



FA FAMILY NEWSLETTER

#39

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Researchers at the Fanconi Anemia Scientific Symposium ask questions of a presenter.

Seventeenth Annual Fanconi Anemia Scientific Symposium

The 2005 Scientific Symposium was held at the Intercontinental Hotel in Geneva, Switzerland from September 29 – October 2, the second time that the meeting was held in Europe. In 2000, the Symposium was held in Amsterdam and was highly successful in recruiting scientists from Europe to research FA.

One hundred eighty-six participants attended the three-day conference, including many researchers new to the Symposium. Researchers from Algeria, Argentina, Brazil, Canada, France, Germany, Japan, India, Israel, Italy, Poland, Spain, Switzerland, The Netherlands, the United Kingdom, the United States, and Turkey were represented. Oral presentations were made by 45 scientists, and there were 68 poster presentations. Topics covered included FA gene discovery, hematopoietic

stem cell transplantation, the function of FA proteins, carcinogenesis and leukemogenesis, and experimental therapeutics.

At the Presenters' Dinner, Hans Joenje, PhD, Free University, Amsterdam, whose lab has led the world in the discovery of FA genes, made an excellent presentation entitled *FA Research: A Retrospective and the Road Ahead*.

The evaluations of the Symposium were overwhelmingly positive. Evaluators remarked very favorably on the mix of basic science and clinical talks. One new researcher wrote that the Symposium was his "first one and I hope to be in the others. It was excellent since I've been studying this disease since my graduation. I'm so happy to be here...." Another wrote: "Excellent, as I came to the FA field from breast cancer. I should

note that the proportion of very good researchers per person is one of the highest in the field." And, from a researcher in the United Kingdom: "This conference is the first that goes in my diary. I rearrange teaching, home life, to ensure I am here." ♦

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Update on Transplants at Memorial Sloan-Kettering Cancer Center

Farid Boulad, MD, Memorial Sloan-Kettering, reported on 19 alternate donor transplants performed at his center from May 1998 through June 2005. Two patients were not included in survival data because their time post-transplant was not yet long enough to evaluate outcomes. Boulad's protocol included total body irradiation, fludarabine, cyclophosphamide, and the immunosuppressive drugs anti-thymocyte globulin and tacrolimus. Sixteen patients received peripheral blood stem cells with potent T-cell depletion; three received T-cell depleted bone marrow. Nine patients had mismatched related donors; 10

had unrelated donors. Ten patients had a history of infection; 10 had advanced disease, including myelodysplastic syndrome (5 patients) or acute myelogenous leukemia (5 patients). Fourteen had been transfused, and 15 had taken androgens prior to transplant. Four patients were older than 20.

Thirteen of 17 patients were alive at the time of Boulad's presentation (74%); 12 were alive disease-free (68%). No patient developed acute or significant chronic graft-versus-host disease. Three patients relapsed with leukemia; two of these patients died of their disease. Two patients succumbed to infections.



Farid Boulad, MD

Boulad noted that immune recovery was quite rapid in this population. These results are encouraging, given the compromised health status of these patients pre-transplant. ♦

Characteristics of FA Patients in Complementation Group J

Our Fall 2005 *FA Family Newsletter* brought news of two new gene discoveries: *FANCM* and *FANCI*. *FANCM*, along with 7 other known FA genes, is part of the "core complex" and functions upstream of *FANCD2*. This complex is still poorly understood, but is known to play a role in recognition and repair of DNA damage. Two genes are known to function downstream of *D2*: *FANCD1* (identical to the breast cancer susceptibility gene *BRCA2*) and now *FANCI*.

At our Scientific Symposium in Geneva, Arleen Auerbach, PhD, The Rockefeller University, founder of the International Fanconi Anemia Registry (IFAR), discussed the characteristics of patients in the FA-J complementation group, and

compared these patients to those in the other known downstream complementation group, FA-D1.

FA-J is a rare group, comprising only 1.6% of all FA patients in the IFAR. Auerbach has studied 11 FA-J patients to date, all of whom shared at least one copy of the same mutation in their DNA. Unlike patients in FA-D1 who develop malignancies prior to age 5, cancer risk appears much smaller in this group. Only one patient developed a malignancy (chronic myelomonocytic leukemia), which occurred during the teen years.

All of these patients in FA-J had major congenital malformations (all were short; 90% had radial ray defects; 60% urogenital defects; and 50% ear abnormalities, among other findings). On average, these patients



Arleen Auerbach, PhD

experienced bone marrow failure at age 5 1/2. ♦

Italian Transplant Center Reports Impressive Early Results

Franco Locatelli, MD, from Oncoematologia Pediatrica IRCCS Policlinico San Mateo, Pavia, Italy, reported on alternate donor FA transplants at his center. Fourteen patients from the ages of 2 to 17 were transplanted using a preparative regimen including fludarabine, low-dose cyclophosphamide and anti-thymocyte globulin. Patients did not undergo irradiation. The stem cell sources were bone marrow (9 patients) and peripheral blood stem cells (5 patients). Four donors were HLA partially matched relatives; their

grafts were T-cell depleted using positive selection of CD34⁺ cells. Nine of the 10 unrelated donors were very closely matched; unrelated donor grafts were not T-cell depleted.

Ten of the 14 patients were transfusion-dependent at the time of transplant. Patients did not have advanced disease (myelodysplasia or leukemia). All but one engrafted, and that patient successfully engrafted with a second donor. Five patients developed acute graft-versus-host disease (GVHD); one experienced extensive chronic GVHD.

Of the 14 patients transplanted, 13 are alive and well (93%). One patient died of an invasive fungal infection and GVHD. Mean time post-transplant is 2.5 years.

Additional patients and a longer follow-up are needed to assess the safety and efficacy of this approach. These early results, using a non-irradiation protocol and primarily closely matched alternate donors, are most encouraging and deserve further investigation. ♦

Transplant Update from the University of Minnesota

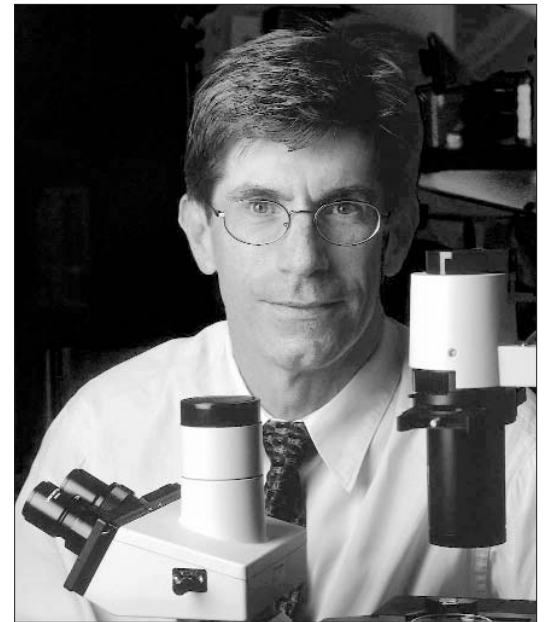
John Wagner, MD, discussed transplant outcomes and risk factors using unrelated or mismatched related donors at the University of Minnesota transplant center. Although matched sibling donor transplants are associated with a success rate of 100% at two years, transplants using alternate donors are more risky.

Beginning in 1995, Minnesota has used three different protocols with alternate donor transplants. Outcomes have significantly improved with each major change in the treatment plan. The first protocol (1995-1999), using cyclophosphamide (CY) and total body irradiation (TBI) resulted in a survival rate of only 31% at 6 years. A second protocol (1999-2004) incorporated fludarabine in addition to CY-TBI. The survival rate in 31 patients markedly improved with 58% alive at 4 years post-transplant. More recently, a third protocol was opened (August 2004), which used the same fludarabine and CY-TBI but with thymic shielding in order to protect the

thymus gland and potentially improve immune recovery. Fourteen patients were enrolled, with 76% alive at 1.8 years.

