

FA FAMILY NEWSLETTER

#32

A Semi-annual Publication of the Fanconi Anemia Research Fund, Inc.

Fall 2002



FA Family Meeting Returns to Camp Sunshine

Forty-three FA families converged on Camp Sunshine on the shores of Sebago Lake, ME, for the 12th Annual FA Family Meeting. Families who had attended the Family Meeting at Camp Sunshine in the mid-90s were delighted with the complete renovation of the facility. A beautiful new conference center which symbolically welcomed young, teen, and adult FA family members with small, mid-size, and large doors provided an excellent site for the scientific program as well as for the activities for the youngsters. Old-time families were delighted to find that the trailers of years past had been replaced with sparkling new living units. Perhaps most impressive, however, were the volunteers who greeted families, tuned into their needs, and did everything possible to make the Camp Sunshine experience a wonderful one

for our group. From all accounts, they succeeded admirably.

Families wasted no time renewing old acquaintances and, for the new families, marveling that they were actually meeting other FA families. Camp Sunshine staff organized many activities to help families get to know one another, including hosting a banquet for the parents, complete with candlelight, white tablecloths, and prime rib. A karaoke program topped off that particular evening. FA children and their siblings seemed to enjoy every minute of their activities, which included arts and crafts, a sleepover, a masquerade ball, and a stage show. Families were also able to pay their respects to deceased FA family members during the Memorial Balloon Release. A special lakeside memorial service for Travis Massino

continued on page 17

The Breast Cancer Gene, *BRCA2*, is an FA Gene, *FANCD1*

In one of the most important FA science developments of recent years, researchers have discovered that one of the FA genes is also a known cancer susceptibility gene.

The June 2002 issue of the journal *Science* printed an article entitled "Biallelic Mutations of *BRCA2* Cause Fanconi Anemia." This article documents the discoveries made by the

continued on page 24

HIGHLIGHTS

Clone with Chromosome 3 Abnormality Predicts MDS, AML in FA Patients	2
John Wagner Reports on Transplant Outcomes, Stresses Importance of Timing.....	3
Harris Reports on Transplant Outcomes	3
Preimplantation Genetic Diagnosis	4
Family News.....	10
FA Regional Meeting	18
Fundraising	19

MEDICAL NEWS

Clone with Chromosome 3 Abnormality Predicts MDS, AML in FA Patients

Wolfram Ebell, MD, of Humboldt University, Berlin, stunned many at the Family Meeting with the news that a clone with a subtle abnormality on chromosome 3 can predict the evolution to myelodysplastic syndrome (MDS) or acute myelogenous leukemia (AML) in FA patients. This abnormality, characterized by duplicated material on chromosome 3, always appears in the same location on this chromosome. It is not detected by routine cytogenetics, but rather by a process called spectral karyotyping. More than half of the patients considered normal on a cytogenetics analysis had this

abnormality on chromosome 3. Unlike other clonal abnormalities in FA patients, this clone never disappears, but becomes progressively more prevalent and often leads to monosomy 7, a clone often associated with AML. The risk of MDS or AML is 90% for patients who exhibit this particular clone. Eighteen of 53 FA patients tested by a Berlin laboratory were positive for this clone. This clone can be followed in the blood as well as in the bone marrow. Ebell believes that the presence and progression of this clone can help patients plan the timing of a bone marrow transplant. ♦



Wolfram Ebell, MD

Walsh Presents Gene Therapy Trial Update and Plan for Future Trials

Christopher Walsh, MD, University of North Carolina Gene Therapy Center, presented results of his gene therapy trial for FA patients in FA-A. Four patients enrolled in this trial. Two and a half years after gene transfer, one patient has had a significant increase in the number of peripheral blood cells carrying the *FANCA* gene.

Several factors have impeded the success of this trial. Walsh used a retroviral vector to transport the corrected gene into stem cells. This vector can enter only dividing cells, thus correcting a small proportion of stem cells. In addition, all FA patients, despite age and blood counts, have significantly fewer stem cells (10 to 100 times fewer) than the normal population. Walsh states we need to

identify additional sources of stem cells and find better vectors to carry the corrected gene into these cells.

Walsh's lab has developed several new lentiviral vectors, which appear to be far superior to his retroviral vector. He has corrected the FA defect in mice using these vectors. Based on this data, he has received approval from the National Gene Vector Lab to manufacture these vectors for a clinical trial. He now needs approval from the FDA to initiate a clinical trial. Walsh's laboratory has also identified a new population of cells that act as hematopoietic stem cells. He is presently studying the potential of these cells to expand after gene transfer. By next year, Walsh hopes to have treated several FA patients in FA-A using this new approach. ♦

FA Research Fund Supports Work on Adult Stem Cells

During the past year, FARF has given two grants to the University of Minnesota to study the potential of multipotent adult stem cells (MASC) as a novel treatment for patients with FA. Drs. Catherine Verfaillie, Bruce Blazar and John Wagner are collaborating on these studies.

MASC cells can be isolated from the bone marrow. They can be grown in large quantities and can differentiate into a variety of different cells and tissues (*e.g.*, liver, gut, lung). It is conceivable that MASC cells could correct both the diseased bone marrow and other tissues in an FA patient. These cells might help repair damaged tissue following a bone marrow transplant. It is possible that these cells might help prevent or treat cancer in FA patients. ♦

John Wagner Reports on Transplant Outcomes, Stresses Importance of Timing

Between April 1999 and April 2002, seven FA patients have undergone matched sibling donor (MSD) transplant, and 36 patients have undergone matched unrelated donor (MUD) transplant at the University of Minnesota. Radiation has been eliminated as part of the protocol for MSD transplants; all seven MSD patients survive.

Of the 36 patients receiving unrelated transplants, 25 were standard risk patients. These patients had aplastic anemia or early myelodysplastic syndrome (MDS). A patient with an abnormal clone but less than 5% blasts in the bone marrow is considered standard risk. Patients were infection-free and under the age of 18. Of these 25 patients, 81% survive. In contrast, only 33% of patients with high-risk disease, defined as those with recurrent infections, poor organ function, or older age, survive. For patients with advanced MDS or acute myeloid leukemia, only 20% survive.

Given the promising outcomes for patients with matched sibling donors and for standard risk patients, Wagner believes that these patients should go to transplant before the development of leukemia, advanced MDS or infection. This group of patients should consider transplantation before undergoing androgen therapy. The transplant should be considered (meaning that a donor search should be initiated) when one of the following occurs: ANC consistently below 1000; hemoglobin below 10; platelets below 30,000.

However, patients with high-risk disease (recurrent infections, poor organ function or older age) should delay transplant, with the hope that new therapies may become available.

These patients should consider androgen therapy, hematopoietic growth factors such as G-CSF, and transfusions. Patients with advanced MDS or leukemia should go to transplant since new approaches may improve present outcomes.

The University of Minnesota has developed two new treatment protocols especially for high-risk patients. See the article by Wagner and Margaret MacMillan in the *Science Letter* for a detailed description of these new approaches.

In the past, factors such as mosaicism, prior use of androgens, and blood transfusions appeared to decrease the likelihood of surviving a



Drs. Wagner, Harris, and Ebell respond to questions from FA parents after their individual presentations.

bone marrow transplant. Wagner stated that, with the use of fludarabine, these might no longer be risk factors. However, transfusions pose a transplant risk when patients suffer iron overload. If iron levels are high, patients need to be on desferal. Wagner has found no evidence that physical malformations increase the risk of transplantation. ♦

Harris Reports on Transplant Outcomes

Richard Harris, MD, Cincinnati Children's Hospital, reported on bone marrow transplant outcomes at the August Family Meeting. Twenty-nine patients received marrow from a matched sibling donor. Patients received low-dose Cytoxan and thoraco-abdominal irradiation (400 cGy). Follow-up is from one month to 13 years. Of 29 patients, 24 are alive; projected 5-year survival is 86%.

Harris reported on 12 alternative (not a matched sibling) donor transplants at Cincinnati utilizing their new fludarabine-based regimen. The preparative regimen consisted of low-dose Cytoxan, total body irradiation (450cGy), anti-thymocyte globulin (ATG) and fludarabine. Six patients had been on androgen therapy. Seven patients had a 6/6 match; 5 had a 5/6 match. Five patients received bone marrow; 7 received peripheral blood stem cells (PBSC).

Eight of 12 patients are alive, with follow-up from one to 35 months. Six of seven patients receiving PBSC are alive, and none experienced graft-versus-host disease (GVHD). Of the 5 patients receiving bone marrow, three experienced significant GVHD and two survive.

Opportunistic infections were frequent, in spite of efforts to prevent this complication. Three patients died of infection; one patient died of pulmonary failure plus infection.

