



May 2013

# FA Family Newsletter

issue 53

A semi-annual publication of the Fanconi Anemia Research Fund, Inc.

Symposium News

## Participants Find Inspiration and Excitement at Annual Symposium



**Grover C. Bagby, MD, receives Lifetime Achievement Award**

The 24<sup>th</sup> Annual Fanconi Anemia Research Fund Scientific Symposium, held last September in Denver, Colo., was attended by 175 scientists, clinicians, and family representatives from 15 countries.

Eleven sessions over four days included the ever-popular FA 101, an introduction to the medicine and biology of Fanconi anemia designed for those new to FA treatment and research as well as long-time veterans. Forty-six scientists presented abstracts in sessions such as Drug and Small Molecule Therapeutics; FA Protein Structure and Function; Genome Engineering and Stem Cells; and Carcinogenesis and Human Papillomavirus. An additional 52 abstracts on a wide range of related topics were presented as posters.

Jakub Tolar, MD, PhD, University of Minnesota, Minneapolis,

facilitated two exciting special sessions on the first full day of the meeting. The first session, Bone Marrow Transplantation: Point/Counterpoint in the Landscape of Change, explored questions vital to patients and families considering transplant (see article on page 9). In the second session, The Pursuit of Stem Cell Expansion, panelists discussed the latest findings in hematopoietic stem cell expansion and the therapeutic significance for people with FA (see article, page 5). Both sessions generated great interest among participants and led Dave Frohnmayer, cofounder of the

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*Twenty-four adults with FA came together at the Fund's Meeting for Adults with FA in Austin, Texas. See related articles starting on page 13.*

## Symposium Overview

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Fund, to pronounce, “This was the single best day in translational research in the history of the Symposia.”

The annual Symposium gala dinner was again a moving celebration illustrating for all in attendance how much has been accomplished and how much work remains.

Ken Atkinson, MD, a parent and active fundraiser, spoke about his family’s experience with FA. Two of Ken and his wife, Jeanne’s, four children had FA. Their daughter Kendall succumbed to complications of FA at age 20 and their son, Taylor, passed away at age 18. Ken and Jeanne founded the Kendall and Taylor Atkinson Foundation; daughters Allison Adams and Whitney Langlois founded Kaps for Kendall. Both organizations raise funds for FA research and family support.

Grover Bagby, MD, Oregon Health & Science University, Portland, Ore. and chair of the Fund’s

Scientific Advisory Board since its inception in 1989, received the Fund’s Lifetime Achievement Award. A founding director of the OHSU Knight Cancer Institute and hematologist for more than 35 years, Dr. Bagby has focused on FA research for the past 25 years. He was saluted for his passionate curiosity, dedication to inquiry and superb organizational and leadership skills. In accepting the award, Dr. Bagby told the old parable about a group of blind men each touching one part of an elephant to learn what it is like. In the story, the man who feels the elephant’s side says it is like a wall, the man who feels the tail says it is like a rope, and so on. The moral of the story is, as Dr. Bagby told the gathered researchers and clinicians, “we need each other.”

Participant evaluations attested to the meeting’s value. One participant wrote, “It is of utmost importance for FA researchers to attend this annual symposium, not only for the scientific value but for the approach to real

**“The single best day in translational research in the history of the Symposia.” – Dave Frohnmayer**

problems of FA families.” Another noted, “This meeting has become my top priority. While emphasizing rigorous basic research, clinical progress, and honest scientific exchange, it reminds the community each year that FA families do not have the luxury of time.” Finally, “I loved this meeting! You seem to have figured out how to keep it balanced and exciting.” ■



## Testing Service for FA Patients

### Testing for Potentially Beneficial Cancer Therapy

The Knight Diagnostic Laboratories at Oregon Health & Science University have recently made available new molecular tumor tissue tests designed to identify potential treatment targets in cancer and to predict the likelihood of benefit for patients treated with the latest therapeutics.

**This new testing is available at NO CHARGE to FA patients.**

### For more information, contact:

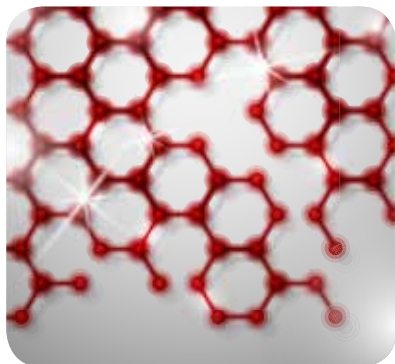
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## Presentations Highlight Aldehyde Research



A majority of researchers at the Scientific Symposium commented that the role of aldehydes in the Fanconi anemia pathway is an exciting area for further

research, since it may more fully explain why Fanconi anemia patients develop bone marrow failure, congenital anomalies and cancer. Aldehydes also provide a new target to develop small molecule therapies to improve these problems.

Aldehydes are highly reactive substances that can injure cells, particularly if they react with DNA in a way that FA cells cannot repair. A common example is formaldehyde.

Some of the aldehydes that can harm cells are endogenous or formed within the body as a result of normal metabolism, such as the processing of alcohols, amino acids, lipids, etc. Some are from outside the body or exogenous, like a number of drugs and environmental agents, including the ethanol found in alcoholic beverages we drink.

To prevent aldehydes from causing damage, they are first broken down by the cell, using enzymes called “aldehyde dehydrogenases.” If the aldehyde persists and causes DNA damage, the working Fanconi anemia pathway repairs it. With a defect in an FA gene, damage to cells will accumulate.

### Aldehydes and Bone Marrow Failure

Researchers at the laboratory of K.J. Patel, MD, PhD, MRC Laboratory of Molecular Biology, Cambridge, UK, are conducting research to explain the relationship between aldehydes and bone marrow failure in FA. Gerry Crossan, PhD, presented work showing that the identity of the enzyme responsible for aldehyde detoxification for hematopoietic stem cells (HSCs) is the aldehyde dehydrogenase ALDH2. HSCs that lack both ALDH2 and FANCD2 genes are much more damaged than those lacking either

ALDH2 or FANCD2 alone, when exposed to an aldehyde. Interestingly, this seems to be a feature of the HSC’s only, since more mature and specialized blood progenitor cells do not show more damage.

Juan Garaycochea, PhD student at the MRC, did experiments with mice deficient in both ALDH2 and FANCD2. These mice had a strong predisposition to leukemia and developmental abnormalities, as previously demonstrated by Frederic Langevin, PhD. They also show a large decrease in the number of HSCs compared to normal mice. Furthermore, those double mutant mice that do not develop leukemia go on to develop bone marrow failure, caused by an accumulation of DNA damage in the blood stem cells. Researchers conclude that endogenously generated aldehydes are a potent source of DNA damage that is repaired by the Fanconi DNA repair pathway.