Over the past year, research has focused on the identification of risk factors that predict survival and the development of novel treatment strategies to improve further upon the transplant results. While androgens, transfusion history, and age have all appeared as risk factors in past alternate donor transplant analyses, current studies limited to recipients of fludarabine with CY/TBI (the standard treatment today) suggest that only a history of systemic fungal or gram-negative bacterial infection prior to transplant predicts poor survival. Without history of infection, the probability of survival was 77% at 4 years in the 31 patients treated in the second protocol.

In 2006, new trials with lower dose radiation, chemotherapy only and infusion of multi-potent adult



John Wagner, MD

stem cells (MASC) from the donor at the time of transplant will be explored. While the first trial with MASC will assess safety, researchers hope that MASC will reduce toxicity and improve survival. This is based on observations in lab models that MASC migrate to areas of tissue injury and effect repair. The latter study will begin in the second quarter of 2006. ♦

Cincinnati Transplant Expert Recommends FISH Analysis of Bone Marrow

Since the fall of 2002, Heidemarie Neitzel, PhD, Institute for Human Genetics, Charite, Berlin, has recommended that the bone marrow of FA patients be studied for a subtle abnormality on chromosome 3, which is closely associated with progression to myelodysplastic syndrome (MDS) or leukemia. Standard cytogenetic studies often miss this chromosomal abnormality, so Neitzel recommended that marrows also be studied using FISH (fluorescence *in situ* hybridization) in addition to standard testing.

Richard Harris, MD, Cincinnati Children's Hospital, confirmed this conclusion at the 2005 Scientific Symposium. Researchers in Cincinnati studied the incidence of clonal abnormalities in 87 FA patients using standard cytogenetic testing and compared these findings with an analysis using FISH.

Patients were sorted into three groups: Group 1 consisted of patients who had developed myelodysplasia or leukemia and also had abnormal clones based on standard cytogenetics. Group 2 consisted of patients with abnormal clones who had not yet developed MDS or leukemia, and Group 3 included patients with normal cytogenetics based on standard testing, who had not yet developed MDS or leukemia.

FISH was then used to probe for three specific abnormal clones: those involving 1q and 3q gains (extra copies of the long arm of chromosome 1 or 3), and those involving abnormalities on chromosome 7 (only one copy of the chromosome, which is called monosomy 7), or loss of the long arm of chromosome 7, which is 7q deletion. Of 44 patients who had abnormal clones based on standard testing, 27 had one or more

of the above abnormalities using FISH. **Among patients who had not developed an abnormal clone by standard cytogenetics, 14 of 43 patients had abnormalities of chromosomes 1, 3 and/or 7 based on FISH analysis.**

Patient survival was highly correlated with clonal abnormalities. For example, of the 21 patients in the first group, only 4 survive, all following a bone marrow transplant. Of the 43 patients in Group 3, 33 survive.

Harris concluded that 3q and 1q gains are seen in a large proportion of FA patients. When they involve >10% of the marrow, there is a strong correlation with progression to MDS or leukemia. Gains in 3q are more closely associated with MDS or leukemia than gains in 1q. In the Cincinnati series, gains in 3q preceded chromosome 7 abnormalities.

Standard testing is not sufficient to detect all serious clonal abnormalities. Harris strongly recommends performing a FISH analysis for 1q and 3q gains and for monosomy 7 and 7q deletions. ♦

Cancer Prevention Tested on FA Mice

Markus Grompe, MD, is using a mouse model to determine if different therapies might decrease malignant tumors in FA mice. He noted that no therapies currently exist which address the life-threatening problem of cancer in FA patients. Grompe's lab has produced a strain of mice with the mutant gene *FANCD2*. These mice develop malignant epithelial tumors at about one year of age.



Markus Grompe, MD

Grompe stated that the drug tempol (which has anti-oxidant properties) hastens tissue healing and is effective in delaying the onset of cancer in mice bred to be defective in another cancer-prone genetic disease, telangiectasia. It is believed that tempol reduces DNA damage induced by free oxygen radicals and thereby significantly slows down the process of tumor formation.

Grompe's lab has generated a large number of *d2* mice, and is treating half of the group with tempol and half with a placebo. After six months of treatment, the tempol treated mice had fewer tumors than the controls. Grompe is optimistic, but needs additional time before he can confirm these results. ♦

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.*

Clonal Chromosomal Abnormalities in FA

Betsy Hirsch, PhD, University of Minnesota Medical School, stated that detecting clonal chromosomal abnormalities and understanding their significance in FA patients is an important component of patient care. Hirsch studied 127 FA patients and found clonal abnormalities in 39%. Most abnormalities resulted in a loss or gain of chromosomal material; 79% of the abnormalities involved the long arm of chromosomes 1, 3 and/or 7. Frequently, chromosome 3 abnormalities were seen in combination with abnormalities of 1 and/or 7. In those cases, the first abnormality to appear was usually the gain of material on chromosome 3. Over time, patients developed secondary abnormalities. Notably, these clones were not transient; all persisted and many increased or evolved over time.

Hirsch tested patient bone marrows using three methods:

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Squamous Cell Carcinoma in FA Patients

In 2003, David Kutler, MD, New York University School of Medicine, published laboratory results indicating that squamous cell carcinoma (SCC) tumor samples from 21 FA patients out of 25 were positive for the human papilloma virus (HPV). This finding suggested that immunization against HPV might help prevent these cancers in FA patients. However, these data could not be confirmed by the study of Ruud Brakenhoff, PhD, Vrije Universiteit Medical Center, The Netherlands.

Brakenhoff studied ten SCC tumors from FA patients. These samples came from the following areas: head and neck (6); esophagus (2); and anogenital region (2). Only one tumor sample out of ten, an anogenital lesion, was positive for HPV. Analysis of genetic alterations such as p53 mutations that distinguish HPV from non-HPV-induced tumors confirmed the absence of HPV in these tumors.

Based on previous work, Brakenhoff stated that large precursor lesions usually precede SCCs. In the oral cavity these can present as white or red areas in the mucosa. The majority of these lesions, however, cannot be seen by the naked eye. A simple screening technique (obtaining brushed samples of the oral mucosa) can identify chromosomal changes characteristic of these lesions, and provide an early test for identifying non-invasive precursor lesions in the oral mucosa. ♦



Ruud Brakenhoff, PhD

National Cancer Institute Study of FA Patients

Neelam Giri, MD, Clinical Genetics Branch, National Cancer Institute (NCI), discussed results of an ongoing study of 45 FA patients at the NCI in Bethesda, Maryland. Specialists at NCI's clinics evaluated 21 patients; 24 responded by questionnaire only. The age range of this cohort of patients was 2-49, with a median age of 16.

Patients enrolled in this study experienced a much higher percentage of abnormalities than those reported in the literature. All 45 patients were evaluated for blood abnormalities: 82% had aplastic anemia; 38% with cytogenetics data had cytogenetic abnormalities; 19% had myelodysplastic syndrome, and 4%

developed leukemia.

Fifty-six percent of patients evaluated had hearing defects. Ear, nose and throat specialists evaluated 20 patients. Twelve of these patients had oral leukoplakia (white patches in the mouth); 4 had erythroplakia (red patches in the mouth); and 4 of 7 biopsies performed at NCI were positive for squamous cell carcinoma.

The endocrine evaluations of all 45 patients found that 69% had one or more endocrine disorders, including short stature, hypothyroidism, growth hormone deficiency and glucose intolerance, among other findings. Of 39 patients, 46% had elevated liver enzymes; one had a benign liver tumor. Reproductive study of 9



Neelam Giri, MD

females and 9 males revealed that 7 females had infertility and premature

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Weidong Wang Receives *Award of Merit*

At the FA Scientific Symposium in Geneva, Dave Frohnmayer, on behalf of the Board of Directors of



Weidong Wang, PhD

the Fund, presented Weidong Wang, PhD, National Institute on Aging, NIH, with the Fund's highest award, the *Award of Merit*.

In presenting the award, Frohnmayer recognized the exceptional contribution that Wang has made to the field of FA research through the discovery and elucidation of *FANCL* and *FANCM*. Because of his brilliant work, Fanconi anemia has advanced significantly into the much broader scientific arena of the cancers that affect the non-FA population.