Based on his experience, Harris prefers PBSC to bone marrow. With PBSC he is able to harvest a very large dose of stem cells, reducing the risk of graft rejection. At his center, the PBSC collections can be more thoroughly depleted of T-cells than bone marrow collections, thus reducing the risk of GVHD and improving outcomes. ♦

Preimplantation Genetic Diagnosis

Mark Hughes, MD, Wayne State University, spoke about Preimplantation Genetic Diagnosis (PGD) at our Family Meeting. Researchers began to work on PGD 13 years ago, in response to the need to diagnose genetic diseases in fertilized eggs before a pregnancy occurred. This procedure can also be used to test for HLA antigens, thereby determining if a pregnancy might provide a matched sibling donor for a later transplant. Through the technologies of PGD and *in vitro* fertilization, several thousand healthy babies have been born.

Fertile couples are sent to a clinic dealing with infertility problems. The mother takes hormones, which

stimulate her ovaries to produce multiple eggs. The eggs are collected, fertilized with the husband's sperm, and allowed to grow for three days, dividing from one cell to 8 cells. One cell is then removed from each blastomere (pre-embryo), and tested for HLA antigens and the absence of the genetic disease. With FA, there are 3 chances in 4 that a blastomere will be free from FA, and 3 chances in 16 that any one blastomere will be free from FA and will be an HLA-matched donor for an FA sibling.

Hughes, working in collaboration with Arleen Auerbach, PhD, The Rockefeller University, and John Wagner, MD, University of Minnesota, has worked with many

FA families from complementation groups A, C and G. Several mothers of FA children are pregnant with healthy fetuses and transplantation matches.

Cost of this procedure depends greatly on the cost of *in vitro* fertilization at a given clinic. These costs (per attempt) vary from \$11,000 in New York City to \$4,500 in some clinics in the Midwest and Canada. Some health insurance companies have begun covering the cost. Success of PGD varies from one *in vitro* clinic to another, and parallels the success of that clinic's *in vitro* fertilization program for all couples. Most clinics now have success rates between 45% and 50% per IVF attempt. ♦

FA and Cancer Closely Linked

Alan d'Andrea, MD, Dana-Farber Cancer Institute, stated that by focusing on FA, a rare disease, scientists will learn a great deal about cancer in the general population. In several respects, cancer cells resemble FA cells. Under the microscope, cancer cells have a similar appearance to FA cells. The chromosomes in cancer cells break and fuse back together in the wrong places. Chromosomes in FA cells also break and fuse inappropriately in response to DNA damage. D'Andrea believes that if we can find out what causes chromosomal breaks in FA, we would learn a great deal about what causes cancer in general.

D'Andrea discovered two years ago that the FA genes work directly with the breast cancer genes to repair DNA damage. Last June, he announced the exciting discovery that the cancer susceptibility gene, *BRCA2*, is also a Fanconi anemia



gene, *FANCD1*. D'Andrea suspects that FA-D1 carriers with certain disease mutations have an increased risk of developing cancer.

D'Andrea believes that the connection of FA with cancers in the general population will help speed FA research. A great deal is already known about the breast cancer susceptibility genes; this knowledge now has direct relevance to FA. Drugs designed to benefit FA patients should help patients with some cancers. ♦

Researchers Request Blood, Bone Marrow

Laboratory research is critical to the development of new clinical trials. Research depends on the availability of patient marrow and blood. At our recent family meeting, Chris Walsh requested bone marrow samples, and John Wagner asked for blood and bone marrow. If you are planning to do a routine CBC or bone marrow aspiration in the near future, please seriously consider donating a small additional sample for research. Contact one of these labs for information on how to send a sample:

Christopher Walsh
University of North Carolina
phone: (919) 966-9116
e-mail: cwalsh@med.unc.edu

John Wagner, MD
University of Minnesota
phone: (612) 626-2961
e-mail: wagne002@umn.edu

Hand and Arm Differences in FA

Scott H. Kozin, MD, of Shriners Hospital for Children, Philadelphia, described the arm and thumb anomalies that affect many FA patients, and discussed therapies that can improve the function of the hands and arms. In an FA patient, the radius (a bone in the forearm) can be incompletely developed or entirely missing. All patients with this complication need treatment.

The initial treatment for the absent radius is stretching, both by the therapist and the caregiver. Splints are used to maintain the hand in a straight alignment. Without treatment, the hand will develop a perpendicular relationship to the forearm. In very young children, stretching is usually recommended every diaper change and is crucial to the overall success of treatment.

In patients with a missing or incompletely developed radius, the only substantial bone in the forearm is the ulna. Surgical treatment involves placing the wrist on top of the ulna. This process is usually performed at about 1 year of age. Unfortunately, while the initial results of surgery can be impressive, it is difficult to maintain the correction. Stiffness is also a possible complication. Recent efforts to improve outcomes include the use of an external fixator to stretch the tissues prior to surgery. The external fixator has also been used to lengthen the forearm, usually when the child is 8 to 15 years of age. This is a difficult, lengthy process, requiring much effort on the part of the patient and family.

Thumb anomalies include missing, misshapen or extra thumbs. A thumb that is slightly smaller than normal can be reconstructed to improve motion and use. If the thumb is missing or is a floating

thumb (missing a stable base), the index finger can be moved to the thumb position. The floating thumb could be removed first or at the time of index finger transfer. This procedure is called pollicization. It is performed between 6 months and 2 years of age, and requires a skilled surgeon who is comfortable with this procedure. The success of pollicization depends upon the flexibility of the index finger prior to surgery. A mobile index finger provides an excellent digit after transfer to the thumb position. A stiff index finger

continued on page 23



Scott H. Kozin, MD

Transplant Results and Observations from our Transplant Expert in Germany

Wolfram Ebell, MD, of Humboldt University, Berlin, reported on 21 FA transplants at our recent Family Meeting. Ebell suspects that radiation induces solid tumor malignancies in later years, so has eliminated it from his conditioning protocol. Engraftment is achieved by using fludarabine, high stem cell doses, T-cell antibodies, and low-dose busulfan.

Eight patients received stem cells from matched sibling donors; 13 had alternate donors. Eleven patients had severe aplastic anemia, six patients had myelodysplastic syndrome, and 4 had leukemia at the time of transplant.

All 8 patients with matched sibling donors, and 7 of 13 with alternate donors survive. Of the 6 who died, 3 died of infection and 3 of leukemia. Of the 11 patients with aplastic anemia, 10 survive. Of the 6 with MDS, 4 survive. Only one of 4 patients with AML survives.

Ebell draws several conclusions from these results:

- Radiation is not essential for matched sibling or alternate donor transplants.
- Toxicity with the present protocol is very low.
- Engraftment with the present protocol is acceptable.
- Infections pose a considerable risk.
- If a patient has AML, chances for a successful transplant are greatly reduced.
- Ebell believes that it is possible to go to transplant too early. Some patients will improve spontaneously. Ebell still recommends a trial of androgens prior to BMT. ♦

Blanche Alter Helps New Families Understand FA; Discusses Cancer Risk

Blanche Alter, MD, MPH, National Cancer Institute, presented two sessions at our Family Meeting in August. New families benefited greatly from her comprehensive overview of this disease (see *Science Letter*, “FA 101”). Alter also addressed the sobering topic of FA and cancer. This information is difficult for all families to hear. However, knowing the risks allows for appropriate screening and early intervention, with the hope of improving survival outcomes (see *Science Letter*, “Cancer in FA”).

Alter presented data from two sources: a review of 1300 reports of FA in the medical literature, and an analysis of 145 responses to her Pilot Study survey. Her findings include the following:

- FA patients who undergo transplant appear to develop oral cancer at an earlier age than non-transplanted FA patients. In the literature, there are 12 reports of oral cancer following BMT, and the median age of these patients is 21. This is younger than the median age of 28 years in the 26 untransplanted FA patients with oral cancer. The numbers are very small but statistically significant. The reasons for this observation are not yet known.
- FA patients develop cancer at much younger ages than those in the general population. Median age for developing leukemia is 14; median age for solid tumors other than those of the liver is 25. Liver tumors can be benign (adenomas) or malignant (hepatomas). Median age for developing either type of liver tumor is 13, and is mostly a complication of long-term androgen usage.

- FA patients experience a far greater risk of developing cancer compared to those in the general population. For example, the risk for an FA patient to develop any cancer was 50-fold; for solid tumors, it was 48-fold. When analyzing cancers prevalent in FA patients, the risks are even higher.
- The types of cancer seen in FA patients are specific and unusual (myeloid leukemia, liver tumors, head and neck cancer, esophageal cancer, and gynecologic cancer, especially vulvar cancer).
- The maximum risk for AML is age 16, and it appears to decline in subsequent years. However, the risk for solid tumors rises slowly during childhood and then increases steeply, with no sign of reaching a plateau.
- Myelodysplastic syndrome (MDS) does not always progress to AML in FA patients. Of 23 patients in the Pilot Study with MDS, 19 did not develop leukemia. And five patients developed leukemia without a previous diagnosis of MDS.