Asuka Hira, MD, Kyoto University, Japan presented her lab’s analysis of Japanese FA patients who are ALDH2 deficient. Approximately 50% of the Japanese population are normally ALDH2 deficient. Hira’s work supports the hypothesis that aldehydes are toxic

Aldehydes are highly reactive substances that can injure cells, particularly if they react with DNA in a way that FA cells cannot repair.

to HSCs, and the FA pathway is counteracting this damage. The researchers determined that 23 of 55 FA patients had one ALDH2 mutated gene allele, 2 had both ALDH2 mutated gene alleles, and 30 were normal for both alleles. The two homozygous cases were both gravely ill. In all 25 cases where the patients were deficient in at least one of the ALDH2 alleles, bone marrow failure was strongly accelerated, but the deficiency did not affect the development of MDS or leukemia. Both FA patients with an ALDH2 mutation and those with normal ALDH2 experienced the same rates of developing MDS or leukemia. Interestingly, body weight at birth and number of physical anomalies were not significantly affected by the lack of ALDH2.

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## Aldehyde Research

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### Aldehydes and Developmental Defects

Nina Oberbeck, from the MRC, presented her work on mice embryos. By examining different genetic combinations of mothers and embryos, she concluded that the mother's ability to break down aldehydes determined the existence of DNA damage in the embryo and the embryo's subsequent developmental defects. The work also showed that the placenta did not protect the embryo by breaking down these aldehydes and therefore did not protect the embryo from DNA damage.

These findings open areas for further exploration. For example, could developmental defects in FA be reduced by drugs like cysteamine that mitigate the damaging effects of aldehydes? Could a pregnant mother's complete abstinence from alcohol or observance of a low-fat diet reduce her endogenous production of aldehydes and therefore reduce defects?

### Aldehydes and Cancer

Leslie Ann Cruz, PhD, from Daria Mochly-Rosen's laboratory at Stanford University, Stanford, Cal., presented a poster, which described the work of Che-Hong Chen, PhD and her attempts to find small molecules that can reduce DNA damage and development of cancer associated with aldehydes.

Acetaldehyde is an aldehyde produced after alcohol ingestion. The researchers used an alcohol intoxication model in mice treated with Alda-1 (a small molecule activator of ALDH2) and Alda-89 (a small molecule activator of ALDH3, which is another aldehyde dehydrogenase). They found that acetaldehyde breakdown with Alda-89/Alda-1 treatment was significantly better compared to Alda-1 treatment alone.

Since ALDH3 is normally expressed in the mouth and esophagus, where many of the solid tumors associated with exposure to aldehydes occur, their next studies will be to determine whether recruiting ALDH3 to metabolize toxic aldehydes reduces upper aero-digestive cancer risk in rats and mice. ■

## TALENS: A New Gene Editing Technique



Mark Osborn, PhD, University of Minnesota, Minneapolis, states that achieving the goal of developing the optimal gene therapy approach for FA is "the highest priority in my lab."

Gene therapy holds great promise for treating numerous diseases. This therapy often relies on a viral delivery

system to transport genetic material into cells. A critical limitation of this strategy is that the virus transporting the therapeutic gene can integrate into a location in the patient's genome that causes harm, such as cancer.

In contrast, gene editing specifically targets a typographical error in the DNA code for replacement with the normal sequence. Molecular "scalpels" can be designed that preferentially excise the damaged DNA. The "wound" is sutured using a powerful and highly accurate cellular repair pathway called homologous recombination. The end result is the permanent

correction of the mutated DNA to normal DNA.

One of the most powerful gene editing reagents, called "transcription activator like effector nucleases" or TALENS, functions as "molecular scissors." TALEN proteins exist in nature and are used by bacteria to alter the gene expression of the plant species they colonize.

**The end result is the permanent correction of the mutated DNA to normal DNA.**

Research specialists at Iowa State University, Ames, Iowa and the University of Minnesota, Minneapolis, re-engineered these proteins to generate highly specific tools for gene correction in human disease. A group at the University of Minnesota has shown the ability of TALENS to correct the human *FANCC* gene. This work provides proof of concept for TALENS in FA therapies. As the TALEN and gene therapy fields converge to define the optimal gene therapy approach, a new therapeutic tool will become available to the FA community. ■

## The Pursuit of Stem Cell Expansion



Fully functional blood stem cells can now be expanded in culture, an approach that could revolutionize stem cell transplants and eventually gene therapy.

Jakub Tolar, MD, PhD, University of Minnesota, Minneapolis, noted that a general rule of blood and

marrow transplant is that “the higher the number of immunologically-matched hematopoietic stem cells (HSCs) available from the donor, the better for the patient’s engraftment and outcome.” HSCs are required in relatively high numbers on the day of transplant for the graft to take permanently. In umbilical cord blood transplants, however, the number of stem cells is limited.

Researchers in the laboratory of Hans-Peter Kiem, MD, University of Washington, Seattle, have tested use of expanded stem cells in a nonhuman primate model and observed very rapid neutrophil engraftment. After transplant, two of three animals did not require any red blood cell or platelet transfusions.

The significant delay in white cell recovery following cord blood transplants leads to an increased risk of

infection and is a critical barrier to successful outcome, according to Colleen Delaney, MD, Fred Hutchinson Cancer Research Center, Seattle. Dr. Delaney described a study to determine if cord blood cells, expanded in the laboratory, could hasten the time to engraftment. Twenty non-FA patients received partially matched double cord blood transplants. They were first infused with unmanipulated cells and, after four hours, were given cord blood stem cells expanded in the laboratory. Time to engraftment (defined as an ANC >500) was 12 days, instead of a median of 25 days without cell expansion.

**Stem cell expansion could change the field of transplant as we know it.**

Anthony Boitano, PhD, Genomics Institute of the Novartis Research Foundation, San Diego, stated that researchers at his center have identified a molecule (SR1) that creates a 17-fold increase in the number of functional HSCs. Using these manipulated cells, phase one/two clinical trials are underway for non-FA patients.

Dr. Tolar concluded that these advances will “change the field of transplant as we know it.” ■

## Effectiveness of HPV Vaccines in Individuals with FA

No published studies have determined if individuals with FA inoculated with a human papillomavirus (HPV) vaccine have mounted sufficient antibodies against HPV. Blanche Alter, MD, MPH, National Cancer Institute, Rockville, Md., has now determined the post-vaccine “titer” level for ten FA patients vaccinated with Gardasil. Titers measure the relative amount of protective antibodies mounted in response to a vaccine. Of these ten patients, nine had sufficient titers. One male, seven years post-transplant, had low titers.