Dr. Wang joins the distinguished group of Manuel Buchwald, PhD, The Hospital for Sick Children; Hans Joenje, PhD, Free University; Alan D'Andrea, MD, Dana-Farber, and Markus Grompe, MD, Oregon Health & Science University, past recipients of the *Award of Merit*. ♦

Researchers Receive *Discovery Award* for Complementation Group FA-B

As reported in the Spring 2005 edition of the *FA Family Newsletter*, researchers from Free University, Amsterdam, the National Institute on Aging, NIH, and Oregon Health & Science University collaborated on the discovery of the gene for the Fanconi anemia complementation group B and its unusual x-linked inheritance. In recognition of this discovery, Dave Frohnmayer presented the

Fund's *Discovery Award* to the following members of these laboratories: A. Ruhikanta Meetei, PhD; Marieke Levitus, PhD; Yutong Xue; Annette Medhurst, PhD; C. Michel Zwaan, MD, PhD; Chen Ling, MS; Martin Rooimans; Patrick Bier; Maureen Hoatlin, PhD; Gerard Pals, PhD; Johan de Winter, PhD; Weidong Wang, PhD; and Hans Joenje, PhD. ♦

Have All FA Patients Been Assigned to a Known Complementation Group?

No. Arleen Auerbach stated that 43 patients in the International Fanconi Anemia Registry (IFAR), or 7%, have not yet been assigned to any complementation group. In addition, Helmut Hanenberg, MD, Children's Hospital, Düsseldorf, Germany, has an additional 20 FA patients he is unable to assign to a known group. Hanenberg concludes that at least two more FA genes have not yet been identified. ♦

Researchers at First FA Scientific Symposium Honored

The first FA Scientific Symposium was held in Portland, OR, in 1989. From that meeting, the fledgling FA Research Fund received direction that set the pace for subsequent symposia and the research that has accelerated the science relating to Fanconi anemia. In gratitude, on behalf of the Board of Directors, Dave Frohnmayer presented the *Founder Award* to the following living members of that pioneering group: Blanche Alter, MD, MPH, National Cancer Institute*; Arleen Auerbach, PhD, The Rockefeller University*; Grover C. Bagby, Jr., MD, OHSU Cancer Institute*; Manuel Buchwald, PhD, The Hospital for Sick Children; Markus Grompe, MD, Oregon Health & Science University*; Richard Gelinas, PhD*; John Hansen, MD, Fred Hutchinson Cancer Research Center; Robb Moses, MD, Oregon Health & Science University; Giovanni Pagano, ScD, Italian National Cancer Institute*; Colin Sieff, MB, BCH, Dana-Farber Cancer Institute; Nasrollah Shahidi, MD, University of Wisconsin School of Medicine; Thalia Papayannopoulou, MD, University of Washington School of Medicine; and Margaret Zdzienicka, PhD, Leiden University Medical Center*.

* denotes researchers who were present in Geneva ♦



Some of the recipients of the Fanconi Anemia Research Fund Discovery Award for FANCF and FANCM.

Researchers Receive *Discovery Awards*

In September 2005, articles documenting the discovery of *FANCF* and *FANCM* were published in *Nature Genetics*. In recognition of those discoveries and the exceptional collaboration of FA researchers, the scientists whose work was published were honored at the Presenters' Dinner at the FA Scientific Symposium. On behalf of the Board of Directors, Dave Frohnmayer presented *Discovery Awards* to the following researchers:

- Paula Rio, PhD, Eunike Velleur, BS, and Helmut Hanenberg, MD, Children's Hospital, Heinrich Heine University, Düsseldorf, Germany;
- Thiyam Ramsing Singh, PhD and Amom Ruhikanta Meetei, PhD, Cincinnati Children's Hospital Research Foundation, Cincinnati, OH;
- Inderjeet Dokal, MD, Hammer-smith Hospital, Imperial College, London, UK;
- Shobbir Hussain, PhD, and Christopher Mathew, PhD, Guy's Hospital, King's College, London, UK;
- Elhaam Elghalbzouri-Maghrani, Wouter Wiegant, Barbara Godthelp, PhD, and Margaret Zdzienicka, PhD, Leiden University Medical Center, Leiden, The Netherlands;
- Claire Attwooll, PhD, and John Petrini, PhD, Memorial Sloan-Kettering Cancer Center, New York, NY;
- Wendy Bridge, Roger Franklin, Cassandra Vandenberg, and Kevin Hiom, PhD, MRC Laboratory of Molecular Biology, Cambridge, UK;
- Stacie Stone and Maureen Hoatlin, PhD, Oregon Health & Science University, Portland, OR;
- Jurg Ott, PhD, Kelly Milton, BA, Rashida Henry, MS, Sat Dev Batish, PhD, Sandra Barrall-Rodriguez, PhD, Orna Levrán, PhD, and Arleen Auerbach, PhD, The Rockefeller University, New York, NY;
- Kornelia Neveling, MS, Reinhard Kalb, MS, and Detlev Schindler, MD, University of Wuerzburg, Wuerzburg, Germany;
- Chen Ling, MS, Yutong Xue, and Weidong Wang, PhD, National Institute on Aging, NIH;
- Marieke Levitus, MSc; Jurgen Steltenpool, PhD, Martin Rooimans, Gerard Pals, PhD, Annette Medhurst, PhD, Patrick Bier, Yne de Vries, PhD, Quinten Waisfisz, PhD, Fre Arwert, PhD, Johan P. de Winter, PhD, and Hans Joenje, PhD, Free University, Amsterdam, The Netherlands. ♦

Use of Logo

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 step is necessary to be sure our messages are accurate and consistent and helps to avoid legal complications. We are happy to collaborate on fundraisers and mailings.

Blake Underriner

by Mary Underriner

Blake was diagnosed with Fanconi anemia when he was 14 years old. During a high school sports physical, we learned he had blood abnormalities. Six weeks after a diagnosis of myelodysplastic syndrome, we learned that he had Fanconi anemia. Most of the doctors he saw did not think that he had FA, because he had few of the characteristics. Two months after the diagnosis, on November 9, 2000, he had an unrelated bone marrow transplant at the University of Minnesota.

When he returned home from the transplant, we were able to find competent tutors for Blake while he recovered. High school is a challenging time in everyone's life, but Blake handled the re-introduction well.

After spending only six weeks at school during his freshman year, he returned as a sophomore. Many of his friends were unsure how to deal with him, but he did what he had to do and made his friends feel comfortable. The majority of his teachers were understanding and supportive.

Blake is now nineteen, a sophomore at Gonzaga University, and very healthy. However, he is constantly vigilant about his health. He is aware of what he needs to watch for and be aware of. He has had two visits to the ENT in the last two months. He has dermatologists in his home city of Billings, MT, as well as in his college city of Spokane, WA. He manages his own health. As his mother, I still am aware of the risks



Blake Underriner

and the signs of further cancers, but do trust Blake to take care of himself. He values his health and his life, and is very involved in bone marrow drives and *Relay For Life* events. ♦



Nikelle Schaefer and Cocoa Puff

Nikelle Schaefer

My name is Nikelle Schaefer. I am 35 years old and am afflicted with FA. I was diagnosed at the age of seven after becoming ill with a urinary tract infection. Blood work revealed low platelet counts, which led to further testing and the eventual FA diagnosis. I have had a healthy and medically uneventful life to this point. I was hospitalized and received a blood transfusion in January 2000 after contracting the flu. I was discharged after four days and have had no serious problems since. I have had colds and flu but always recover without medical intervention. I have yearly oral and gynecological examinations, none of which has revealed any abnormalities. My doctor also makes sure I receive a flu shot every fall.

I graduated from high school and went on to college where I received an AA degree in Library Sciences. After graduation I held several jobs, including librarian assistant. In 1998, as my blood counts began to decline [platelets 130,000 in 1980; 82,000 in 1993; 50,000 in 2000; and 45,000 now], I decided to quit working. My stamina was waning and working eight-hour shifts five days a week was becoming physically draining. I was also concerned about the exposure to germs in the library environment. With blood counts declining, it became even more of a concern that my immune system might not withstand a serious illness. It seems as though that was a good decision

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My Journey with Fanconi Anemia

by Danielle Sacks

The folks at the Fanconi Anemia Research Fund asked me to write about my journey with Fanconi anemia. It started at birth, because of my diminutive, full-term birth size; hands without thumbs; and arms which had no radius bones. None of my pediatricians felt there was anything wrong with me other than these skeletal issues.