Alter offered guidance on screening for hematologic disease and for solid tumors. Patients should have blood counts at least every 4 months, and an annual bone marrow aspirate, biopsy, and cytogenetics (a study of the chromosomes in dividing bone marrow cells).

Head and neck cancer screening includes an examination of the oral pharynx, the throat, and the region down to the vocal cords (this requires insertion of a flexible scope into a nostril and down the throat). Comprehensive oral screening should be done annually, starting at age 10 in untransplanted patients, and within the year after transplant at any age. Monitoring for gynecologic cancer should begin at age 16 or earlier. Skin examination should be done as part of an annual physical. Pain, sores, or lesions that persist for more than a brief time should be brought to the attention of a physician. Patients on androgens (or who have previously received androgens) should have an annual ultrasound of the liver, as well as liver enzyme tests 3-4 times per year. ♦



FA parents listen carefully to presentation of FA treatment and research findings.

Alter Receives Lifetime Achievement Award

At a banquet during the FA Family Meeting at Camp Sunshine, Maine, Dave Frohnmayer, vice-president of the FA Research Fund's Board of Directors, presented Blanche Alter, MD, MPH, with the Fund's Lifetime Achievement Award. Alter, a cancer expert from the National Cancer Institute, is only the second recipient of this honor. The award was presented with great fanfare and much appreciation. Teens attending the Family Meeting marched into the auditorium to the tunes of *O Canada* and *The Star Spangled Banner*, bearing US and Canadian flags, in recognition of both Alter's country of birth and her newly-acquired US citizenship. In presenting the award to Alter, Frohnmayer cited her exceptional accomplishments and her unparalleled dedication to her FA patients.

The inscription on the award aptly describes Alter's contributions:

With profound gratitude for pioneering greater understanding of Fanconi anemia and for tireless dedication to helping FA patients and families worldwide. Your gift of self as a resource to FA families and to the FA Research Fund as a teacher, physician, scientist, and friend has value beyond measure.

Alter's commitment to FA patients and their families is well known and made the Family Meeting particularly appropriate as the site of the presentation of this award. The youngsters in attendance added their recognition to the Lifetime Achievement Award by presenting Dr. Alter with a colorful hand-made card bearing their handprints and their very best wishes. ♦



Blanche Alter, MD, MPH receiving the Fund's Lifetime Achievement Award from Dave Frohnmayer

Hormones and Fanconi Anemia

Susan R. Rose, Professor of Endocrinology at Cincinnati Children's Hospital Medical Center, discussed the importance of identifying and treating endocrine problems in FA patients. Endocrinology is the study of how hormone messages interact in the body. Among other things, hormones affect growth and development.

Many FA children have hormone problems. The only large study on this subject was by Dr. Michael P. Wajnrajch and appeared in *Pediatrics* 2001; 107:744. This study of 54 patients revealed that 72% had insulin resistance, 25% had glucose intolerance, 46% had low growth hormone peak, and 36% had hypothyroidism. Wajnrajch suggested performing "endocrine evaluation in all FA children because correction of

these endocrinopathies may improve growth, final height, and overall quality of life."

During the past five months, endocrinologists at Cincinnati Children's Hospital Medical Center have done endocrine testing in 12 FA children, in order to better understand growth problems. Short stature was identified in 58% of these children. Of this small study group, every child had an endocrine deficiency. Either glucose intolerance (often a precursor to diabetes) or diabetes was identified in every child. Insulin levels were elevated in 63% of those who were old enough to test. Abnormal thyroid tests were found in 83%; and low growth hormone peak was identified in 62% of these patients.

Rose recommends that all FA patients undergo a careful and

systematic baseline evaluation. Growth should be monitored yearly; if growth rate continues to be slow, endocrine tests should be repeated. When problems are identified, hormone therapy can help to optimize growth and promote good health. ♦

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.

Oral Cancer Precautions and Recommendations

Stephen Engroff, MD, DDS, Fellow in Oral and Maxillofacial Oncology at the University of Maryland Medical Center, reported on oral cancer at our recent Family Meeting. Engroff stated that 90% of oral cancers are squamous cell carcinomas. Treatment has become much more successful in the early stage of this disease. Early-stage lesions (less than 2 cm) have an 85-90% cure rate; stage 3-4 lesions have only a 20-30% cure rate.

Three types of premalignant conditions are implicated in oral cancers of FA patients:

Leukoplakia is the most common premalignant condition. Engroff defined leukoplakia as “a white patch or plaque of oral mucosa that cannot be rubbed off and cannot be characterized as any other disease.” In the general population, depending on the site, up to 40% of leukoplakias will go on to become cancer within 5 years. In FA, the percentage could be higher.

Mixed lesions are even more suspicious than leukoplakia. They are “thick and white, with associated red areas.”

Erythroplakia is a red patch of oral mucosa. With erythroplakia, the changes that have occurred in the tissues of the mouth are more frequently dysplasia, carcinoma *in-situ* or frank carcinoma. A high percent of erythroplakias become malignant.

Premalignant lesions should be biopsied. Toluidine blue selectively stains areas undergoing a higher rate of cell division, and can be helpful in identifying the appropriate area for biopsy.

There are several treatment options for premalignant and malignant lesions. If biopsy of a premalignant lesion shows thickening or

progression to dysplasia, the lesion needs to be removed. Surgical excision, laser treatment, or photodynamic therapy can be effective. With photodynamic therapy, the patient is given medication, which is taken up rapidly in dividing cells. Light is applied, which causes destruction of these lesions.

Malignant lesions must be removed. Today, there is no effective chemotherapy for oral cancers. Radiation poses problems with salivation and wound healing and is not ideal for FA patients. Surgical removal remains the mainstay of treatment for oral squamous cell carcinomas in the FA population.

Oral cancers can return rapidly and have a “field characterization,” meaning that more than one spot is often affected.

Engroff recommends aggressive screening to detect premalignant and malignant lesions as early as possible. Specifically:

- FA patients should undergo an oral examination upon diagnosis and every 3-4 months thereafter.
- The dentist should be told that the patient has FA and that FA patients are at high risk for oral cancer.
- The entire oral cavity must be examined.
- FA patients should be aggressive in following up on suspicious-appearing areas. Don't just “wait and see.”
- FA patients should avoid behaviors that increase the likelihood of oral cancers, such as drinking and smoking.
- Chinese green tea might reduce the incidence of these cancers. ♦



Grompe Wins *E. Mead Johnson Award*

Markus Grompe, MD, from Oregon Health & Sciences University, has been awarded the *E. Mead Johnson Award for Excellence in Pediatric Research*. This is the most prestigious award given by the Pediatric Academic Society/Society for Pediatric Research. Grompe, a long-time researcher into Fanconi anemia, recently isolated the *FANCD2* gene, further contributing to the knowledge of the FA pathway. He also manages the FA Cell Repository at OHSU. ♦

Comprehensive Care Center Established

The Fanconi Anemia Comprehensive Care Center was established at Cincinnati Children's Hospital Medical Center in January 2002. The Center offers a weeklong clinical assessment of FA patients and opportunities to participate in clinical research studies. Research studies will include gene therapy, blood and marrow transplantation, novel androgens (oxandrolone), and endocrine evaluations. Consultation will be available on a wide range of specialties, including ear, nose and throat; orthopedics and hand surgery; gastroenterology; nephrology and urology; and dental. The Center is establishing an FA cell repository of bone marrow, blood, skin and tumor samples. Investigators can apply to the Fanconi Anemia Comprehensive Care Center for access to tissue samples and clinical information. For questions, contact Robin Mueller, the FACCC coordinator, at 513/636-3218 or email her at robin.mueller@chmcc.org. ♦

Fanconi Anemia Comprehensive Care Program Established in Minnesota

The University of Minnesota has established the Fanconi Anemia Comprehensive Care Program at Fairview-University Medical Center, a treatment center for patients with FA. Care is individually tailored to meet the unique needs of each family. A wide range of services is provided, including surgical correction of congenital anomalies; bone marrow transplantation; hormone replacement therapy to correct short stature, thyroid insufficiency or diabetes; cancer treatment; voice reconstruction; and genetic counseling for preimplantation genetic diagnosis.



Drs. D'Andrea and Joenje field questions from FA parents regarding the genetics of FA.

Hans Joenje Describes the Importance of Molecular Diagnosis

Hans Joenje, PhD, Free University Medical Center, Amsterdam, The Netherlands, states that 95% of all FA patients have mutations in one of the seven known FA genes (*FANCA*, *FANCC*, *FANCD1 [BRCA1]*, *FANCD2*, *FANCE*, *FANCF* and

FANCG). It is therefore now possible to do "molecular diagnosis," *i.e.*, the determination of the defective gene and the disease-causing mutations in that gene, on the vast majority of FA patients. Some mutations are more severe than others. This knowledge can help families and their physicians devise an appropriate treatment plan. Knowing which gene is defective is essential for preimplantation genetic diagnosis, access to gene therapy trials, carrier detection, and earlier and more reliable prenatal diagnosis. Knowing the specific disease mutations provides the greatest accuracy, and is most helpful when making decisions concerning clinical care.