One FA patient, studied both three and five years after vaccination, consistently exhibited titers in the normal range. Dr. Alter concludes that for most FA patients, Gardasil provides protection against HPV similar to what is achieved in non-FA individuals. ■

**For most FA patients, Gardasil provides protection against HPV similar to what is achieved in non-FA individuals.**

## HPV Not Detected in FA Head and Neck Cancers in Two Small Studies



*Blanche Alter, MD, MPH; Susanne Wells, PhD*

The role of the human papillomavirus (HPV) in potentially causing cancers affecting FA patients is still a major unresolved controversy. Two recent reports, based on extremely small numbers of FA patients, suggested that HPV might play a role in gynecological cancers, but these studies did not detect HPV in the head and neck squamous cell carcinomas (HNSCCs) from these FA patients.

Blanche Alter, MD, MPH, National Cancer Institute, Rockville, Md., studied nine tumors from individuals with FA. Three were cancers of the oral cavity, two were



oropharyngeal cancers, and four were vulvar/vaginal cancers. The only cancer positive for HPV was one of the four gynecological cancers.

Laboratory findings of Susanne Wells, PhD, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, and Maura Gillison, MD, PhD, Ohio State University, Columbus, Ohio were similar to those from NCI. Of 10 cancers studied, nine of nine FA head and neck cancers were negative for HPV. The one FA vulvar cancer was HPV positive.

**The role of the human papillomavirus (HPV) in potentially causing cancers affecting FA patients is still a major unresolved controversy.**

Studies consistently show that HPV is often implicated in gynecological cancers in women with FA, but that HPV alone cannot explain the high incidence of head and neck cancers in the FA population. Vaccination is still recommended for all individuals with FA. ■

## Mouse Studies Find a Higher Immune Response to Gardasil than Cervarix in FA-deficient Mice



HPV plays a significant role in causing certain cancers in the general population. It has been implicated in some FA cancers as well. Two commercially available vaccines, Cervarix and Gardasil, are highly effective in preventing HPV infection in the general population.

Mice deficient in Fancc provide an appropriate preclinical model to test HPV vaccine response in FA, according to Blachy Davila Saldana, MD, Oregon

Health & Science University (OHSU), Portland, Ore. Dr. Saldana presented the work of Jason Taylor, MD, PhD and his investigators at OHSU at our fall 2012 Symposium. Dr. Taylor found that FA-deficient mice, treated with Cervarix, mount far fewer antibodies against HPV than non-FA (wild-type) mice. However, both wild-type and FA-deficient mice mount a similar antibody response to Gardasil. These mouse studies suggest that Gardasil might be more effective than Cervarix in protecting FA patients from HPV.

The ultimate test of the effectiveness of Cervarix and Gardasil in preventing HPV in individuals with FA will have to come from studies on humans, since mice and humans do not share an identical immune system. ■

## Solid Tumors and FA



David Kutler, MD; Robert Sclafani, PhD; Chantal Stoecker, MSc; Ian Mackenzie, DDS, PhD

One-third of FA adult survivors will develop head and neck squamous cell carcinomas (HNSCC), vulvar cancers and other solid tumors by age 40. Not only does the DNA repair defect characteristic of FA patients lead to earlier onset of cancer, it compromises the patient's response to many conventional chemotherapeutic agents. The following is a summary of some thought-provoking presentations on prevention, early detection, and novel approaches to treatment of tumors in FA patients.

### HNSCC Treatment for Fanconi Anemia Patients in the IFAR

David Kutler, MD, Weill Cornell Medical Center, New York, presented his group's study of the management and outcome of FA patients with HNSCC. Researchers studied patients enrolled in the International Fanconi Anemia Registry (IFAR) who developed HNSCC and were treated in the United States. The chart on page 8 summarizes their data.

FA patients have a high risk of developing aggressive HNSCC at an early age. They can tolerate complex surgeries to treat the cancer, but careful post-operative care is needed. Their poor tolerance of radiation and chemotherapy makes additional treatment difficult. However, radiation should be used for high-risk cancers because of the poor survival of these patients otherwise. Further study of FA patients' response to various treatments should be initiated, to establish appropriate doses while limiting toxicity.

### A Novel Treatment with Resveratrol

Robert Sclafani, PhD, University of Colorado, Aurora, Colo., gave an exciting presentation on the effect the nutraceutical resveratrol can have in inhibiting and perhaps eliminating cancer, particularly in FA patients. Resveratrol is found in many plants, including red grape skins, peanuts and some berries.

Previous animal studies on FA mice done by Marcus Grompe, MD's group at the Oregon Health & Science University, Portland, Ore., showed resveratrol caused no toxicity. Dr. Sclafani's studies on cells from FA patients showed that resveratrol selectively stopped HNSCC and ovarian cancer cells with no effect on normal cells. Resveratrol achieves this by damaging cancer cell DNA during the replication phase, thereby activating the body's own process to destroy damaged cells. This process is actually enhanced by the DNA repair defect in FA cells.

Sclafani's group is doing further experiments on FA HNSCC cells to test the hypothesis that resveratrol accomplishes its effect by partially slowing an enzyme used in DNA replication (called polymerase alpha) which causes the DNA damage. Next, they will test cells where they have knocked out genes that they have previously identified as potential resveratrol sensitizers to identify new pathways that could be targeted by drugs to enhance resveratrol's effect.

Dr. Sclafani hopes resveratrol will eventually prove to be a safe, non-toxic and inexpensive compound to either prevent and/or treat HNSCC in FA patients.

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## Solid Tumors and FA

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Population of FA patients studied	25 with HNSCC; 12 male, 13 female
Age cancers developed	Mean age of 33.5 years, range 15 to 48 years; median 30
Location of cancer	Oral cavity 20; larynx 3; oropharynx 1; unknown 1.
Risk factors	20% had tobacco and alcohol risk factors; 9 had prior bone marrow transplant
HPV status of the tumor	20 underwent HPV testing of their primary cancer, with 15/20 of the specimens HPV positive
Surgery treatments	23 had surgery; 5 developed a total of 8 post-operative complications; no post-operative deaths
Radiation management	12 received post-operative radiation therapy, average dose of 5278 cGy (range 2500 to 7020)
Toxicities from radiation	High-grade mucositis 9/12; dysphagia 8/12; and pancytopenia 6/12; only 4/12 survived
Survival	5-year overall survival was 27%, with a cause-specific survival of 41%

### HNSCC Cell Lines as Tools to Develop Novel Treatments for FA Patients

Chantal Stoecker, MSc and Johan de Winter, PhD, Vrije Universiteit Medical Center, Amsterdam, Netherlands, presented a poster describing how their group established three HNSCC cell lines from tissue obtained from three FA patients who had squamous cell carcinoma (mouth mucosa FANC-A; floor of the mouth FANC-C; and tongue FANC-L). These FA-HNSCC cell lines will be used for the development of novel treatment options, including more targeted therapies and perhaps preventive treatments.