At age five, my hand surgeon tried to centralize my wrist on my remaining ulna bone. Apparently, no one told him my platelets were down to 8,000. So, my heart stopped beating, and I was immediately pulled out of the surgery. I survived that scare, but my parents quickly took me to National Children's Hospital in Washington, D.C. It was there that a geneticist took one look at me and said "Fanconi anemia—you are a textbook case." Too bad my pediatrician had not read about that possible diagnosis in medical school. Of course, in 1979 not much was written about this disease, but I could tell my parents were not happy with the prognosis. I had a particularly virulent form of the FA-C gene, the IVS-4 mutation, predominantly found in descendants of Eastern European Jews.

During the next four years my platelets were so low that general bruising and bleeding of mouth, gums and nasal passages occurred frequently. My red cells finally began their descent, and my breathing became labored. A six-week trial with androgen therapy failed to rally my dying bone marrow. Fortunately, my brother's bone marrow was a 6/6 match, and I received a bone marrow transplant on January 23, 1984, a kind of re-birthday I still celebrate each year. After battling with fungal infections and exceedingly high temperatures, I was able to return home

after six weeks of hospitalization. The chemotherapy protocol at that time was quite toxic to FA patients, but somehow I managed to survive. I was kept sheltered from other people, even my 12-year-old brother, and schooled at home for over a year. My immune system is much stronger now, but I don't believe it is 100%.

We were thrilled with the success of the transplant but understood my very high risk for solid tumor cancers as a young adult. We, therefore, made regular trips to medical specialists like gynecologists, endocrinologists, dentists, and oral surgeons. While a teenager, I had a ventricular-peritoneal shunt placed in my head to drain cerebral spinal fluid that was blocked by a benign fatty tumor between the 3rd and 4th ventricle in my brain. We found out about that anomaly after my Dad unknowingly took me on the Mountain Railroad roller coaster at Disney World, and the seaweed in my brain (as my brain surgeon described it) did not enjoy the ride with us.

At age 19, my endocrinologist noted that my thirst and frequent bathroom trips were possible symptoms of diabetes, and a glucose tolerance test showed glucose levels in the 500's. I received multiple daily shots and glucose testing, and counted carbohydrates. My diabetes is much better controlled today, thanks to an insulin pump which provides insulin through my stomach 24 hours a day. However, my eyesight is poor, especially distance vision and depth perception.

My mouth has always been of concern due to widespread leukoplakia and erythroplakia, the white and red patches which often turn cancerous. At age 25, the first of these patches on my tongue was confirmed as an early stage squamous



Danielle Sacks

cell carcinoma; that patch is currently in remission after surgery. Other patches would later also prove to be cancerous. In the meantime, at age 28, squamous cell carcinoma of the vulva appeared. I was told by a doctor at NIH that I would need extensive surgery, removing several organs near the vulvar region. We discussed the possibility of radiation instead, but were informed that radiation was way too risky for FA patients. Fortunately, the tumor had not spread and after minimal surgery, it, too, is in remission.

At age 30, however, a more serious head and neck squamous cell carcinoma appeared at the back of my throat behind my pharynx. Six months after its removal by surgery via my neck, at the age of 31, a tumor showed up on my carotid artery and another one on my left neck lymph node. Now, we had to face another crossroads to decide whether carotid artery surgery was indicated. Our head and neck surgeon said that surgery presented a very high risk of a stroke. The alternative of radiation was also problematic. The literature on FA patients who had received radiation indicated

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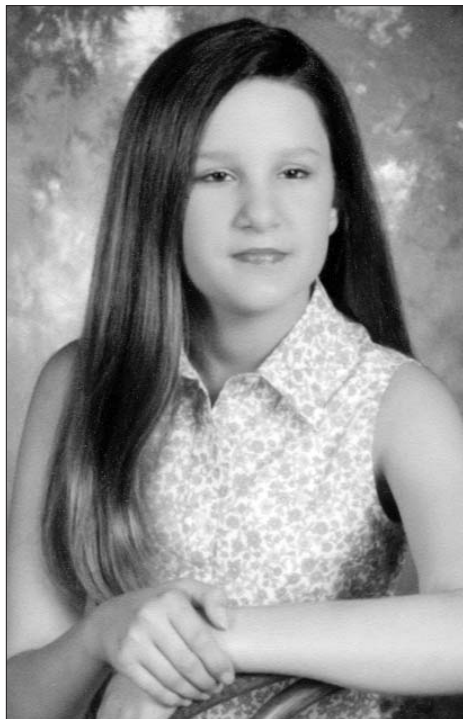
Life after Transplant x 2

by Pamela Heilig

Our family began our journey in dealing with Fanconi anemia in 1999. Both our daughters, Morgan (6) and Brea (8), were diagnosed between November 1999 and March 2000. Through a long process, we found the wonderful Dr. Farid Boulad at Memorial Sloan-Kettering, who agreed to proceed with their transplants.

We were blessed to have their fraternal aunt, Donna Williams, as their donor. Aunt Donna was a 5/6 match, which allowed us to proceed with a peripheral stem cell transplant for Brea in October, 2000. In 2003, we followed the same process again with Aunt Donna for Morgan.

Both the girls had their rough spots during transplant, but are thriving now. Of course, they are both considered "high medical maintenance." So what is normal now for our family? Things are certainly not as bad as they could be, but are still sometimes a little intense. But, not to



Brea Heilig

worry, we find a balance and have resumed some semblance of normalcy.

Brea and Morgan both have the genotype of *FANCG* which directly affects the endocrine system. Brea is 5 1/2 years post-transplant, and she has Type I diabetes, which requires her to have an insulin pump. Her thyroid numbers slide in and out of normal parameters (but no medicines yet), and she takes hormone replacement therapy which involves two medications. We continuously watch her mouth for leukoplakia which, thus far, comes and goes. Last, she takes medication for a lesion on her scalp. Her growth plate has closed, and she is a beautiful 4' 9 1/2", 80 pound, happy teenager in honors classes in high school with a 4.678 GPA. She is a cheerleader, loves horseback riding, and takes drivers education. Naturally, we go back to Memorial Sloan-Kettering for check-ups every six months.

Morgan is 2 1/2 years out of transplant, and she is adjusting to the sixth grade. She has been plagued with pulmonary problems which always result in pneumonia. She is on asthma medications and suffers from some emotional problems for which she takes medications. Due to this, we are seeking a tutor for her at school. Overall, Morgan is your typical 12-year-old, going to school dances and hanging out. She has an upcoming surgery to re-build her left ear drum to repair FA-related anomalies. Morgan is also followed every six months at Memorial Sloan-Kettering for routine check-ups.

Overall, our family has a very normal life. We have all just encompassed the little idiosyncrasies into our lives and know that things were once much worse. We look at each day with thankfulness to God for what he has done for us. We have



Morgan Heilig

learned to live in the moment and take nothing for granted. Life really can resume a degree of normalcy, maybe not to the degree it was prior to the diagnosis of FA, but to a degree that sure isn't bad! ♦

National Cancer Institute Study of FA Patients

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ovarian failure; 3 males had hypogonadism (low testosterone); and 5 had hypogonadism (small genitals). All 8 females tested and 4/5 males tested who were older than 18 years of age had osteopenia or osteoporosis. Of 45 patients, 11 had 12 cancers at a median age of 29, including five head and neck cancers, three vulvar, two skin, one brain tumor and one nasopharyngeal lymphoma.

Giri concluded that FA patients should be evaluated frequently in comprehensive subspecialty clinics to detect and manage the many complications that develop. Systematic screening for malignancies is critical for early detection and treatment of cancer in this population. ♦

Living with Fanconi Anemia

by Marcia Reardon

In 1987, at the age of 16, I was diagnosed with Fanconi anemia. Twelve years later, in 1999, I had a 6 out of 6 matched unrelated donor bone marrow transplant at the University of Minnesota.