Dr. Gerard Pals (g.pals@vumc.nl) at the Free University Medical Center, Amsterdam, provides molecular diagnosis for all known FA genes. Joenje states the turnaround time is 1-3 months, and the price is reasonable. Patients for whom no mutations can be found are referred to the research division at no further cost. ♦

University of Minnesota physicians have developed protocols that have drastically improved outcomes for patients undergoing BMT with unrelated donors. Scientists at the University of Minnesota continue to research ways to improve treatment for FA patients. The focus of current research efforts includes use of Preimplantation Genetic Diagnosis to create a healthy HLA-matched sibling donor; Multipotent Adult Stem Cell Therapy to treat tissues of the body other than just the marrow; and gene therapy. ♦

FAMILY NEWS

Surviving the First Year

By Carol Siniawski

A long time ago, I redefined “success” for myself. It was not about whether Jake lived or died, as I believed that was in hands bigger than mine. Instead I chose to define success by three things: 1) not having any regrets, as Jake’s parent; 2) ensuring that Jake had a high quality of life, regardless of how long I had him; and 3) always telling the truth, even if it hurt. That definition served me well while Jake was alive and serves me well now that he has moved on to heaven.

Dr. Harris was incredibly patient with me and my 5 million questions. That was my way of ensuring I wouldn’t have any regrets. I asked questions when I wasn’t sure and learned to trust my gut when it was screaming at me. I learned how to trust my son, when he was really speaking to me. And we talked a lot, about everything, conversations I would never have had, if his life were not in grave danger. We would talk about the decisions we needed to make, the options, the possible outcomes, his preferences. Jake was always part of the decision, for as long as I can remember. His body was only 10 years old, but his mind matured at 4 times the normal rate. By the time we got to transplant, he had already learned that he could trust what I told him.

Good thing I have my faith. I fell away after he was diagnosed, but eventually found my way back. I have really clung to the *Serenity Prayer* over the years. It has helped me focus on things I can change and

to let go of things I truly cannot change. Letting go can sometimes be very empowering. I have found peace in sorting my troubles into these two categories.

Jake packed a whole lot of living into his 10 years here on Earth. He swam with dolphins, had a helicopter ride over an active volcano, attended a Mass celebrated by Pope John Paul II, sat in the cockpit of the Raptor and the Stealth, toured a Navy frigate and Air Force One, rode in a Hummer, was the Grand Marshal of a parade, and so on. I cherish all the photos I took and the memories they bring back. Jake inspired people to consider returning to the church, giving more to charities and not taking life for granted. That was my 10-year-old son. I am so proud of him and how he handled his illness with courage, grace and a smile.

Eventually, the complications from the transplant took over, and Jake was born into eternal life a few months short of his 11th birthday. Figuring how to get through the next year without losing my mind was an entirely new task, and I was not ready for it.

I take comfort in knowing that I did my best. I have no regrets. I was successful, as I defined it all those years ago. God’s plans for Jake were not aligned with mine. But Jake knew that whatever God had in store for him, He would take care of him and never leave him. Jake also knew that we’d all be together again someday. We even agreed that Jake would save a seat for me. Jake died knowing



Jake Siniawski

that I loved him. He knew I was proud of him. To some degree, all of that helped me get through the first year after his death.

We decided early on that we might as well dedicate some time and energy to grieving, as it wouldn’t go away by itself. We decided to pay homage to Jake at every major event: holidays, birthdays, trips, hobbies, the simplest of family activities. We hoped that, by investing the time this first year, maybe next year we could enjoy the event again. It was all painful. We had to learn how to deal

continued on page 11

Surviving the First Year

continued from 10

with guilt over laughing and having fun. We had to learn how to deal with guilt from not thinking about him every minute of every day. I don't think I smiled much those days.

We learned that our son Justin, Jim, and I grieved in different ways and healed at different rates and speeds. Some days I'd be up and Jim or Justin would be down or vice versa. This went on for months and months, but we stuck together and weathered the rough roads. It would have been so much easier to just give up and give in to the sadness. It takes

a lot of work, energy, and dedication to crawl out of that hole. We looked out for each other. It was that wonderful teamwork that helped get us to today.

I had really expected that my grief would get a little better every week or maybe even every month, but it would always be trending upward. Boy, was I wrong. It was always two steps forward and one step back. The overall trend was upward, but the curve was not smooth, but very jagged with sharp dips down. This realization was very discouraging. When would it end?

Going through Jake's personal belongings was not as hard as it

could have been. Because I still have Justin, I didn't need to get rid of Jake's clothes or his toys. We placed the most treasured items on shelves for safekeeping. Each of us picked out one or two things that really meant something to us. I chose a few items for Jake's two best friends and for the extended family. Sharing Jake's possessions actually helped me get through his stuff. Justin wanted to move into Jake's bedroom and sleep in his bed. I didn't object, but it meant I had to clean out the drawers and it was emotionally exhausting. I understood Justin's request, but did it at my own pace.

continued on page 23

Ruthie and Sharon Saunders from Israel Attend the Family Meeting

by Sharon Saunders, Jerusalem

Sometimes, when things get to Ruthie and me, we feel like animals in a zoo; a contained unit of two. The "situation," as we call the terror in Israel, makes life even weirder. We needed to break out. And break out we did—Camp Sunshine was only 4 days long, but for us it will always be a long, lovely summer memory. Everyone outside of camp was now the zoo, and we were free!

Yes, there were interesting and informative (and sometimes scary) seminars by experts in the ever-enlarging field of FA research. But there were also families showing off their new babies and toddlers, courageous pre-teens and teenagers, and post-transplant young adults. We were able to celebrate life and mourn and grieve for those who died with the understanding that this was our life—this was how FA families live. The 4 days rolled past my eyes in a kaleidoscope of a silvery lake and pine trees, little Abbey Stuart in her Pebbles costume, memorial balloons



*Back Row: Sharon Saunders, Andrea and Bob Sacks;
Front Row: Ruthie Saunders and Danielle Sacks*

reaching skyward, Ruthie and Dani doing the chicken dance, karaoke, and a festive dinner with moms in earrings with flashing lights, and more and more.

I feel tremendously indebted to the staff at Camp Sunshine and the

Fanconi Anemia Research Fund for all the hard work they did in making this respite "just what the doctor ordered."

Peace and love to all of you. ♦

In Kare of Kory

by Annette Bevelhymmer

Kory's diagnosis of Fanconi anemia was thrown at us in April 2000. We had very little time for research of this "bomb" before we met with Dr. Richard Harris at Cincinnati Children's Hospital. We were told that Kory needed a bone marrow transplant fairly soon because of his platelet count, which fell as low as 11,000 at one point. We chose to go to transplant in January 2001.

Kory seemed to breeze through the transplant. He actually slept during the infusion of his new marrow while several of us prayed around his bedside. His 100% donor sign was hung on his door on day +15!! I had visions of thanking his wonderful, generous donor a million times but knew that would not be possible for at least a year.

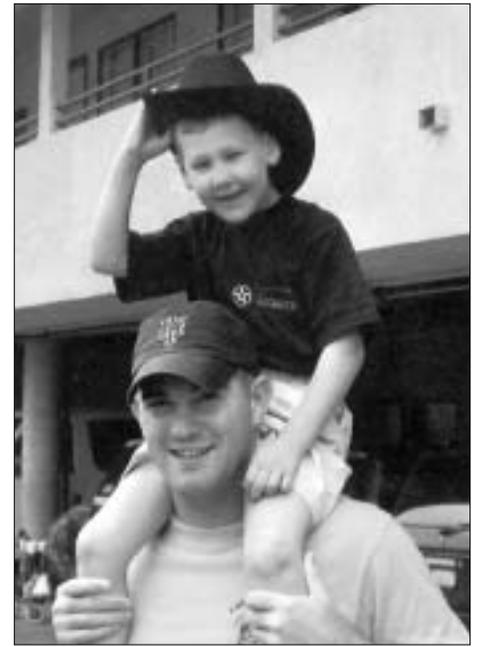
Kory left the hospital on day +25 after an uneventful hospitalization. Well, the road ahead was much more eventful. Kory started his winding road with a reaction to platelets at the clinic. A few days later, he had diarrhea and some vomiting and underwent scopes to check for GvHD. A couple of days later he was admitted to the hospital again for administration of TPN and lipids because his nutritional status was not adequate. The course that Kory took for the next several months was quite rocky. He was eventually diagnosed with chronic GvHD, which really started the bumpy ride. Massive doses of steroids for the GvHD precipitated many grueling problems such as hypertension, diabetes, and osteoporosis, to name a few. Weight gain was also a problem for Kory.