### Therapeutic Resistance in Head and Neck Cancers

Ian Mackenzie, DDS, PhD, Barts and The London Medical School, London, presented his investigation of how some HNSCC cells lacking Fanconi gene function

develop three ominous abilities: the ability to cause local tumors, the ability to travel to distant tissue and cause tumors (metastasis), and the ability to become resistant to chemo- and radio-therapies. For this transformation called EMT (epithelial-mesenchymal transition) to occur, the cell needs a signal from a protein produced in a separate pathway called EGF (epidermal growth factor).

Mackenzie's group concluded that if you can block EGF, then the cells do not transform and cell death follows. They examined how well three existing cancer treatments, Cetuximab (also known as Erbitux), Erlotinib and Tyrphostin could block EGF so that EMT would not occur.

This specific targeting of particular cancer cells is a better way to treat FA patients for whom the side effects of DNA-damaging chemo- and radio-treatments are severe. ■

Save the Date!

25th Annual Fanconi Anemia Research Fund Scientific Symposium  
October 24-27, 2013 • Hyatt Regency Houston  
Houston, Texas • [www.fanconi.org](http://www.fanconi.org)



## Bone Marrow Transplantation: Point/Counterpoint

One of the most exciting sessions during the Scientific Symposium was a series of debates concerning decisions and questions facing parents and individuals with FA. Experts with differing opinions gave a lively defense of their positions. This thought-provoking exchange highlighted the difficulty families face in choosing the best treatment options. Larger patient numbers and improving data will help to clarify choices when facing a crucial crossroads.

### Should danazol be offered before transplant for bone marrow failure in FA?

#### YES

Helmut Hanenberg, MD, Indiana University, Indianapolis, made the case for offering danazol, a very mild synthetic androgen, to a certain subset of FA patients. He acknowledged that those with myelodysplasia (MDS) or leukemia need to be transplanted immediately, but patients with a clinically milder disease and/or declining blood counts in the absence of MDS or leukemia should be offered this option. Danazol was well tolerated and did not show masculinizing side effects in a recent study of eight patients with FA. Seven of these patients had a robust blood count response, some for several years. Danazol can provide precious time to make decisions or find an optimal donor. Some patients, perhaps as many as 30%, may never need a stem cell transplant. If necessary, patients can still go to transplant after danazol.

#### NO

Margaret MacMillan, MD, University of Minnesota, Minneapolis, stated that ten to twenty years ago patients wanted to buy time since transplant outcomes were so uncertain. However, survival following bone marrow transplant has improved greatly and toxicity has decreased significantly. In most cases, there is no longer any need to delay transplant by going on androgens, even androgens as mild as danazol. If there is an appropriate donor, the downside of taking danazol is that patients might lose the most optimal time to proceed to transplant.

### Should radiation be used in the conditioning regimen for FA transplants?

#### YES (with certain patients)

The answer depends primarily on the type of donor available, according to Margaret MacMillan, MD, University of Minnesota, Minneapolis. Neither radiation nor busulfan is used at her center when transplanting

patients with matched sibling donors. The protocol for patients with alternative donors includes radiation.

Minnesota has achieved impressive survival rates with a conditioning regimen including total body irradiation (TBI) of 300 rads for patients with alternative donors. The probability of survival is now 92% for patients with no prior history of transfusions or opportunistic infections.

Dr. MacMillan stated that both TBI and busulfan have significant, but different, toxicities. TBI carries a risk for cataracts and hypothyroidism whereas busulfan can cause alopecia, veno-occlusive disease and hemorrhagic cystitis. Neither is more likely than the other to increase the risk of post-transplant malignancies.

In a trial of busulfan for nine patients with advanced disease, the toxicity rate was unacceptable, with the exception of *BRCA2* patients who tolerated this therapy well. The standard of care at this center remains cyclophosphamide, fludarabine, TBI300 and thymic shielding.

#### NO

Farid Boulad, MD, Memorial Sloan-Kettering Cancer Center, New York, stated that studies of non-FA patients show two factors consistently associated with increased risk of secondary malignancies post-transplant: graft-versus-host disease and radiation. TBI is also associated with organ toxicity, growth impairment, gonadal dysfunction and other post-transplant complications.

Memorial Sloan-Kettering and other centers have reduced the risk of GvHD using T-cell depleted transplants. In an effort to reduce the risk of radiation toxicity post-transplant including the risk of secondary malignancies, Dr. Boulad and others have initiated a multi-center trial, substituting busulfan for radiation.

To date, 27 patients have been treated on this protocol at four institutions. GvHD has been minimal (two patients developed grade 1; one patient developed grade 2 GvHD). Twenty-three of the 27 patients are alive and well.

Dr. Boulad asks: Why use radiation if there is an alternative which leads to a comparable outcome? ■

## Transplant Outcomes from Curitiba, Brazil



Carmem Bonfim, MD, Federal University of Parana, Curitiba, Brazil, presented a follow-up of 126 patients transplanted at her center from October 1983 to October 2009 who survived two or more years post-transplant. Today, 108 of these patients survive.

Survival outcomes have improved dramatically in recent years: 73% of patients transplanted between 1983 – 2003 survived more than two years, compared to 97% of patients transplanted from 2003 – 2009. The transplant regimen now includes 60mg/kg cyclophosphamide; patients are not given radiation or busulfan. In spite of these excellent results, Dr. Bonfim expressed concern about the long-term problems patients encounter post-transplant.

Patients frequently experienced an increase in endocrine problems post-transplant. Chronic GvHD (cGvHD), infections and malignancies were the most frequent causes of death. Eleven patients developed squamous cell carcinoma of the tongue and only three

are alive, one with active disease. Patients with cGvHD developed this complication much earlier and at a younger age than patients who did not have cGvHD. But three patients with cancer did not develop cGvHD.