Although I had a successful transplant, I have had several subsequent health issues. Shortly after transplant I was diagnosed with autoimmune hemolytic anemia, a form of graft-versus-host disease. As a result of treating the anemia with high doses of prednisone, I developed medicine-induced diabetes, several bouts of pneumonia, and severe osteoporosis that resulted in several collapsed vertebrae, causing me to lose seven inches of height. In addition to the vertebrae, I have developed necrosis in the hip and knees. To control the anemia, I have had my spleen removed.

I have also had two episodes of cancer. In the spring of 2000 I developed Epstein-Barr virus B-cell lymphoma in the small intestine, which required surgery to remove a segment of the intestine. In the fall of 2004 I developed thyroid cancer and had my thyroid gland removed.

Having said all of the above, I am now 35 years old, and I am doing well. I have not had any major health problems in over a year. I exercise regularly to help with my aches and pains in the back and joints. I have reduced my prednisone to 7 mg a day, and I no longer have diabetes. I realize that at any time something new could develop, but I will continue to enjoy what for me is good health with my family, friends, and pets.



Marcia Reardon

I, like all of you, hope that one day researchers will develop a cure for FA. Until then, I wish everyone afflicted with FA much luck. I also hope that my experiences can offer some hope to others who have FA. ♦

One Camper's Experiences at a *Hole in the Wall* Gang Camp

Becca Tzimmerman, age 23, had a bone marrow transplant at Memorial Sloan-Kettering in 2004 under the guidance of Dr. Farid Boulad. In response to a question on our listserv, she related her experiences attending a Hole in the Wall Camp in Connecticut:

To anyone who doesn't know about the *Hole in the Wall Gang Camp*, it's a great place. I went there for three years in a row when I was younger. There's a lot to do: horseback riding, fishing, canoeing, camping and playing all sorts of indoor and outdoor sports. There is a place for those who are creative to do a newsletter. You can write poems and short stories or whatever. There are crafts you can make. They have a pool. They have obstacle courses that you go through with your teammates.

Each child is assigned to a cabin by age. There is the red cabin, blue cabin, green cabin, and a yellow cabin as well. Best of all, there was the purple cabin—it was awesome!

There are special events each year for kids of all ages. There are clowns there. One of them is called "Noodle." She's funny. And there is a lady who pretends to be a fairy. She plays a flute for the kids if they want her to, just before bedtime. She also tells nice stories for the younger groups.

It's great. I wish I could go back there myself. I loved it there. ♦

Hole in the Wall Camps

Hole in the Wall Camps are the world's largest family of camps for children (usually ages 7-15) with serious illnesses and life-threatening conditions. They were the dream of actor Paul Newman, who started the first camp in 1988 and has been the driving force ever since. There is one adult for every two children, nurses who distribute needed medications, and specially trained counselors who can relate to the individual needs of the campers. These camps are free of charge. Unlike Camp Sunshine, they are for kids only, not families.

The Association of Hole in the Wall Camps
265 Church Street, Suite #503
New Haven, CT 06510
phone: 203-562-1203; fax: 203-562-1207
email: info@holeinthewallcamps.org
www.holeinthewallcamps.org

With Faith and Science: Our Pre-Implantation Genetics Diagnosis Experience

by Marina Ravelo

On November 26, 2005 the world welcomed Fabian Ravelo, who weighed in at 7 lbs., 9 oz., and was 21 inches long. After two long and emotional years, we had Ivan's matched sibling donor!

In November 2003, we got the call we had been waiting for: our mutations had been identified. We were able to proceed with Preimplantation Genetics Diagnosis (PGD). I immediately contacted my husband Pedro's insurance company and mine. Illinois is one of the states that covers *in-vitro* fertilization (IVF). We were both initially denied because we were not infertile and PGD was not deemed to be medically necessary. Pedro's company covered IVF for infertile couples, but not PGD. We wrote a letter explaining that we already had one child who was affected by FA and that the combination of IVF and PGD would almost guarantee that we could have a healthy child. After a couple of months, the insurance company agreed to extend benefits to us for the PGD and IVF.

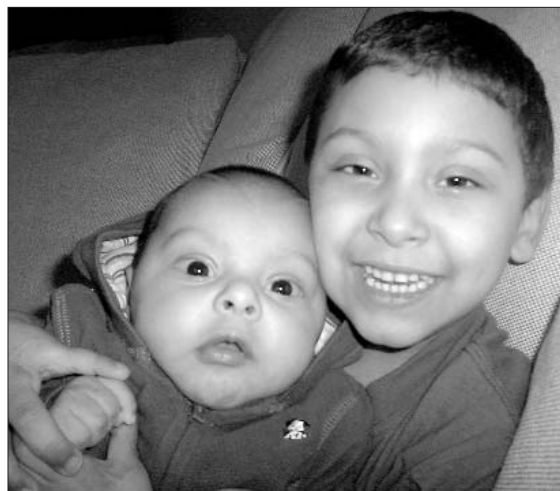
After the insurance was approved, we were referred to a prestigious Chicago hospital and quickly made an appointment to start the process. We explained that we wanted to have a healthy baby who could also become Ivan's donor. We were only the second family they had helped using PGD. That should have been a red flag to us, but we were assured that they were a great IVF group. In July that year, I started my hormone shots and produced about 13 eggs—not a great amount, but good enough. The embryos were biopsied, and we were told that we had three perfect matches. I thought I was dreaming when I heard that. It seemed too good to be true. We

transferred two of the three. As I sat on the table, already imagining the babies growing inside of me, the lab technician came in and gave me the lab report. The report clearly read "no FA, but HLA status could not be confirmed." I almost fainted. They had implanted two embryos that were not known to be matches! I could not believe how they could have gotten it wrong, since everyone at the clinic knew how crucial it was to have the embryos disease-free and HLA matched. They apologized, but all I could think of was that, if these embryos took, I could be pregnant with healthy twins who may not be able to help Ivan—and that I would not be able to try again until next year. In the end, these eggs did not produce a pregnancy. I was reassured that this would not happen again and that they would be careful next time. I truly believed they wanted to help us, so we continued with them. We tried again in September and in December, but had no luck. We were ready to continue, when I got a call from the IVF doctor. He wanted us to succeed and, since we had tried three times already with his clinic, he thought maybe we should seek another clinic. We agreed.

I called the Reproductive Genetics Institute (RGI) in Chicago. They were local, and all of the testing would be done in-house. We walked in with little hope, but were willing to try again. How could I not do everything possible to help Ivan? I had to keep trying. RGI did things a little differently, from the testing of the embryos and adjusting of my

medication. I started again in February 2005 and produced 20 eggs, the most I had produced. From the 20 eggs, 15 embryos were created. From those 15, only one was a perfect match. But there was a slight problem. The embryo was not growing at the pace the doctors would have liked. I began to cry. I was so sure this was a bust again. However, RGI still seemed optimistic. They transferred the one embryo and, 10 days later, I got the call I had been waiting for. I was pregnant, finally!

We ended up about \$15,000 in debt even with the help of insurance, but it was worth every penny. The road seemed endless. I tried so many things to help me get pregnant. I took up yoga to stay calm and focused through the rigorous shots and doctor appointments. I started eating organic food and had acupuncture done during cycles. I don't know if it helped in getting me pregnant, but I felt a little more in control. In the end, what I got for my hard work and perseverance was a beautiful healthy boy, the only person who could save Ivan's life! ♦



Fabian and Ivan Ravelo

In Loving Memory

Samantha Baber
11/3/90 – 1/7/06

Valeska Dietrich
6/24/85 – 12/27/05

Robin Moroney
8/8/63 – 12/20/05

Lindzy Westmoreland
3/3/83 – 8/17/05



My Journey with Fanconi Anemia

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a low probability of success, even though my Dad had been in contact with one FA adult patient who survived radiation for head and neck cancer a while ago and was still doing well.