These complications kept Kory and me close to the hospital longer than we had hoped, but the one event that almost caused Kory to give

up was his longest stay in the hospital in June. Kory developed shingles, continued to vomit and have diarrhea, requiring another scope. He then showed signs of meningitis and had a lumbar puncture, which was positive. This was followed by severe abdominal pain and more tests showed a duodenal hematoma (a complication from the scope). That wonderful finding bought him a nasogastric tube for continuous suctioning. He still vomited around this and was found to have pancreatitis. He was on a continuous pain medication infusion, not to mention ALL the other medications he now required. Many people, professional and non-professional, would come in to tell me, "things just don't seem to be going in the right direction. Kory has seemed to have given up, and maybe you should get things in order." This I did **not** want to give in to, so I decided that, if I could take Kory back to our "home away from home," I could help him gain back his will. After a long meeting with all involved in Kory's care, I was able to do just that! We left the hospital in August (after a long 7 weeks). Kory and I had our job cut out for us, but I was determined! He crossed many hurdles and on October 26th, Kory and I went back HOME!

In January 2002, Kory had a fabulous one-year post-BMT anniversary party. The day after...he fractured his left arm.

On February 14th I was called with some fantastic information—the name and address of Kory's donor. His name is John "Jack" Gorman. He is in the Marines and stationed in California. When Kory was asked what he wanted to do for his special wish, he said, "I want to go to



*Kory on the shoulders of his donor,
Jack Gorman*

California and meet my donor, Jack!" That is exactly where Special Wish sent all of us. Jack met us at the airport in his uniform, and Kory would not leave him alone the entire time we were there. Kory spent most of his time on Jack's shoulders. We are so thankful to him, and he has been added to our "family." ♦

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.

What a Fabulous Opportunity!

by Brandi Stuart

When my husband, Greg, and I decided to go to the FA Family Meeting back in the spring, we had no idea how the experience would impact our lives. Our daughter Abbey was diagnosed with FA about a week after she was born. As you all know, the numerous doctor visits and seemingly endless explanations to doctors about your FA child's condition can become quite frustrating. We simply hoped that the FA Family Meeting would help us to make the correct decisions at the right times for our daughter's health.

Upon our arrival at Camp Sunshine, we were immediately greeted by the outstanding volunteers. Never before have I seen such a large group of people who were truly unselfish and loving. They were so helpful and ready to take on any task. Without them the camp could not have run so smoothly.

Our experience at the FA Family Meeting was invaluable. We were extremely impressed by the caliber of the speakers, and even more impressed with their willingness to answer questions during and after the presentations. Not only were we able to find the answers to many of our questions, but we were also able to obtain some much needed advice for Abbey, not just generalized information.

Equally as beneficial were the friendships we made at the camp. Before the meeting we had never met another family who had a child with FA and knew exactly what we were going through. Now that we personally know other families dealing with FA, we no longer feel so alone. We are so grateful for the experiences, whether good or bad,



Greg, Abbey and Brandi Stuart

which have been shared with us. These new friendships have a big place in our hearts.

We strongly recommend the FA Family Meeting to everyone who is close to an FA patient. Not only will you come away learning a great deal about your loved one's condition, but you will form a special support group with other wonderful families at the camp. The information we came away with has given us even more determination to fight this terrible disease and has helped to put us on the right track for Abbey's health.

Our family would like to thank all the people at FARF and Camp Sunshine who made this FA Family Meeting such a positive experience. We would also like to express our extreme gratitude to FARF and the scholarship program for making our trip possible. We look forward to making the FA Family Meeting a yearly tradition. ♦

Grandparents Attend the FA Family Meeting

by Jay and Susan Stuart,
Syracuse, Utah

Abbey's birth was followed by one of the longest and most difficult seven days. We had a grandchild who was a tiny 2 lbs., 15 ounces, was missing both thumbs, had a serious blockage of the stomach, and an ear that was not completely formed. The Children's Hospital in Salt Lake City was not sure of the "syndrome" or the diagnosis. It was very frightening not to know what the problem was or what else to expect in the future. We were very fortunate that within a week we had a diagnosis and were able to gather information concerning her condition. The most helpful resource turned out to be printed information from the Fanconi Anemia Research Fund. Our doctors had "limited" experience with this

continued on page 21

Dawn Ann Kalman

by John and Irene Kalman

Dawn Ann, our first child, was born in 1963 at a birth weight of 6lbs., 4oz. Dawn's childhood and her annual check-ups through high school were normal, although she did have quite a few colds and ear infections. After high school Dawn decided to stay at home and attend the University of Bridgeport. She was determined to get her degree and graduated in 3 years, by attending all year around. She was a little pale in 1985 as she pushed herself to get finished. She graduated with a Bachelor of Science degree in Management, ready to get on with her life. For a graduation present she wanted to go to Europe, and my husband John and I took her for 3 weeks in August of 1985. We went to several countries, and Dawn had a wonderful time.

In September 1985, Dawn called and told me she did not feel very well; the symptoms sounded like the flu. After a bone marrow aspiration, she was diagnosed with aplastic anemia. Dawn was put on birth control pills to stop her period because she could not stop bleeding. Dawn spent practically the whole month of October 1985 in the hospital until the hematologist told us there was nothing else he could do.

We opted to go to Brigham and Women's Hospital in Boston and saw Dr. Joel Rapoport. He put Dawn on oxymetholone, as neither John, myself nor our son was a match for a bone marrow transplant. Dawn stopped the birth control pills and started oxymetholone, 150 mgs., 3 times daily. Dawn had numerous horrendous side effects, which I'm sure everyone who has been on this drug knows about.

In September of 1987 Dr. Rapoport left Brigham and Women's

Hospital and assumed a professorship which included the development of the bone marrow transplant program at Yale New Haven Hospital, so we transferred to the Yale Clinic. Dawn never did complain about anything except the awful symptoms she was getting from the oxymetholone. She finally started to complain that she wanted off the horrible pills. Finally, by August 1989, after tapering off, the dosage was reduced to 50 mg. every other day. John and I were getting worried that Dawn could die and tried to talk to her, but Dawn was not listening and wanted off the pills. Finally Dr. Rapoport told her she could stop taking the pills, and she took her last one on September 14, 1989. Dawn was relieved and swore she would never go back on oxymetholone again.

On Thanksgiving Day of 1989 Dawn did not feel well and found that she had a lesion by her vagina. She had a platelet transfusion and had a biopsy done on November 30, which revealed that she had squamous cell carcinoma. Dawn had a vulvectomy and several lymph nodes removed. At this time Dr. Rapoport decided to do a chromosome test and informed us that Dawn had Fanconi anemia. "What's that?" He explained everything to us, and I guess we just went into shock. Dr. Rapoport and our family physician were shocked, as Dawn had no obvious signs of FA. I remember calling Lynn Frohnmayer and discussing FA with her. Lynn was wonderful with the help she gave to me and then sent me some literature.

Dawn was in the hospital for the month of December 1989, to recover from the operation. She also got an infection, which required removal of all stitches and clamps in order to



clean the wounds. She received antibiotics and several red cell transfusions. Dawn took a whirlpool bath every day to have her wounds cleaned, and she finally came home on December 30, 1989.

Finally by the end of May, 1990 Dawn was doing wonderfully. She could not have radiation or chemotherapy, so she had 2 laser treatments and she was fine. She had to have visits with the gynecologist twice a year. For some unknown reason, Dawn's counts came up, and she somehow existed on platelets of 32,000 to 50,000, WBC of 2,400 to 3,000, and hemoglobin between 9 and 10 for the next 12 years without any medication whatsoever. Visits with Dr. Rapoport had gone from 4 times a year down to twice a year until 2001.

In 2001 all of Dawn's blood counts started fluctuating. In May she had high fevers for about a week. She had pneumonia in the right lung and was admitted to Yale New Haven Hospital. She had to get a platelet transfusion plus antibiotics and spent 3 days in the hospital. In July we went to Florida, and Dawn was more tired than usual. She started complaining about her knees aching and about swelling in her legs

Dawn Ann Kalman

continued from 14

and feet. Dr. Rappeport was more concerned about her falling blood counts than the swelling, which was getting worse. Dawn started to swell all over her body. Dr. Rappeport did suggest oxymetholone, which Dawn did not want to hear about. She started going to the clinic at Yale for platelet and red cell transfusions. In November she had a chest x-ray and found that she had pneumonia in her left lung. Dawn, who normally weighed about 110 lbs, now weighed about 140 lbs. She saw the endocrinologist, who put her on medication for the swelling, as she had developed Cushing Syndrome. A chest x-ray then revealed a tumor in her left lung, which was confirmed by biopsy to be small cell carcinoma. The cancer had already metastasized to her liver.

