael Williams

Up to $999
Peter & Donna Abramov
Lily & Keith Baggett
Barbara Bedoya
Diane Bradley
Eric & Jennifer Bray
Richard Briga
Ed & Barbara Brookover
Joelle & Joachim Carvahlo
Lynnette Chandler
Tyler & Teresa Clifton
Elaine Cockman
John & Kim Connelly
Richard Day
Charles & Dahne Deeks
Carol Dillon
Nathan & Ann Eckstadt
Kay Eubanks
Ezat & Laila Faizyar
David & Mary Ann Fiaschetti
Susan Gannon
Gary & Melody Ganz
Mitzi Gerber
Pat & Maria Gleason
Beatriz Goris
Michael Greenberg
Mitchell & Tirzah Haik
Frank & Kelly Hamilton
Helen Healey
Roger & Eleanor Herman
Irene & John Kalman
Leardon Keleher
Shaid & Melvina Khan
Erik Kjos-Hanssen
William Knupp
Kayla Lackey
Peg LeRoux
Rene LeRoux
Gayle Licari
Bill & Jackie Lucarell
Allison & Steve McClay
Cecelia Meloling
David Meves
Jose Monroy
Griff & Cecilia Morgan
John & Betty Mozisek
Kenny & Lisa Myhan
Bob & Alice Nicolson
Ron & Fredi Norris
Kevin & Lorraine O'Connor
Robin Paulson
Leighsa & Stephen Perlish
Hal & Bobbie Porter
Ken & Margaret Ramsing
Pedro & Marina Ravelo
Marcia Reardon
Les & Nancy Ross
Glenn & Maureen Russo
Ron & Elesa Schaefer
Beatrice & Severt Score
Bryan & Karen Siebenthal
Connie Simpson
Jim & Carol Siniawski
Jeff & Debby Slater
Bruce & Kerri Timperley
Nancy & Reese Williams
Barry Wood

Journey with Jacob

by Rachel Grossman

Our journey with Jacob began in December 1998. After going through three long years of medical concerns, we found out that Jacob had been misdiagnosed and that he had FA. We soon found out that our daughter Talia was a match and, in May of 2002, we went to see Dr. Wagner at Fairview Hospital at the University of Minnesota. He stated that we should go to transplant over the summer, so we started the transplant process on June 26, 2002. Dr. Wagner and his team took every precaution to protect Jacob, and he went through the entire process with success. He left the hospital on Day 14, and we went home on Day 64.

We returned from transplant elated from all of the help that we received from the medical staff at Fairview, FARF, family and friends. We decided that we had to give back. Through many discussions, we decided to hold a fundraiser. Would it be a dinner theatre, formal dance or a dinner with a silent auction? After doing some research, we came up with the latter. Never in my wildest dreams did we feel that we would be raising $50,000. We had a small committee of friends that quickly rushed to make the event a success. Our goal was to try to obtain as many donated items as possible. The restaurant where the event took place donated the wine and the appetizers. One friend whose husband owns a family business generously donated all of the centerpieces, baskets of toys, which were later donated to the Ronald McDonald House. The entertainment was discounted, and the piano was rented. A friend who is a graphic designer did an incredible job on the "save the date" cards and the invitation.

All of the silent auction items were donated. A chef on our committee donated a catered meal, which sold for around $700. One committee member's husband is an editor at the Oprah show, and we were able to secure two tickets to the show. The most amazing thing on the auction list was a basket that had American Girl doll books. Our daughter, Talia, wanted this and made a bid for the item. No one wanted to bid against her, but one person asked me if he could make a bid for Talia. The books are worth $50 and sold for $500! We had so many donated items that we sold balloons for $10 that had prizes in them. We knew that not everyone could afford this event but could participate in the evening by buying a balloon without buying a more expensive silent auction item.

The other main factor in the success of the event was our Master of Ceremonies, Art Norman of NBC 5 News here in Chicago. He was incredible. Our night would not have been so successful without him. He energized the room!

There were few challenges with this event, almost as though it was meant to be. Most of the people involved outperformed themselves. We set out to raise $10,000 and raised five times that amount. The paper work was a hassle but, the more organized we were, the better the event went. When it was over, it took a while to come down from the excitement!

Our future with Jacob would not be possible without our family and friends beside us. We knew that it was our turn to give to others. Those who have been there before us have paved Jacob's path. They have given us the hope and understanding that we can make it though each and every day. Without that journey by other FA families and researchers, our present would not be the same. I do believe that our contributions to the FA Research Fund make a difference. We have seen the difference! What tomorrow will bring is unknown, but we love the smiles and the laughter that Jacob brings to us today. ◆

Fundraising Assistance

Almost all of the donations (85 percent) to the FA Research Fund are raised by FA families. If you are not now involved in raising funds for FA research, we very much need your help. The staff of the Fund will be happy to assist you. We'll help you write or edit your fundraising letter; photocopy it; provide the postage; and mail it from our office, using your mailing list. If you're going to hold a fundraising event, we'll provide similar help.

The FA Research Fund asks FA parents to make certain that any event they hold is covered by liability insurance. This insurance for a one-time event is often available through a family's homeowners insurance as a relatively inexpensive insurance rider. Please contact the Fund if you need assistance obtaining or paying for this required insurance.