After a second opinion with a surgeon at Memorial Sloan-Kettering who insisted that this type of cancer must be stopped by radiation, we went ahead with 7 weeks of treatments. The end result is that my esophagus is, at least temporarily, closed, and I have to eat through a stomach feeding tube, which leaks. In fact, it has been replaced or fixed eleven times, but still leaks. The good news is that it is a great weight reduction program! More importantly, however, my head and neck surgeon and otolaryngologist are absolutely amazed at how normal my previously cancerous and precancerous head and neck regions look after the radiation therapy.

I can also report that the gynecological surgeon who removed my vulvar cancer says that he has now treated two FA adult females successfully with radiation. I think we are finding out that technological advances in radiation machinery and therapy are allowing FA adults more options than we ever had before.

I can also tell you that my Dad is working hard as a board member of the Fanconi Anemia Research Fund to locate new therapies that could help repair our DNA to avoid cancer. He is also looking for clinical trials open to FA patients to secure even better opportunities to conquer their cancers and, along with the research funded by FARE, find cures for the cancers that threaten all people.

I want to thank all the donors to the FA Research Fund. You have made a huge contribution to the Fund's efforts to find cures for FA and extend our lives. The future for FA patients has never looked brighter. ♦

Nikelle Schaefer

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because I have remained healthy and have been able to travel a lot with my parents. We visited friends in Europe one year and just this summer traveled to New York, Ohio, Georgia, and Florida.

As a child my parents decided against any intervention, opting instead to monitor my blood, schedule regular doctor's visits, feed me a nutritional diet, and do all they could to limit my exposure to germs and disease. When I became an adult, I concurred with my parents' decision and have decided against a bone marrow transplant or androgen treatments. Not knowing what side effects I might experience is a serious concern for me. As previously mentioned, I have had no pain or suffering as a result of my FA and am not willing to tamper with my quality of life at this point.

About six months ago, my blood counts began to decline at a faster rate. I am now seeing my doctor once a month for blood work, and it appears that blood transfusions may be forthcoming. I am not feeling ill or weak, so only time will tell. Because it is the cold and flu season, I have avoided crowds and spent a lot of time at home, staying warm and enjoying my cat, Cocoa Puff.

I know FA can affect different people in different ways and our decision not to intervene may not be an option for others. I am only sharing my story as a means of showing how my parents and I have chosen to deal with the disease. ♦



Abby Williams

Hope Achieved

by Kim Williams

Our daughter Abby is four years old. She was diagnosed with FA in 2002. When people hear about Abby's condition, their first response is a desire to offer us hope. This past year we asked them to back that up with financial donations to the Fanconi Anemia Research Fund. By providing much-needed funds for research, they are giving us "hope." Hope for a long and happy future for our daughter.

On February 6, we hosted our first fundraising event, "Artisans for Abby." We had written fundraising letters for four years, with some success, but wanted to do more. This event raised more than all four of our letters combined. But, more than the money, Mike and I really did get the "hope" that our friends, neighbors, co-workers, and family wanted us to have.

Their generosity was amazing. Few people turned down our requests to come or, at least, buy a ticket. Our hope to have 30 auction items was quickly met and exceeded. On the day of the auction, we received more than 15 auction items, so that our total number of auctioned items exceeded 100. With all of these items, we not only raised money. We raised an awareness of Fanconi anemia in our community. We raised our spirits. And, we filled our hearts with hope for our future, for the future of the Fanconi Anemia Research Fund, and for the future of FA patients everywhere. ♦

Firefighters Hold Benefit for Will Bloxom

The Princess Anne Volunteer Fire Company (PAVFC) in Princess Anne, Maryland, recently held its Eleventh Annual Winter Banquet, with proceeds benefiting the Fanconi Anemia Research Fund in honor of Will Bloxom, the nephew of PAVFC Vice-president Keith Widdowson. The event featured a barbeque buffet, auction, and dance as well as an educational table with display boards and information about Will, FA, and the Fund. The event raised over \$10,000 for FA research. Will's family is most grateful to the PAVFC, donors, and attendees for a successful event.

From an early age, Will loved it when Uncle Keith took him to the fire hall to see the trucks, try on the gear, and hang out with the firefighters. He often rode in the fire trucks during the town's annual Christmas parade. In a heartfelt ceremony, PAVFC President Kenny Walston said they considered Will as one of their own. He presented Will with his own helmet and made him an honorary lifetime member of the Princess Anne Volunteer Fire Company. Will's uncle Keith spoke briefly about Will and FA. He effectively explained the concept of an orphan disease and stressed the importance of grassroots fundraising

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Princess Anne Volunteer Fire Company President Kenny Walston with Will and Randy Bloxom

AGIA Foundation Raises Funds for Fanconi Anemia

Pat Kilkenny, chairman of Arrowhead General Insurance Agency, Inc. (AGIA), Inc, has been touched by the plight of two separate FA families. An alumnus of the University of Oregon, who also has served as a Trustee of the University of Oregon Foundation, Pat knows Dave and Lynn Frohnmayer and has donated to the Fanconi Anemia Research Fund for years. Then, three years ago, his fraternity brother at the University of Oregon, Glen Shearer and his wife, Peg Padden, were suddenly confronted with FA when their oldest son, Jake, was diagnosed at age 21 with FA-related acute myelogenous leukemia. Sadly, Jake died at age 23 from complications of a bone marrow transplant. Always mindful of

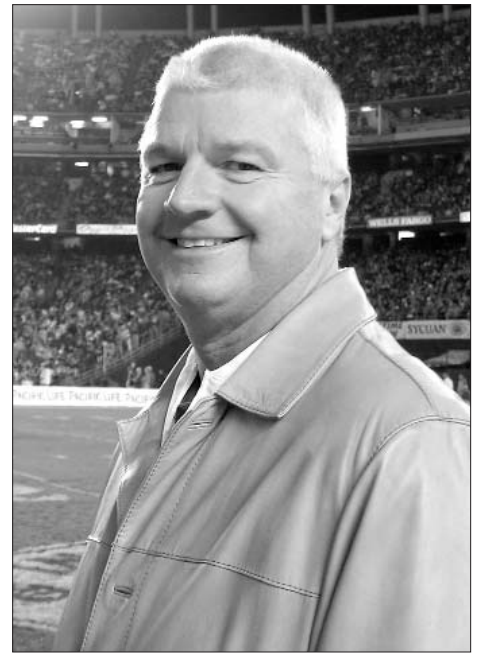
the importance of philanthropic service, Pat and his wife, Stephanie, decided to do everything they possibly could to help eradicate this disease.

“Stephanie and I are broken-hearted by our friends’ losses,” Kilkenny said. “Hopefully our collective efforts will help make a difference for the Fanconi Anemia Research Fund.”

Pat, along with other fellow Arrowhead employees, created the AGIA Foundation, raising money to benefit the FA Research Fund and St. Vincent de Paul charity, as well as other section 501(c)(3) medical research organizations.

The employees of Arrowhead and

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Philanthropist Pat Kilkenny

How You Can Help

Your donations have helped move this fatal disease from an orphaned status in 1989 to a disease with treatments that now buy precious time for FA patients. As the genetic basis of Fanconi anemia continues to be deciphered, your donations are also having an impact on the lives of millions in the general population. We continue to move to the mainstream of scientific interest. To help us in this fight, consider these ways to donate:

Gifts to celebrate an occasion: If you are celebrating a birth, a birthday, an anniversary, a graduation, a marriage or other gift-worthy event, consider asking that donations be made to the Fund in honor of the reason for the event.

Gifts to commemorate a loved one: Families who have lost a loved one may ask that a donation to the FA Research Fund be made in memory of the deceased individual. The Fund has received many thousands of dollars from caring people who have responded to obituary announcements.

Bequests: If you are preparing or reviewing your *Last Will and Testament*, consider making a bequest to the Fund.

Matching Gifts: Many employers will match the charitable gift of an employee. This is an excellent way to double your donation.

Gifts of Appreciated Property: Donors who have property that has gained greatly in value (stock, vacation homes, art items, etc.) can avoid tax liabilities and provide enormous support by gifting this property to the Fund. Please contact us for helpful advice and suggestions.