In December Dawn had her first phase of chemotherapy (Taxol) and received red cell and platelet transfusions every 4 days. She spent Christmas home and was feeling good under the circumstances. She then

went to the clinic and completed two more phases of her chemotherapy. She was off of chemotherapy until February 18. In the meantime the oncologist said the tumor in the lung was down by 75%, but the chemo had done nothing for the liver.

Dawn started the 2nd phase of the chemotherapy on February 18, of carboplatin and etoposide for 3 days in a row. She then started to get mouth sores and throat sores. On the 25th of February she was admitted to Yale New Haven Hospital as she was in significant pain. She was put on morphine for the pain, given platelet and red cell transfusions, and took Neupogen, since her white cells had dropped to 200. For the next 2 weeks Dawn was unable to eat solid food, and it was quite hard for her to swallow any liquids. Her total bilirubin went to 22.1, and she was becoming quite yellow. She was also put on antibiotics because her white cells were so low that they were not responding to the Neupogen. She was being fed intravenously for about 5 days.

Dawn finally realized that, even

though her white counts might come back, she had to make a decision about what to do for the next round of chemotherapy. Because of the pain she was in, she decided that she wanted everything stopped. She invoked her Living Will, which meant she would receive the morphine in a constant drip and oxygen. I must hope that, whenever our time comes, we will have the strength that Dawn had to make this decision. If Dawn had not had Fanconi anemia, maybe she would have had more of a chance of living. At least we know that Dawn is not suffering and is in a better place than we are, and we shall meet again. In the meantime, we try to get through one day at a time. It is not supposed to be like this, parents should go before their children. But Dawn is now at peace. We know that, in Dawn's short life here on earth, she touched many lives and will never be forgotten. Thank you everyone for all of your condolences and support. If you want to talk, please call or e-mail us.

1-203-375-6817

itcjk@optonline.net

In Loving Memory

Christopher Danchisko

3/24/81 - 9/2/02

Caleb Glover

9/9/96 - 4/12/02

Kacie Goodwin

7/23/94 - 4/27/02

John Thomas Greer

8/26/01 - 5/23/02

Dawn Kalman

12/4/65 - 03/27/02

Megan Morings

3/16/80 - 1/24/02

Shaykinah Williams

9/6/96 - 5/29/02



2002 Family Meeting at Camp Sunshine



Campers of all ages and sizes are welcomed to Camp Sunshine

"Peaceful and beautiful location."

"Amazing speakers!"

"We have had the most wonderful time and gained expert knowledge."

"First time at Camp Sunshine. Everything perfect."

"Camp Sunshine is wonderful! The volunteers are wonderful!!"

"I think Camp Sunshine was a wonderful experience. The volunteers were absolutely wonderful. I think our family will definitely make the FA meeting a yearly vacation."

"Thanks for a wonderful event!"



Friends and family release memorial balloons on the shore of Sebago Lake in honor of deceased loved ones



CC Bray ready for the Masquerade Ball



Samuel Boudreau and a volunteer Hells Angel enjoy a Harley.



Amy and Jon Frohnmayer dressed for fun at the Masquerade Ball

FA Family Meeting Returns to Camp Sunshine

continued from 1

was held by his family, which included a bagpipe rendition of *Amazing Grace*, played beautifully by Mishan Blecher.

FA families were honored once again by the presence of first-rate researchers and clinicians who shared progress and research results with the parents. For the first time ever, a hand surgeon spoke to the group:

Scott Kozin, MD, from Shriners Hospital in Philadelphia. He was tremendously helpful to families in providing them with information about hand and arm surgery and its benefits and limitations. Stephen Engroff, MD, DMD, from the University of Maryland School of Medicine, presented information on squamous cell carcinoma of the head and neck, including physical symptoms and self-examination guidelines. Other researchers and clinicians who presented their research and took time to talk with families were Blanche Alter, MD, MPH, National Cancer Institute; John Wagner, MD, University of Minnesota; Richard Harris, MD, Cincinnati Children's Medical Center; Wolfram Ebell, MD, Berlin; Christopher Walsh, MD, PhD, University of



Brandi Stuart and Jennifer Bray enjoy karaoke.

North Carolina, Chapel Hill; Alan D'Andrea, Dana-Farber Cancer Institute; Franklin Smith, MD, Cincinnati Children's Medical Center; Charmaine Jacobs, Bloemfontein, South Africa; Hans Joenje, PhD, Free University, Amsterdam; Mark Hughes, MD, PhD, Wayne State University; and Susan Rose, MD, Cincinnati Children's Medical Center. As always, Nancy Cincotta, MSW, facilitated many coping sessions, and Andy Eichenfield, MD, performed admirably as the Camp Doctor.

The FA Research Fund extends its thanks to the staff and volunteers of Camp Sunshine for making the Family Meeting such an enjoyable and worthwhile experience and to the physicians and researchers who took time out of their busy schedules and traveled a great distance to share themselves with us. ♦



Memorial Service for Travis Massino

FA REGIONAL MEETING

FA Regional Meeting Held in Cincinnati

The FA Research Fund held a regional meeting at Children's Hospital Medical Center in Cincinnati on Saturday, July 27, 2002. Sixteen FA parents from as far away as Los Angeles and Calgary, Alberta, Canada, attended this excellent conference. Franklin Smith, MD, the Chief of the Pediatric Hematology/Oncology Division at Children's Hospital, welcomed the group and gave a synopsis of the hospital's Fanconi Anemia Comprehensive Care Center. He was followed by presentations on androgens and cytokines by Michael Jeng, MD, Stanford University Medical Center and on gene therapy for FA by David Williams, MD, Cincinnati Children's Hospital and from James Croop, MD, PhD, Indiana University Medical School. Richard Harris, MD, made a presentation on the bone marrow transplantation program at Children's Hospital, and

Laurie Bailey, MS, discussed prenatal genetic testing, including pre-implantation genetic diagnosis and *in vitro* fertilization. During the afternoon session, Susan Rose, MD, presented information on the endocrine issues faced by FA patients, and Thomas Kiefhaber, MD, presented on surgery for thumb and arm anomalies. Participants also had an opportunity to debrief and to discuss coping with FA with psychologists Kathy Vannatta, PhD, and Cindy Gerhardt, PhD. Toward the end of this very busy but informative day, the participants were given a tour of the bone marrow transplant unit at the hospital.

We extend our thanks to the doctors and staff of Cincinnati Children's Hospital Medical Center for their exceptional generosity and kindness in making special arrangements for participants to stay at a

reduced cost at the Marriott Hotel on campus, arranging for a shuttle from the airport, and organizing such a comprehensive scientific program. Judging from the evaluations completed by the participants, the meeting was a tremendous success:

"Everything was so interesting and helpful. We should have attended one sooner. Thanks to everyone."

"Very nice facility."

"Really like the location at the hospital—more convenient for the presenters. Was catered really well—excellent choice of food and refreshments—nutritious and very convenient, maximizing the meeting time."

"Wow! Getting the binder in advance was great—10 minutes through it the evening before really helped me pace when I wanted to take notes, pictures, videos, whatever!"

"Great to have a hospital tour. Holding the meeting at a hospital allows us to also check out a potential treatment center."

"Presentations were fabulous: clear, concise, interesting and very well laid out. The slides and binder notes were awesome. Thank you for your kind and thoughtful considerations!"



Left to Right: Thomas Kiefhaber, MD; Patrick Kelly, MD; Richard Harris, MD, Susan Rose, MD; James Croop, MD; Franklin Smith, MD; David Williams, MD; Kathy Vannatta, PhD; Laurie Bailey, MS; Michael Jeng, MD; and Cindy Gerhardt, PhD

FUNDRAISING

Currency from Many Countries Collected for FA Research

During the past 10 months, Ralf and Cornelia Dietrich and other German FA families collected more than 3,000 pounds of coins and bills from European and many other countries. This fundraising activity began in Portland, OR at the FA Scientific Symposium last November. With a plastic cup, Ralf asked for coins from other participants with the words: "This is a test for a fundraising campaign we will start when I'm back at home in Germany. We only want your little coins, nothing that 'hurts.'" After an hour or so, the cup was almost full.

At the end of 2001, 12 European countries started to use the Euro instead of their individual currencies. With the help of newspaper articles explaining the project, Ralf and Cornelia began to collect old coins in the Christmas market of their hometown of Unna. In addition to German coins, they wanted to collect Italian lira, Spanish pesetas and Austrian shillings. Many people in Unna had

followed newspaper articles about two of the Dietrich children and their struggles with FA. Townspeople knew that their eldest daughter, Sarah Ninja, passed away in September of 2001. The mayor of Unna lent his support as the official patron of this fundraising campaign.