Dr Bonfim writes these poignant yet hopeful words: “In the beginning, our poor patients (who didn’t have a chance to go to a dentist EVER) got diagnosed very late. Our country is big and they didn’t have money to come back to our unit. Now we have family meetings; we teach them how to take care of themselves and be their own advocates, and we are very clear about the

**Transplant survival outcomes have improved dramatically in recent years.**

‘known’ cancer risks. Survival is MUCH, MUCH better after transplantation, but it can be even MUCH, MUCH better if we try to prevent or detect cancer earlier. So, transplanted and non-transplanted patients should ALWAYS take care, lifelong!” ■

## Long-term Follow-up of Patients After Alternate Donor Transplants



Farid Boulad, MD, Memorial Sloan-Kettering Cancer Center, New York, discussed post-transplant complications experienced by a cohort of 21 patients who had survived disease-free for at least one year, following an alternative donor transplant. Patients ranged in age from 4.5 to 35 years. Eighteen patients

received 450 rads of TBI as part of the conditioning protocol, and three were conditioned with busulfan followed by T-cell depletion. None of these long-term patients developed chronic GvHD.

One patient experienced a relapse of myelodysplastic syndrome three years post-transplant. Two patients developed squamous cell carcinoma, one of the vulvo-vaginal area (with dysplasia present pre-transplant) and one of the tongue. Cancers occurred 3.7 and 7.2 years post-transplant, at the ages of 27 and 28.

Eleven of the 21 patients, including four multiply transfused, had low-normal ferritin, while 10 patients

had high ferritin levels. Four patients were confirmed to have iron overload.

Endocrine and metabolic abnormalities were common. These included primary hypothyroidism in 11 patients, hyperglycemia in four patients, and hyperlipidemia in six patients. One patient developed insulin-dependent diabetes.

Patients often experienced gonadal dysfunction post-transplant. Of ten males who could be evaluated, six had evidence of germ cell dysfunction, and all six evaluable females had ovarian dysfunction, with normalization in two females. One female had a successful pregnancy after TBI.

### Post-transplant patients need multi-disciplinary follow-up.

Patients with FA can be cured of their hematologic disease with alternate donor transplants, but these patients remain at risk for a variety of complications. Post-transplant patients need multi-disciplinary follow-up. Dr. Boulad noted that there is a tendency for poor compliance concerning post-transplant care in this population. ■

## Twenty Years of Alternative Donor Transplantation at the University of Minnesota



Between 1990 and 2010, 127 FA patients underwent alternative (non-sibling) donor hematopoietic cell transplantation at the University of Minnesota, Minneapolis using one of five consecutive clinical trials. No other transplant center has transplanted more FA patients using

alternative donors. Stem cell sources included bone marrow or cord blood from related donors (n=7) or unrelated donors (n=120).

All patients received cyclophosphamide and total body irradiation (TBI). Sequential changes were made to prevent graft-versus-host disease (GvHD), graft failure and infections to enhance survival. GvHD risk was greatly reduced by the use of T-cell depletion in 1994. The introduction of fludarabine in 1999 was a “game changer” and greatly increased patient engraftment and survival. Thymic shielding has hastened immune recovery and reduced post-transplant infections. The lowest effective dose of TBI was determined to be 300 rads. With each new protocol, patient survival improved.

Margaret MacMillan, MD stated that the overall survival for all five protocols was 61%. Poorer survival was associated with transfusions prior to transplant, invasive fungal or gram-negative infections, seropositivity for cytomegalovirus, and use of cord blood instead of bone marrow. Age is also a factor, since younger patients do better, yet Dr. MacMillan emphasized that one should not go to transplant just because of age.

For patients on Trial 5 who had no transfusions or infections before transplant, survival was 92%. Patients on Trial 5 who had been transfused or presented with serious infections had a 67% survival.

The University of Minnesota transplant program will

### No other transplant center has transplanted more FA patients using alternative donors.

continue to modify the transplant protocol for patients receiving alternate donor transplants, in an on-going effort to improve FA patient outcomes. ■

Since 1989, the Fanconi Anemia Research Fund has awarded **183** research grants to **99** researchers at **54** institutions totaling **\$15.3 million**. For details, go to [www.fanconi.org](http://www.fanconi.org).

## New FA Gene Therapy Trial Announced in Europe

European researchers, under the leadership of Juan Bueren, MD, CIEMAT, Madrid, announced that a five-year gene therapy project for FA-A patients opened on January 28, 2013. The stem cell collection phase is now open, but the gene therapy component is awaiting final authorization. This European Consortium (EUROFANCOLEN) is composed of FA researchers and gene therapists who have developed the therapy protocol after years of preclinical and clinical research.

The clinical trial will use new drugs to collect high numbers of hematopoietic stem cells from FA patients. These cells will then be exposed to lentiviral vectors that carry the therapeutic *FANCA* gene. Lentiviral vectors show improved safety and efficacy compared to vectors used in previous clinical trials.

The gene therapy trial will initially enroll five FA-A patients. The objective of this project is to develop a safe and clinically efficient gene therapy protocol for FA-A patients. ■

## Small Molecules Testing Meeting Leads to New Clinical Trial

The Fanconi Anemia Research Fund convened a Small Molecules Testing for Fanconi Anemia meeting in Portland, Ore., Nov. 2-3, 2012, that was attended by 38 participants. The meeting's overall objective was to form a federation of researchers willing to test prioritized small molecules (drugs or compounds) and identify candidates for clinical trials. Discussion focused around three key questions: 1) What small molecules might modify the FA cellular phenotype *in vitro* or *in vivo*? 2) What mechanistic insight might be exploited to guide subsequent work? 3) What is needed to move these agents to clinical trials?

As a result of the meeting, a group of researchers is designing a clinical trial using N-acetylcysteine (NAC). NAC is an efficient pro-drug for cysteine, an amino acid that regulates a number of redox reactions, including DNA synthesis and the repair of oxidative DNA damage. As FA patients show strong evidence of redox imbalance and DNA damage in bone marrow, the researchers hypothesize that oral NAC may be a beneficial therapy in FA. Oral NAC has been used for almost 50 years for other conditions including cystic fibrosis and has proven safe for children and adults. The current plan allows for enrollment of up to 40 FA patients starting late this year. Watch for more information as this trial moves forward. ■

## Advances Made in Correcting Appearance of Wrist and Arm in Children with Absent Radius

By Scott Kozin, MD

Many children with FA are born with partial or total absence of the radius. Complete absence of the radius is the most frequent variant, and causes the hand to become perpendicular to the forearm. Correction of the angular appearance of the wrist and the bowed appearance of the arm is sometimes accomplished by a surgical treatment known as "centralization," which involves placing the wrist on top of the ulna. Sometimes straightening the ulna may also be necessary. Although the initial correction is impressive, it usually does not

last and the arm reverts to its original appearance. A new method, involving transfer of a toe (without the skin) to support the wrist, shows considerable promise. The toe is placed adjacent to the wrist and spans from the ulna to the wrist bone. The arteries and veins are reconnected within the arm so that the bone and growth plates survive. The toe and its growth plates grow along with the arm, providing stability. Correction has been maintained in approximately 50% of cases. Please contact me at [skozin@shrinenet.org](mailto:skozin@shrinenet.org) for additional information. ■