Sales on eBay: If you sell an item on eBay, you can designate that all or a portion of the proceeds be given to the Fund through their MissionFish program (www.missionfish.org).

United Way or Combined Federal Campaign: If you work for an organization covered by either of these organizations, consider making a donation via your workplace and asking your colleagues to do the same.

Donations Online: Look for the PayPal button in the Donations section of our web page (www.fanconi.org)

Donations by Telephone: Call us at (541) 687-4658 or toll free at (800) 828-4891.

Donations by Mail: 1801 Willamette Street, Suite 200, Eugene, OR 97401.

2nd Annual Valentine Fanconi Anemia 5K Run/Walk

by Peg Padden

It's hard to believe how different our lives were three years ago at this time. Our wonderful, caring, enthusiastic 21-year-old son Jake, who loved life more than anyone I've ever known, was a junior in college in Montana. He had rarely been sick a day in his life when he was diagnosed with Fanconi anemia. He needed a bone marrow transplant immediately. Although our youngest son Spencer was found to match Jake's bone marrow, doctors soon diagnosed Spencer with FA, too.

Sadly, all of you reading this know the feeling of absolute terror when receiving this devastating news. It was a nightmare which, unfortunately, did not go away. Somehow I had to muster up the strength to deal with this new life.

Jake's doctor gave us the FA newsletter—the same one you're reading right now. I had no intention of reading it. I couldn't. I just had to focus on taking care of Jake. I saw Spencer start reading it. I wanted to shout, "Don't read it!" but, of course, I didn't. I remember Spencer saying, "There's a support group for parents of kids with Fanconi anemia that you and Dad can join." I remember thinking that that is NOT a group I want to belong to.

As most of you know, Jake had a transplant a few months later and tragically passed away a few months after that.

All of you know that our hope lies in research, that research takes money and, if we don't raise money for FA research, no one else will. What I'm not sure you all know is that there is a benefit that goes beyond the money that I truly never would have imagined. That benefit is realizing that so many wonderful people out in the community

(beyond family and friends) are empathetic, kind, and generous, and really want to help.

I just organized the 2nd Annual Valentine Fanconi Anemia 5K Run/Walk in Portland, OR. I am happy with the amount of money we raised but, to tell you the truth, I'm equally happy with the incredible people I encountered along the way. I want to tell you about some of them:

When Spencer's doctor, Peter Kurre, heard about the 5K, he contacted OHSU's public relations people who sent out information to all the employees via e-mail. He then contacted a science reporter who put an article about us and the upcoming 5K in the *Oregonian* a week before the event, gave me the name of a group that might sponsor us (they did, to the tune of \$2,500), and suggested that I e-mail all the OHSU FA researchers there to invite them to join us. I did, and the response was phenomenal. One of the researchers, Maureen Hoatlin, put posters and brochures around campus and included a notice about the 5K in a press release about a new FA discovery (Yea!) in her lab. Approximately 50 FA researchers and their family members participated, including a whole group from Grover Bagby's laboratory wearing "Bagby Lab" T-shirts. I'm still somewhat floored by the whole thing!

When Jake was in 1st – 3rd grade, he had a very good friend named Katie. Jake changed schools after that and, as far as I know, never saw Katie again. Katie e-mailed me when she heard about the 5K and said she wanted to help. She was there the day of the event, cheering people on.

An 18-year-old girl e-mailed me saying she wanted to volunteer. She did, and she was great! A guy

e-mailed me saying he'd be happy to time people at the race and get it online afterwards. I was thrilled, since I had absolutely no idea how to do that. He brought his clock and PA system, so we didn't need to rent them, and he's going to help me organize things next year. Two other running guys I'd never met volunteered and were fantastic. After the run, a woman who's coached track for 25 years asked me if I'd like to have her help me organize it next year. Let me think about that...YES!!

The woman doing T-shirts asked me how to get on the bone marrow registry, participated with her family, and is going to volunteer next year with her ham radio group so if anyone gets hurt, they can get the word out.

When some banners I had posted advertising the race had to be moved because of sudden road work, the guy from the city took a collection in his office to help pay half of the cost to move them and the guy who put them up matched the other half.

A 5th grade girl at the school where I teach came into my classroom with her savings of \$62 (mostly in ones) a few days before the run. She asked me to give it to the doctors to help my son. She also told her pediatrician about the run, and he entered the race.

The point is: we're not alone in this effort to defeat FA. I realize now that, even though I obviously still wish I could go back to my old life, I know I can't. I'm going to do everything in my power to raise money to help Spencer and EVERYONE else out there with FA. And, I know that, among all the sadness in this FA world, there's really a tremendous amount of goodness in it too. ♦

Your FA Research Dollars at Work in 2005

During 2005, the Fanconi Anemia Research Fund awarded \$1,393,830 in research grants to the following projects:

Investigator: Ruud Brakenhoff, PhD, Free University Medical Center, Amsterdam, The Netherlands	Investigator: Patrick Kelly, MD, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
Title: <i>Genetic Progression of FA Squamous Cell Carcinoma and Development of a Non-invasive Screening Method for Precursor Lesions</i>	Title: <i>Gene Transfer for Patients with FA Genotype A</i>
Amount: \$265,800	Amount: \$101,196
Investigator: Johan de Winter, PhD, Free University Medical Center, Amsterdam, The Netherlands	Investigator: Duane Lehtinen, PhD, and Thomas Hollis, PhD, Wake Forest School of Medicine, Winston-Salem, NC
Title: <i>A Knock-Out Mouse for Fancm</i>	Title: <i>Crystallographic Studies of the Fanconi Anemia L Protein</i>
Amount: \$96,000	Amount: \$64,000
Investigator: Sara Fagerlie, PhD, Fred Hutchinson Cancer Research Center, Seattle, WA	Investigator: Sue Richards, PhD, Oregon Health & Science University, Portland, OR
Title: <i>Establishing an FA Canine Model</i>	Title: <i>Development of a Comprehensive Clinical Program for FA Diagnosis: A Molecular Approach</i>
Amount: \$75,246	Amount: \$172,307
Investigator: Laura Haneline, MD, University of Indiana School of Medicine, Indianapolis, IN	Investigator: Susan Rose, MD, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
Title: <i>Preclinical Analysis of Potential Therapeutic Agents Targeted to Enhance FANCC/- HSC Function</i>	Title: <i>Thyroid Hormone in Children with FA</i>
Amount: \$176,813	Amount: \$47,687
Investigator: Niall Howlett, PhD, and Thomas Glover, PhD, University of Michigan School of Medicine, Ann Arbor, MI	Investigator: Holger Tonnies, PhD, and Heidemarie Neitzel, PhD, Institute for Human Genetics, Humboldt University, Berlin, Germany
Title: <i>Role of the FA Pathway in the DNA Replication Stress Response</i>	Title: <i>Multi-Center Study for Correlating the Clinical Data with Clonal Aberrations in Mononuclear Peripheral Blood Cells of FA Patients</i>
Amount: \$152,972	Amount: \$101,688
Investigator: Hans Joenje, PhD, Free University Medical Center, Amsterdam, The Netherlands	
Title: <i>Cloning and Partial Characterization of FANCI</i>	
Amount: \$140,061	

Clonal Chromosomal Abnormalities in FA

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conventional (G-banded) cytogenetics, FISH, and a technique called comparative genomic hybridization (CGH). She concluded that conventional cytogenetics provided the most comprehensive analysis and should be the first choice for evaluation. FISH targeted to the long arm of

chromosomes 1, 3 and 7 provided increased sensitivity for the detection of small clones involving the most common abnormalities. Although CGH can pick up clones missed by the other methods, it is not able to detect clones that comprise only a small percentage (less than 10%) of the bone marrow.

Clonal abnormalities did not go away, and there was an association between the expansion or evolution

of clones and progression of disease. Only 4% of patients with normal cytogenetics had developed myelodysplastic syndrome (MDS) or leukemia. Of patients with abnormal clones, 67% had MDS or leukemia. Detection of abnormal clones signals the need for close surveillance of the bone marrow and can help guide treatment decisions. ♦

Family Fundraising Efforts

In 2005, FA families raised \$1,513,971 for Fanconi anemia research, breaking their record of last year by \$190,351! The Fund also received donations of \$10,942 through the United Way and \$6,821 through the Combined Federal Campaign.