At first the Dietrichs collected the money in a little donation tin. But as the townspeople recognized that they could aid FA research through this project, hundreds of people donated, often with large bags of coins. So, Cornelia and Ralf cleaned their old, very large trash container (which, fortunately, had wheels) and spray painted it gold because of Christmas. In the following days, hundreds of people recognized this large golden trash container in the center of Unna and threw coins and bills into it. Each evening, Cornelia and Ralf took the container home, sorted the money into the currencies of each country, and counted it.

continued on page 22

FA Families Meet Harold & Arlene Schnitzer CARE Foundation Challenge

The Spring 2002 *FA Family Newsletter* contained an article describing the \$60,000 donation by the Harold & Arlene Schnitzer CARE Foundation, which funds part of the International FA Transcription Consortium, led by Grover Bagby, Jr, MD, of the Oregon Cancer Institute. As part of its donation, the CARE Foundation issued a challenge to FA families to raise a

matching \$60,000. We are pleased to report that a number of FA families rose to the challenge and that we have now met the \$60,000 goal. Thanks go especially to the fundraising efforts of Jeff and Judy Hoffman; Deane and Stuart Marchbein; Christie and Randy Kelley; Bill and Jackie Lucarell; and Vicki and Andrew Anton-Athens in meeting this challenge. ♦

Family Fundraising

Did you know that 85 percent of the donations to the FA Research Fund are raised by FA families? While many families hold very successful fundraising events, most funds are raised via holiday letters sent by FA parents to their family and friends. In these letters, FA parents describe FA, how the disease has affected their child or children, and ask for a donation for Fanconi anemia research.

The staff of the FA Research Fund stands ready to assist 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. 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.

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 FA Research Fund if you need assistance obtaining this required insurance.

One last request: Please ask your donors to write their donation check to the "FA Research Fund."

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

A Wonderful Surprise

By Carol Siniawski

We got the call on New Year's Day. I was outside in the back yard. It was cold. My husband was in the house when the phone rang. He came outside onto the back deck, and I could see the excitement on his face.

FA parent Connie Schenone was on the phone, informing us that we won the raffle! Raffle? It took me a minute to remember which raffle. Then I remembered. Months ago, Connie asked us to sell raffle tickets to benefit FA. The tickets only cost \$10, so I just bought them. I never dreamed we'd win an all expenses paid trip for 4 days and 3 nights at a posh hotel in Disney World, Florida!

The trip sparked many emotions. Our family had gone to Disney World in 1993. It was bittersweet. Jake had just been diagnosed, and we were devastated, as you all can understand. It was awful. My firstborn. My only son. My only child. I wanted to run away from home...far, far away. So, we did...to Florida, to Disney World. Is there a better place to run? Jake was only 3 years old at the time, but it was good for Jim and me to make this trip.

Fast forward to the present day, 2002. When Connie called us, Jake had not even been gone one year. Jim, Justin, our second son, and I had already taken our first real vacation without Jake and did okay, but this trip would be different. Jake went to Disney World, but without a sibling. Now Justin would go, also without a sibling.

Justin was excited. Jim and I knew we'd go on the trip, but we were anxious, with Jake's first anniversary coming. Knowing all that, we planned for the worst but hoped this trip might be just what we needed at that time. There is no

doubt we did the right thing. It was an awesome trip. I can't help but wonder if Jake didn't have a hand in this somehow.

The prize included a few nights at Disney World, all expenses paid. Then Jim and I discussed throwing in some of our own money to extend the vacation to include a few days in Florida, outside of Disney. It was well worth it. We spent one day at Sea World, which we knew we would love. Justin has the same love of dolphins and whales that his brother had. We spent one day at the Kennedy Space Center and, again, Jake must have had some influence here, as we were lucky enough to see the shuttle Atlantis launch. It was inspiring. Then, we took one day "off" and just played in the swimming pool and played a lot of miniature golf, which Justin loves.

Then we headed to the Disney Hotel Swan, the grand prize of the raffle. The hotel lobby, the view from our room, the swimming pools, and the service were all incredible. And yes, there was even a miniature golf course within walking distance. One theme park was walking distance from our hotel, but the others were farther and that made the adventure much more fun. There were several options for getting from the hotel to the park: a boat ferry; a long walk; a bus; and then, of course, the monorail—you can even sit in front with the driver! We did them all, several times. Downtown Disney was full of shopping, which included a LEGO store that encouraged you to play with the merchandise. MGM Studios had a cool playground from the *Honey, I Shrunk the Kids* movie. Magic Kingdom had a new Buzz



Carol and Justin Siniawski on a giant ant at Disney World

Lightyear ride with the neatest colors of lights. Animal Kingdom's Tree of Life and Kilimanjaro Safari are both something to see!

The last event of the trip was the icing on the cake. We were at the airport waiting to board, and coach was overbooked. Well, we were seated in first class! It was a great way to end the trip. The seats were huge. It was a fun ending to an already great trip! Thanks Connie! We really needed that to continue our healing process of losing our beloved Jake. Returning to Disney World with Justin was just perfect! ♦

Credit Card Donations

Credit card donations can be made to the FA Research Fund via PayPal. Look for the **PayPal** button below the **Donations** line on the home page of the FARF web site (www.fanconi.org). ♦

Your FA Research Dollars at Work in 2001-2002

Investigator: Hans Joenje, PhD,
Free University, Amsterdam

Title: Complementation Analysis in Fanconi Anemia

Amount: \$56,146

Investigator: Grover Bagby, Jr, MD,
Oregon Cancer Institute, Portland

Title: The Fanconi Anemia Transcriptome Consortium

Amount: \$331,000

Investigator: Hans Joenje, PhD,
Free University, Amsterdam

Title: Characterization of the Fanconi anemia Proteins
FANCE and FANCF

Amount: \$90,104

Investigator: Markus Grompe, MD, and Michael Forte, PhD,
Oregon Health & Sciences University, Portland

Title: Functional Studies of Drosophila FANCD2

Amount: \$42,905

Investigator: Hans Joenje, PhD, Free University,
Amsterdam

Title: Complementation Analysis in Fanconi Anemia

Amount: \$58,707

Investigator: Catherine Verfaillie, MD,
and Uma Lakshmipathy, PhD,
University of Minnesota, Minneapolis

Title: FANCC Gene Correction by Homologous
Recombination in Multipotent Adult Progenitor Cells

Amount: \$105,500

Investigator: Bruce Blazar, MD, and Jakub Tolar, MD,
University of Minnesota, Minneapolis

Title: Multipotent Adult Progenitor Cell Effects on Tissue
Repair after Bone Marrow Transplant in Fanconi Anemia

Amount: \$70,000

Grandparents Attend the FA Family Meeting

continued from 13

disease, and we have learned to appreciate how precious knowledge is.

We were excited with the opportunity to attend the conference at Camp Sunshine, but had no idea how much it would benefit us. As we arrived and experienced for the first time seeing another child with FA and the enthusiastic welcoming and acceptance on behalf of the staff and volunteers, we were very moved. Then came the flood of information. Had it not been for the handouts, question/answer periods and the informal discussions, we would have been quite overwhelmed. What was happening was a grand infusion of

knowledge. In Alcoholics Anonymous, they talk of knowing what you can change and what you can't, and the importance of knowing the difference. We were learning what we can change and what we cannot. We have become armed with the knowledge that gives us some power over what we can change. We also now know doctors, researchers, and wonderful volunteers who can help us with answers to many of our questions. Simultaneously, we received the warm support to help us accept those things over which we have no power.

Small things are a result of duty, but great things result from love. It was obvious that those who are involved in the creation and perpetuation of this organization are exhibiting great love. Those who are doing

research and making medical contributions really do care and desire to find solutions. Those who have been working with fundraising are looking far beyond themselves. Those who volunteered their time and services showed such acceptance, compassion, enthusiasm and unconditional love, they have won our hearts.

As grandparents who attended the family conference, we benefited in many ways. We would like to express our appreciation to all involved and encourage others to become more involved.

We are better for having our lives touched by a child with FA, and we are better prepared and stronger for having blended a week of our lives with all of you. ♦

Family Fundraising Efforts

From January 1 through June 30, 2002, FA families raised \$1,273,608 for Fanconi anemia research. The Fund also received \$10,611 from the United Way and the Combined Federal Campaign. Our special thanks to all of you who have worked so hard to raise critically-needed research dollars.