## Adults with FA Meeting Draws Record Attendance



*Eric Mittelsteadt, age 35. Eric was diagnosed with FA at age 33. He received a bone marrow transplant in 2012 and attended his first Meeting for Adults with FA. "Everyone at the meeting has inspired me in some way."*

Twenty-four adults with Fanconi anemia from ten countries, ranging in age from 20 to 47, attended the Fund's fourth Meeting for Adults with FA in Austin, Texas in October, 2012. Twelve attendees were first-time participants. The participants heard presentations from foremost experts on Fanconi Anemia 101, Adult FA Stem Cell Transplantation, Gene Therapy, Head and Neck Cancer in FA, Gynecologic Considerations, and Nutrition. The meeting included support group sessions for adults with FA, their parents, partners and spouses, and opportunities for oral cancer screenings and FA research studies. The group had a spirited dinner tour aboard an amphibious vehicle, including live music and a plunge into Lake Austin. A good time was had by all.

The fifth Meeting for Adults with FA will be scheduled in spring 2014. ■

*"Fantastic to meet other FA patients for the first time, and to take part in research opportunities."*

*"It was our first time. It was very informative and well-organized. Thank you very much for everything, and for making it possible for us to attend."*

*"The support group meeting was a moving opportunity to connect with others navigating adulthood with FA. Although we all have unique life stories and illness experiences, FA becomes common ground that allows us to share and learn in a place of non-judgment and support."*

*"I feel so fortunate to have an organization meeting the needs of a group so small. I never take it for granted. I hope to give back more than I receive in the near future."*

*"This meeting is so heartwarming to me and my son. I feel a connection to others going through many of the same things we have been through."*

*"It was a real eye opener. Meeting families, patients and friends, and seeing we are not alone."*

*"I appreciate the chance to hear others' FA stories. I learned something in every session. I am so happy that my husband and I could both attend."*

*"Amazing. The highlight is bonding with those who also have FA. We all seem to get along so well very quickly."*

*"I was able to meet so many wonderful people from around the world in our little community. I loved hearing everyone's stories and how FA affects them. It brought me hope for the future."*

# Adults with FA: Trailblazers in the FA Community

By Nancy Cincotta, MSW, MPhil



Only people who live with Fanconi anemia can understand precisely what it means to have FA. The cumulative experience of the adult FA cohort is guiding the medical and emotional road map for this population.

The caring and the connections among persons with FA and their families at the adult meeting was nothing short of remarkable. The ability to discuss life, accomplishments, aspirations, fears and the reality of FA promoted a high level of trust, understanding and camaraderie. There was a “kindness” in the room, among long-time friends and among many who had just met, but who were not strangers to FA.

The meeting in Austin served as an opportunity for the community of adults to learn, connect and grow. The task for young adults is to gain enough expertise about FA to make informed decisions and to ultimately be the primary force in their own care. This gathering allowed for lively dialogue and provided a way to promote and support an enthusiasm about self-care.

As adults grappled with some of the more daunting information from the educational sessions, there was also a feeling of empowerment about the things which are controllable, such as diet. Wisdom came in all different ways. At one point someone advised, “Don’t be afraid of the C word.” Another powerful component of the adult meeting was the extended time with spouses, parents, siblings, cousins and partners. FA affects the whole family.

Fanconi anemia poses inherent challenges and limitations. For example, drinking alcohol has its role in society, yet for people with FA the risks are worrisome. Although medical recommendations suggest severely limiting or abstaining from drinking, there is a pull to fit in, to be social as others are and to have the freedom of those choices.

For more information on the adult experience with FA, please refer back to the summary of Amy Frohnmayr’s presentation in the FA Family Newsletter, Issue 50, Oct. 2011. ■

## Some “truisms” about being an adult with FA

- You are part of a very small community.
- You travel where few have been.
- You reach adulthood and immediately become a role model – a hero to those younger than you with FA, and to every FA parent.
- You are likely to have to make complicated medical decisions in your lifetime.
- You plan your future knowing the possible medical complexities.
- You have additional risk factors that require you to think about your lifestyle choices.
- You may experience closer relationships with your parents, siblings, and partners than many of your peers.
- You may work in partnership with your parents or siblings around your medical care.
- You will have to enter into a dialogue about FA as significant people enter your life.
- You have to consider medical insurance as you make choices in employment.
- You may have “FA Wisdom,” an understanding and appreciation of life unequalled by others.

## Strategies for living with Fanconi anemia

- Maintain hopeful realism
- Engage in life: Aspire to new heights
- Seek independence: Find support
- Experience hope: Mitigate against uncertainty
- Find balance: Impose boundaries and keep FA in its place
- Accept limits: Enhance capabilities
- Allow for setbacks: Applaud accomplishments
- Recognize isolation: Seek friendship
- Empower oneself: Take on challenges

# Eating Well May Help Protect Against Cancer



Many adults with FA are repeatedly warned to avoid harmful activities and substances. In her talk, “Nutrition: Eating Well for Taste and Health,” Carol Ceresa, Registered Dietitian, Veteran’s Administration Medical Center, San Francisco, provided patients with helpful tools to

discover a healthy diet and foods which may help protect against cancer.

Ceresa described the ideal diet as plant-based. She emphasized eating vegetables and fruits, including

whole grains and fat-free or reduced fat dairy products as a nutritional strategy. She encouraged eating lean meats, such as poultry and fish, as well as beans, eggs and nuts. Everyone’s diet should be low in saturated fat, cholesterol, salt and added sugars, and should include protective herbs and spices.

Ceresa highlighted substances and foods (noted in the chart below) that may be especially beneficial in reducing risk for cancer in FA. Of particular note are cancer-fighting properties found in onions, mushrooms, strawberries and the spices turmeric and curcumin. A study of quercetin, a flavonoid and strong anti-oxidant, found that this naturally occurring compound could prevent esophageal and oral cancers. Quercetin is found in onions. ■

Protective foods, spices, phytonutrients	Benefits
Zinc	May help prevent oxidative stress which leads to DNA damage.
Fish and walnuts	Contain omega-3 fatty acids, shown to protect against colon cancer. Walnuts are an excellent source of antioxidants.
Onions	Contain quercetin, which slows cancer cell growth, can stop metastasis and force cancer cells to die.
Curcumin (the active ingredient of turmeric)	Antioxidant and anti-inflammatory properties. These spices inhibit activation of genes that trigger cancer and inhibit spread of cancer cells. Curcumin extract is especially potent.
Rosemary, pomegranates	Powerful antioxidant components; shown to suppress/kill cancer cells.
Mustard seeds, horseradish, garlic and wasabi	Contain allyl isothiocyanates (AITC), which have distinctive healing power.
Mushrooms and Brazil nuts	Mushrooms (especially shitake) contain linoleic acid, shown to have anti-cancer properties. Mushrooms and Brazil nuts contain selenium, which helps protect cells from damage (1 nut/day meets one’s needs).
Thyme	May help prevent age-related reduction in antioxidants.
Strawberries	Shown to decrease the grade of precancerous lesions and slow their growth in most participants in one study.
Pecans, walnuts, avocado, parsley	Powerful sources of helpful antioxidants. Avocados are an excellent source of glutathione, an antioxidant important in preventing cancer. Writes Ceresa: “Research has shown that certain compounds in avocados are able to seek out precancerous and cancerous oral cancer cells and destroy them without harming healthy cells.”