FA families did a fantastic job this year in raising money for FA research. One hundred forty-two families raised funds and, of those, 86 raised \$500 or more. Six families raised \$50,000 or more. Of great importance, FA families combined (without the Frohnmayers) have increased their fundraising to the point that it now totals 60% of all funds raised, compared to the Frohnmayers, at 40% of the total funds. We are delighted that the burden of raising funds for FA research is now being borne by so many more FA families.

We extend our thanks to all FA families who have worked so hard to raise critically needed research dollars while simultaneously spending countless hours dealing with the personal anguish of Fanconi anemia. We are extremely grateful for each effort.

Our fundraising goal for 2006 is \$2 million. We're confident that, with your help, we can meet this challenge. Members of the staff of the Fund will be happy to help you with your fundraising efforts, as will the leaders of the FA Fundraising Teams.

\$500,000 and up

Dave and Lynn Frohnmayer

\$100,000 to \$499,000

Glen Shearer and Peg Padden

\$75,000 to \$99,999

John and Audrey Barrow
Kevin and Lorraine McQueen

\$50,000 to \$74,999

John and Kim Connelly
Alan and Rachel Grossman

\$30,000 to \$49,999

Stuart Cohen and Deane Marchbein

\$20,000 to \$29,999

Peter and Tara Himmelreich
Brian Horrigan and Amy Levine
Todd and Kristin Levine
Tanner and Jessica Lindsay
Mark and Diane Pearl

\$15,000 to \$19,999

Jeffrey and Donna Boggs
Des Murnane and Mai Byrne
Bob and Andrea Sacks
Mike and Beth Vangel

\$10,000 to \$14,999

Ken and Jeanne Atkinson
Chris and Susan Collins
Andrew and Jennifer Gough
Charles and Katy Hull
Reese Williams

\$5,000 to \$9,999

James and Tracy Biby
David and Kim Chew
Joseph and Nancy Chou
Ed and Janice Duffy
Jeff and Beth Janock
Jack and Lisa Nash
Fred and Nancy Nunes
John and Dianne Ploetz
Mark and Susan Trager

\$1,000 to \$4,999

Andrew and Vicki Athens
Cherie Bank
Mark and Linda Baumiller
Darryl Blecher and Diana Fitch
Randy and Nancy Bloxom
Mike and Kerrie Brannock
Donald and Danielle Burkin
Brian and Margaret Curtis
Donna DellaRatta
Pat and Mary DiMarino
Antonino and Marie DiMercurio
Lindsay and Sandra Dunn
Curt and Crystal Fales
Michael Glas and Carol Felmy
David and Mary Ann Fiaschetti
Stephen and Doreen Flynn
Allan Goldberg and Laurie Strongin
John and Martina Hartmann
Keleher, Lila
Kelly, Randy and Christie
John and Karilyn Kelson
Erik Kjos-Hanssen and Turid Frislid
Gregory and Lynnette Lowrimore
Dan and Nikki McCarthy
Gil and Peggy McDaniel

Tyler Morrison and Rachel Altmann
Sheila Muhlen
Tony and Lina Nahas
Robert and Mary Nori
Steve Perkins and Karen Magrath
Derek and Ginger Persson
Pedro and Marina Ravelo
Marcia Reardon
Rick and Lynn Sablosky
Ron and Elisa Schaefer
Bill and Connie Schenone
Irwin and Leona Selden
William and Mary Underriner
Ira and Terry Walker
Marc and Sandi Weiner
Kim and Michael Williams
Sean and Kristin Young

\$500 to \$999

Lezlie Chesler
Jeanette Clark
Tyler and Teresa Clifton
Dottie Day
Gary and Melody Ganz
Pat and Maria Gleason
Michael Greenberg
Robert and Jennifer Kiesel
Ayala Laufer
Eugene and Renee Lemmon
Gianna and Lauren Megna
Adam and Olivia Mindle
Griff and Cecelia Morgan
Ron and Fredi Norris

Up to \$499

Keith and Lily Baggett
Roger and Annette Bevelhymmer

John and Elaine Beyer
 Paul and Tracy Birchall
 Michael and Diane Bradley
 Richard Briga
 Jeff and Darlene Brunson
 Juan and Melinda Burgos
 Joachim and Joelle Carvahlo
 David and Paula Ceresa
 Floyd and Susan Clark
 Bill and Pat Danks
 Charles and Dahne Deeks
 James and Carol Dillon
 Nathan and Ann Eckstadt
 Gene and Lynn Eddy
 Sharon Ellis
 Frederic Engel
 Wendy Epps
 Nanette Vannostran Foster
 Cindy and Brian Gaudet
 Mitzi Gerber
 Maria Godwin
 Todd and Robin Gray
 Sean and Helen Healey
 Roger and Eleanor Herman
 Jeff Hoffman
 Greg and Gail King
 Krisstina King
 Sejin Kwon and Jee-ai Kim
 Peg LeRoux
 Michael and Myra Lewis
 Larry and Gayle Licari
 Eric and Beth Losekamp
 Steve and Allison McClay
 Kevin and Barbara McKee
 Charles and Cecilia Meloling
 John and Betty Mozisek
 Kenny and Lisa Myhan
 Louis and Virginia Napoles
 Kevin and Lorraine O'Connor
 Robin Paulson
 Leighsa Perlsh
 Freddy and Kathy Pharris
 Tom Plummer
 Lynn and Shirley Quilici
 Mario and Yolanda Ramirez
 Jack and Tannis Redekop
 Les and Nancy Ross
 Severt and Beatrice Score
 Thomas and Brenda Seiford
 Bryan and Karen Siebenthal
 Connie Simpson
 Jim and Carol Siniawski
 Chris and Amanda Smith
 Greg and Brandi Stuart
 Marge Zaborney ◆

Theta Chi Raises Funds for FA Research

The University of Oregon chapter of Theta Chi Fraternity raised nearly \$1,600 for the Fanconi Anemia Research Fund during its Fall 2005 Powder Puff Football Philanthropy. ◆



Fraternity brothers (l to r) Matthew Nuernberg, Mike Worthington, and Robbie McEachern present check to University of Oregon President David Frohnmayer, co-founder of the Fanconi Anemia Research Fund.

Fundraising Assistance

Did you know that 85 percent of the donations to the FA Research Fund are raised by FA families? Obviously, we need the efforts of everyone who reads this newsletter!

FA Family Fundraising Teams now exist on a regional level to assist our families with fundraising. If you are unsure how to contact your team leader, contact the FA Research Fund.

The staff of the Fund stands ready to assist each of you with your fundraising efforts. 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 will generate 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."

Our sincere thanks go to all of you for your efforts to raise funds to combat this devastating disease.

Firefighters Hold Benefit

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in battling an orphan disease. He commended the Fund for its outstanding stewardship of funds and remarked on the progress made since Will's diagnosis.

Diagnosed with FA in January 1998 at age 6, Will has since enjoyed remarkably good health. He has managed to live drug- and transfusion-free for eight years. Unfortunately, Will's counts have now declined to a critical level, and his only suitable unrelated bone marrow donor is approaching the maximum allowable age. For these reasons, a bone marrow transplant is being planned for this spring at Memorial Sloan-Kettering Cancer Center in New York City. To stay updated about Will's progress, you can visit www.awill2live.com. ♦

AGIA Foundation Raises Funds

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American Claims Management have made a major commitment to give to charitable causes. In 2005, employees from both companies donated their personal funds and they went into the community to fundraise, competing with each other through car washes, various baked good sales and a marathon sponsorship. These efforts were wonderfully successful, and the Kilkennys and Arrowhead matched the funds raised.

In 2006, the company will continue the outstanding work of the employee-driven fundraising. In addition to these efforts, the AGIA Foundation will be holding the First Annual Golf Classic at La Costa Resort, just north of San Diego. The Golf Classic will take place on April 24, 2006. ♦



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Anemia**

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