\$39,000 and up

Dave & Lynn Frohnmayer
Jeff & Judy Hoffman

\$20,000 - \$39,999

Allan Goldberg & Laurie Strongin

\$10,000 - \$19,999

Christie & Randy Kelley
Bill & Jackie Lucarell
Deane Marchbein & Stuart Cohen
Mark & Diane Pearl

\$5,000 - \$9,999

Lorraine & Kevin McQueen
Rick & Lynn Sablosky

\$1,000 - \$4,999

Vicki & Andrew Anton-Athens
Ken & Jeanne Atkinson
John & Audrey Barrow
Mark & Linda Baumiller
Kelly Bennett
Chris & Susan Collins
Antonin & Marie DiMercurio
Ed & Janice Duffy
Gary & Melody Ganz
Roger & Eleanor Herman
Beth & Jeff Janock
Eric & Beth Losekamp
Gregory & Lynette Lowrimore
Marilyn & Tom Massino
Sheila Muhlen
Jack & Lisa Nash
Luis & Lucina Perez
Jack & Tannis Redekop
Bob & Andrea Sacks
Bill & Connie Schenone
Bryan & Karen Siebenthal

Chris & Amanda Smith
Mike & Beth Vangel

Up to \$1,000

Darryl Blecher & Diana Fitch
Randy & Nancy Bloxom
Ed & Barbara Brookover
Jerome & Blenda Dahlin
Dottie Day
Joseph & Tracey DeMarco
Pat & Mary DiMarino
Gene & Lynn Eddy
Paige Ellis
David & Mary Ann Fiaschetti
Susan Gannon
Andrew & Jennifer Gough
Michael Greenberg
Alan & Rachel Grossman
Mitchell & Tirzah Haik
Mel & Jackie Hardy
Helen Healey
Brian Horrigan & Amy Levine
Charles & Katy Hull
Irene & John Kalman
Leardon Keleher
John & Karilyn Kelson

Currency from Many Countries

continued from 19

The Dietrichs and their friends also sent yellow postal parcels to about 200 bakery shops and pharmacies in Unna and nearby towns. These parcels, emblazoned with the German Fanconi anemia organization logo, contained information about the coin collection. Each postal parcel contained a hole for the insertion of coins. Many people donated coins via this method.

Additionally, Cornelia and Ralf sent a letter to 1,000 German FA families and their friends, asking for donation of outdated coins. Soon the postman came to their house carrying very, very heavy parcels contain-

Peg LeRoux
Gayle Licari
Roberta & Glenn Magill
Steve & Alison McClay
Cecelia & Charles Meloling
Griff & Cecilia Morgan
Andrea Morris
Kenny & Lisa Myhan
Louis & Virginia Napoles
Robin Paulson
Jeff Pederson
John & Diane Ploetz
Lynn & Shirley Quilici
Marcia Reardon
Shirley Ricker
Erik & Lori Salo
Tommy & Brenda Seiford
Irwin & Leona Selden
Jim & Carol Siniawski
Jeff & Debby Slater
Paul & Debra Sundsvold
Mark & Susan Trager
William & Mary Underriner
Bob Walker
Ira & Terry Walker
Marc & Sandi Weiner

ing coins sent from all over Germany.

It took 5 months to collect, sort and count what amounted to more than \$50,000 US dollars. So far, more than \$30,000 dollars have been converted at banks in Germany, Spain, Switzerland, the Netherlands, Denmark, the United States and Canada. French, Italian, and Austrian coins still need to be converted.

The Dietrichs would like to thank everyone who supported this fundraising effort. The Scientific Advisory Board of the German FA organization has agreed that the money will be spent to hire a young scientist for at least one more year at the FA research laboratory of Detlev Schnindler, MD, at the University of Würzburg. ♦

Surviving the First Year

continued from 11

I also found that it was very important to take care of myself. I only got sick once. I was not prepared for how emotionally sensitive I was once I became physically sick. It took about a week to get over the stomach flu and several more days to get better emotionally. That severe setback really caught me off guard. Now I have learned to spend more time and energy maintaining my own health. I exercise a little more, drink more water, watch my calcium intake, have changed my hair style, and even got braces! (Okay, so maybe the last item was pushing it?)

Justin has been doing okay. He talks to us when he is sad and missing Jake. He also has someone at school he can talk to. Several times he wrote a note to Jake, and we tied it to a balloon and set it free.

I have worked outside of the home for 16 years now. Deciding when to go back to work was tough.

About six weeks after Jake died there were four emotional events in the same month: a dedication at a park, the announcement of the Jake Siniawski Award at school, Jake's birthday, and the marrow transplant anniversary. I didn't kid myself. I knew I was not strong enough to work and deal with all of those public appearances, so I put off going back to work for several months. When I did go back, I went back part time. It was almost a year before I returned to full time. Two reasons caused the delay: I was physically exhausted (grieving is very tiring); and my priorities had changed. It was more important to me to spend more time with my family than to get back to work. Fortunately, I work for a great company, and this was okay with my boss. Now I can be very focused on work without feeling guilty about not thinking of my family.

The first anniversary was much harder than I had anticipated. It was miserable. My mind insisted on reliving all of the painful moments of

that last week: bringing Jake home, enjoying the first few days only to have to give that up as his condition deteriorated, honoring his wishes as best I could, making him comfortable in his own home, holding his hand, and watching the last breath leave his infected lungs. It is something I don't wish on anyone. The first anniversary was a bad time, and the deep pain was unexpected, which made it worse.

Now it is several months after the first anniversary. We survived it. We are still learning how to move on without Jake. We still think of him often and talk about him a lot. We are learning to laugh and have fun without guilt. We have survived many of the "firsts." We are learning to take care of ourselves better. We are not done but it continues to get better. We still miss him, but it's not as painful as it used to be. There will still be difficult days. I watch his classmates grow up and mature, and I know Jake won't. I think of him helping another newly inducted

angel every single time I hear of another person dying. I think Jake would make a wonderful "heavenly greeter." He had a great smile and a comforting tone.

I share this with you, not to prepare you for a specific family death, but for death in general. It will happen to all of us and our loved ones. Some people will get some notice. Others will not. Don't waste one minute. Take nothing for granted. Have no regrets. Be truthful. Ensure a high quality of life. Celebrate everything, for life is truly too short. ♦

Hand and Arm Differences in FA

continued from 5

is less useful, but can act as a post during grasping of large objects.

If there is no bone at the base of a thumb (a floating thumb), the thumb cannot be salvaged. Kozin believes it is probably best to remove this thumb and replace it with the index finger. The decision to remove a floating thumb is a difficult one for the family. It is helpful to discuss these issues with the surgeon and others who have been through the same experience.

Kozin stated that Shriners Hospitals do not charge for treatment. ♦



Jim and Justin Siniawski at Disney World

The Breast Cancer Gene

continued from 1

labs of Alan D'Andrea, Dana-Farber Cancer Institute; Markus Grompe, MD, of Oregon Health & Sciences University; Hans Joenje, PhD, Free University, Amsterdam; Christine de Die-Smulders of Academic Hospital in Maastricht, The Netherlands; and Hideyuki Ikeda of Sapporo Medical University, Japan.

Recent studies suggested that the breast cancer genes, *BRCA1* and *BRCA2*, interact with the FA genes in a DNA repair pathway. Among other similarities, *BRCA1* and *BRCA2* tumor cells exhibit chromosome instability and hypersensitivity to MMC, defects characteristic of FA cells. Researchers suspected that one or both of the cancer susceptibility genes might actually be FA genes.

To test this hypothesis, researchers sequenced the breast cancer genes in cells derived from FA-D1 patients.

While no *BRCA1* mutations were found, mutations in *BRCA2* were observed in cells from FA-D1 patients. This established the fact that the *BRCA2* gene and the *FANCD1* gene are one and the same.

It has long been known that the cancer susceptibility genes are involved in DNA repair. This discovery offers additional proof that the primary defect in FA is the inability to repair DNA damage. A great deal is known about the breast cancer genes. FA researchers will benefit from that knowledge.

As a result of this discovery, it is now suspected that some carriers of *FANCD1* might be at increased cancer risk. A *BRCA2* mutation found in Ashkenazi Jews may confer a breast cancer risk as high as 70% by age 70. Other mutations appear to have no increased cancer risk.

Researchers have now identified 7 of at least 8 FA genes. These genes account for 95% of all cases of FA. ♦



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

Newsletter Editors

Lynn & Dave Frohnmayer
Mary Ellen Eiler
Joyce Owen, PhD

Layout and Design

Tanya Harvey, Wild Iris Design

Staff

Executive Director:
Mary Ellen Eiler

Family Support Coordinator:
Suzanne Lauck

Board of Directors

Barry Rubenstein, JD, President
David Frohnmayer, JD, Vice President
Ruby Brockett, Secretary/Treasurer
Vicki Anton-Athens, DPM
Deane Marchbein, MD
Peter von Hippel, PhD
Robert D. Sacks
Michael L. Vangel
Joyce Owen, PhD, Director Emeritus
Lynn Frohnmayer, Advisor to the Board

Scientific Advisory Board

Grover C. Bagby, Jr., MD, Chair
Manuel Buchwald, PhD, OC
Richard Gelinis, PhD
Eva Guinan, MD
Hans Joenje, PhD
Christopher Mathew, PhD
Stephen Meyn, MD, PhD
Raymond J. Monnat, Jr., MD
Maria Pallavicini, PhD
Leona D. Samson, PhD
Kevin M. Shannon, MD
Neal Young, MD

Printing

Image Masters Printers

The Fourteenth Annual International FA Scientific Symposium

DECEMBER 2-5, 2002

Wyndham Franklin Plaza Hotel
Philadelphia, Pennsylvania