## Outcomes for FA Adults Transplanted at Memorial Sloan-Kettering Cancer Center

At the Adults with FA Meeting in Austin, Texas in October, Farid Boulad, MD, Memorial Sloan-Kettering Cancer Center (MSKCC), New York, gave an historical overview of bone marrow transplantation. He then spoke specifically about adult transplant outcomes at his center from April 2001 through March 2012.

Over the past ten years, 12 adults with FA have undergone bone marrow transplants at MSKCC. They ranged in age from 19 to 36 years. Ten of the 12 adults

had been diagnosed with myelodysplastic syndrome or leukemia. Eleven were conditioned using radiation, and one received busulfan. In the future, all patients will be given busulfan as part of the conditioning protocol.

Six did well, but six did not survive their transplant. Dr. Boulad noted that he is optimistic, nonetheless, because having six survivors at these ages and disease severity would not have been thinkable ten years ago. ■

### Study Underway to Detect Oral Cancer in FA

If you or someone in your family is diagnosed with oral cancer, please consider participating in a new research study funded by FARF to determine if saliva can be an early detection tool for oral cancer. Contact Teresa Kennedy as soon as possible after diagnosis and before treatment at [teresa@fanconi.org](mailto:teresa@fanconi.org) or 888-FANCONI. Teresa will coordinate your participation with David Wong, DMD, DMSc, the study's principal investigator. For more information, visit Research Highlights on our website.

## Congratulations!



*Christine Bray (FA) and Donald Morse were wed on March 28, 2013.*



*Lisa Doyle Kinsella (FA) and Terry Kinsella were married June 22, 2012.*



*Nicole Fauver and Rondo Fraley married on August 20, 2012.*



# Hopeful For Our Future Together

By Maly Lee



2011 was a very exciting year for our family. We had pulled through one of the toughest times of our lives just the year before with my husband Eddie's layoff and were now looking forward to a brighter future with his new job. Within just a few months, Eddie was promoted, our oldest child was

choice of preschool and we were anticipating our third child. We actually started to feel that we were finally going to make it.

At my 20-week ultrasound, however, all that changed. The test showed that a few things were amiss with our baby. After numerous examinations, we finally heard the name of Fanconi anemia. That began the first leg of our unwilling journey into FA.

Our baby boy was born on March 13, 2012 and immediately rushed to the NICU. We named him Mason. That night we learned that his stomach was attached to his lungs, so his esophagus ended in a pouch going nowhere. Two days later he underwent corrective surgery, but it was unsuccessful. The gap between his esophagus and his stomach, now removed from his lungs, was too wide for them to repair until he was older.

In the weeks after his birth, we learned many new things about Mason. He had a bicuspid aortic valve, no thumb on his right hand, a non-functional thumb on his left hand, a shortened radius in his right arm which caused a club hand and hearing loss in his right ear. It was a very tough time for us. All the hardship from previous years felt like nothing compared to what we were now facing.

Since FA is genetic, we had our other two children, Jiena and Eddison, tested for it as well. Jiena's results came back positive. Not wanting to let FA destroy us,

we went ahead and searched for potential bone marrow donors. Eddie, our unaffected son Eddison, and I were tested. None of us was a match to either Mason or Jiena so we decided to check the national registry. We received alarming news: only a handful of potential matches came back and our hematologist had no confidence in them matching enough to be donors for our children. Not only that, but we found out that Jiena has one of the rarest tissue types in the world. Her platelets were dropping and her bone marrow cellularity was already at 20%. We felt broken beyond repair.

Still, we were unwilling to give up. Since then, we've been raising awareness non-stop within our Hmong community. We've also started working with the Be The Match organization to register more donors, especially those of color. The University of Minnesota's Gophers football and other teams decided to help us as well. We've been met with a lot of support wherever we've gone. Support has come from within our Hmong community as well. Illnesses typically are not accepted very well if you are Hmong. However, the support we have received so far has been almost overwhelming. It was actually much harder to make our own parents understand. To this day, my in-laws still have faith that the FA will disappear. I wish it were that simple.

Unwilling to give up, we've been raising awareness non-stop within our Hmong community.

Amazingly, because of FA we've learned to slow down and not take things for granted. We now take one day at a time and make every moment memorable. Even medical appointments are now viewed as trips with fun to be had. Mason still has a lot of medical needs that have yet to be addressed, and matching donors still have not been found for him or Jiena. But, we are again hopeful for our future together. For Mason and Jiena, our family will never give up. ■

# Why We Fundraise

By Becky Brinkmann



I admit I was flattered when asked to write an article for this newsletter, but I thought, “are you kidding me?” What in the world can I say that hasn’t already been said and felt by every parent dealing with Fanconi anemia? And then I learned my topic was fundraising!

We finally began fundraising a year post-diagnosis. It was nothing elaborate; we started with a family letter. It seemed important to put our story into words.

Prior to July 2011, we were a normal family, although we have five children: Sydney, 13; Chad, 10; Zach, 6; and Samantha and Summer, 4. That July our world began spinning a bit faster. Sydney had routine blood work done, and the results were unexpected and quite shocking. Her white, red and platelet counts were all extremely low. We contacted St. Louis Children’s Hospital for an appointment in the hematology department.

After more appointments and a stay in the hospital, we heard the gut-wrenching words: Sydney has Fanconi anemia and will require a bone marrow transplant soon. The doctors told us the best hope for a successful transplant is a matched sibling donor. Chad, Zach, Sam and Summer were tested to determine if anyone was her match. We received wonderful news that our ever-active Zach was a perfect match for her. This was a bit of a relief. We thought we were finally given a little breathing room.