When a donation is received, we'll send a letter of thanks from the Fund with a tax receipt, and we'll notify you that a donation has been made in your name. One request: Please ask your donors to write their donation check to the "Fanconi Anemia Research Fund."

Successful Fundraising

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Delia Levine-Horrigan

knew about and approved of what we were doing, but did not get involved in the whole process—which is her way of dealing with all of this.

The response was immediate, and continued throughout the holidays and into January (well past the tax-deduction cutoff). Our appeal brought in almost $20,000 in donations by the end of the year—very gratifying for a first-time effort. [Editor's Note: The Horrigan's fundraising letter raised $28,000 through February 12th!] We have heard from many people for whom our news was truly "new," and they really appreciated hearing about it. Clearly, our letter's personalized character set it apart from the other year-end appeals for donations that most of us receive, as does the status of FA as an "orphan" disease. In other words, if those of us who are affected by it don't do this work of fundraising, who will?

And, yes, we will be doing it again. We are looking for foundations or organizations that might be able to offer matching funds for the next appeal—and we would welcome any ideas or experiences of other families. ◆

Your FA Research Dollars at Work in 2003

During 2003, the Fanconi Anemia Research Fund awarded $953,336 in research grants to the following projects:

Investigator:	Ruud Brakenhoff, PhD, Hans Joenje, PhD, and Vincent van Beusechem, PhD, Free University, Amsterdam
Title:	Development of Virotherapy Using Retargeted Adenoviruses to Eradicate Preneoplastic Lesions of the Oral Cavity and Oropharynx
Amount:	$116,000
Investigator:	Grover Bagby, Jr., MD, Oregon Health & Science University, Portland
Title:	The Fanconi Anemia Transcriptome Consortium (addendum for genotyping)
Amount:	$51,920
Investigator:	Markus Grompe, MD, Oregon Health & Science University, Portland
Title:	Non-Viral Gene Therapy for Fanconi Anemia
Amount:	$213,017
Investigator:	K. J. Patel, PhD, MRCP, MRC Laboratory of Molecular Biology, Gonville and Caius Colleges, Cambridge University, Cambridge, UK
Title:	Biochemical Analysis and Structural Determination of FA E and D2 Proteins
Amount:	$88,172
Investigator:	Inder Verma, PhD, Salk Institute for Biological Studies, La Jolla
Title:	Gene Therapy for Fanconi Anemia Using Lentiviral Vectors
Amount:	$77,227
Investigator:	Margaret MacMillan, MD, University of Minnesota, Minneapolis
Title:	Immune Reconstitution and Opportunistic Infections after Unrelated Donor Bone Marrow Transplantation
Amount:	$90,000
Investigator:	Weidong Wang, PhD, National Institute on Aging, NIH, Bethesda
Title:	Identify New FA Genes and Understand the Disease Mechanism through Protein Association
Amount:	$192,000
Investigator:	Christopher Mathew, PhD, Guy's Hospital, King's College, London
Title:	Funding for Research Materials
Amount:	$9,800
Investigator:	Qishen Pang, MD, Cincinnati Children's Medical Center, Cincinnati
Title:	Role of FA Protein Complexes in Fanconi Anemia
Amount:	$60,000
Investigator:	Seidman, Michael, PhD, National Institute on Aging, NIH, Bethesda
Title:	Repair and Recombination Induced by Targeted Genomic Crosslinks in FA Cells
Amount:	$55,200

Mark Your Calendars

Regional Meeting
Monrovia, CA
Saturday, May 22, 2004

FA parents and adult FA patients are invited to this meeting, which will be held at the Four Points Sheraton Hotel, Monrovia. Presentations will include:

- Fanconi Anemia 101 and Cancer Epidemiology: Blanche Alter, MD, MPH, National Cancer Institute;
- Endocrinology in FA: Susan Rose, MD, Cincinnati Children's Hospital;
- Bone Marrow Transplantation: John Wagner, MD, University of Minnesota, and Joseph Rosenthal, MD, City of Hope Comprehensive Cancer Center;
- Head and Neck Cancer in FA Patients: David Kutler, MD, New York University;
- A tour of the Bone Marrow Transplantation Unit at City of Hope: Joseph Rosenthal, MD.

To register for this meeting, contact Suzanne Lauck at suzanne@fanconi.org or call 1-800-828-4891.

Annual Family Meeting
Camp Sunshine, Sebago Lake, Casco, Maine
Friday, August 13 - 17, 2004

Registration information for this meeting will be mailed to FA families by March 15, 2004.

Life After Transplant

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struggle. After earning a BA in Fine Arts from a reputable NY college, I tried very hard to find gainful employment both in New York and Vermont. I had also sought out help finding employment using state aid, but I had no luck at all. I am 4' 8" tall and still have the appearance of being a young teenager. I found that it was impossible to be taken seriously. So, after a period of time I decided to file for SSD. Benefits were finally awarded to me, and with SSD I am now eligible for Medicare benefits.

Certainly my health and place in this world could be improved, but I am grateful they are not worse. Hopefully one day there will be a cure for FA and many other genetic disorders. Until then, I wish all the people with FA in the U.S. and around the world the very best of luck. ◆

Fanconi Anemia
RESEARCH FUND, INC.

1801 Willamette St., #200
Eugene, OR 97401
phone: (541) 687-4658
(800) 828-4891 (USA only)
Fax: (541) 687-0548
e-mail: info@fanconi.org
web site: www.fanconi.org