Unfortunately, a couple weeks later our hopes were crushed as we were given the devastating news that Zach also had FA and low blood counts. One child with a

life-threatening disorder is hard enough, but now two of our children? The tears came and numbness set in. The questions began flying: How could this be? Why? Are the doctors sure? This just didn’t seem possible. Sydney and Zach are so active and have never shown any signs of illness, much less a fatal disorder. This must sound very familiar to some of you right now.

At this time we feel very blessed that Sydney and Zach’s blood counts have remained stable (low, but stable), and they have been able to remain normal kids with normal activities.

So what do we do now? Now we have to get to work to help find a cure for this challenging disease. We began fundraising efforts for the Fanconi Anemia Research Fund. Over 85% of the Fund’s income comes directly from family fundraising from families just like ours. This organization is amazingly helpful to all the FA families by providing emotional support and funding research. Researchers and specialists continue to try to make the painful transplant process more bearable and successful for patients, and to find better therapies for this disease. But all of this takes money. The simple fact is that we need to fundraise to save our children!

If we who have the most to lose do not fight, who will? We have met families who have lost their children. We have met a family who had to decide whether to continue the fight or to make the most of the time that

**The simple fact is that we need to fundraise to save our children!**

was left. I do not want to have to make those decisions. I do not want to suffer this unbearable, unspeakable loss. We need to fundraise to help the doctors and researchers develop improved treatments and, most of all, to FIND A CURE!

Is our family going to be the fundraising family of the year? Not even a chance. But we can get ourselves out there and help the cause. We can begin to put our mark on FA and find answers. ■

## Before and After a Diagnosis

By Ana Alejandra Tabar Concha



I was born in the Dominican Republic, a small island in the Caribbean with a lot of limitations. I have a wonderful family: parents, siblings, boyfriend, and friends who make me very happy. However, Fanconi anemia has touched my life with great sadness.

When I was fourteen, my family discovered that my oldest brother had a rare disease called Fanconi anemia, which made him weaker and weaker. They also learned that I had FA, but I was not concerned at the time. My family fought day after day to understand and improve my brother's condition. They got him to the US for treatment, where the disease was most known. Unfortunately, my brother died the same year he was diagnosed. This marked a before and after in our lives.

I have always been very active and happy, and I never worried about FA. I've never felt tired or had any limitations in my everyday life. I went to college, graduated, and worked at the same time. I even went to Madrid to work on a master's degree.

A year ago, I started to feel pain in my stomach, and I went to the doctor. My blood counts were very low, and we knew FA was back in our lives. My life turned around again, and became one of constant worry and a desperate search for help.

Doctors say I can't work and must reduce my activities and hobbies to ten percent of what I did before. In the Dominican Republic there's little experience and knowledge of FA. We desperately started looking for other alternatives and information outside of our country.

Through our search, we found Dr. Farid Boulad at the Memorial Sloan-Kettering Cancer Center in New York. Here was the hope we were looking for! Dr. Boulad told me I needed a bone marrow transplant, and I also discovered things I had never imagined about FA.

Dr. Boulad also told us about the Fanconi Anemia Research Fund, a wonderful team that works and fights everyday for our health and well-being. But the really amazing part was just about to begin. I attended a conference for adults with FA. Wow! Such an amazing blessing! I went from feeling alone, that nobody could understand how I felt, to feeling like family with the people I met. These 24 people from around the world had my same disease. Not only that, they were happy people: fighters, heroes, friends, siblings, and wonderful human beings who have been through more painful moments than I have. I also met doctors, researchers, and transplanted and non-transplanted patients.

I decided that FA is not going to imprison me or make me unhappy.

At the conference, I heard others speak about living with FA. They made me realize that we have to fight the disease. I decided that FA is not going to imprison me or make me unhappy, and that I belong to this small group that understands and supports me.

Right now I am in need of medical treatment and a transplant, but I'm without a donor or money for transplant. I am fighting to reach my goal step by step. My fight continues, but I also feel joy and happiness in living my life to the maximum every moment as best I can. ■

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facebook

# Fundraising Connelly Style

By Kim Connelly



A brief description of how we began. John and I met, fell in love, married and planned our lives together down to the color of towels hanging in our master bathroom. Less than a year later, we welcomed our first daughter. After two miscarriages, Evan graced our lives, but

along with him came the diagnosis of Fanconi anemia. We were devastated and overcome with despair. After a year or so, we adjusted to reality and began settling in with FA like an old married couple on a comfy couch. Next came four more miscarriages, three additional daughters, and many comments that we should really get a television in our bedroom! Lastly, we welcomed the caboose of our family, Becca, who sadly has FA, too.

Our lives are busy. We have six children between the ages of two and thirteen. John is president of a US company based overseas and often travels. I am a registered nurse but stay at home as CEO of all things Connelly. The children's activities consist of lessons for flute, drums, piano x3, violin, karate, mother/daughter book club, Girl Scouts x2, robotics, orchestra and band x2, not to mention the social schedule of a thirteen-year-old girl! Our family is very involved in the lives of our extended family and friends, the children's school, our church and our small community. Our daily calendar changes throughout the day, depending on forgotten lunches, illnesses, last-minute study sessions and two-year-old meltdowns! Launching the kids (and husband) out the door in the morning sometimes seems comparable to launching a shuttle into space!

Why, we are often asked, would you repeatedly add fundraising for FARF to your already full docket? We are currently working on our seventh Evan's Enchanted Evening (EEE), a dinner dance with a live and silent auction. We have previously raised funds via cookbooks,

vendor fairs, bake sales, scrapbooking days, non-uniform days, catalog and home parties and an annual Christmas card plea. We know how much time fundraising requires. We adjust to parts of our lives being public, and we are professionals at accepting offers for help, asking for help and being thankful and humbled for help. You've heard the reasons why not to fundraise numerous times. Please, now, let me explain to you why John and I *do* fundraise.

Our initial fundraiser took root after we attended our first FARF regional meeting. When we heard about the research possibilities, we felt like sailors lost at sea finally seeing inhabited land! We knew that the only individuals raising research money would be the small group affected by this rare disease. We jumped in, not knowing what we were doing, and nine months later our first EEE took place. The evening took our breath away with powerful emotions of love and generosity. These emotions still warm our souls today.

Fundraising is as important as finding the right doctors to care for Evan and Becca. If there is no money to fund FA research, FA research will decrease, as will the hope we feel regarding the only part of this disease we *can* control. If the day ever comes when we are grieving the loss of one of our children, I will not look back and wish I had done more for them. Comforting those in our FAMily who have shared the mourning of their FA angel leaves me grieving for the beautiful soul

**Why, we are often asked, would you repeatedly add fundraising for FARF to your already full docket?**

who has passed and wondering if it will be our turn next. We fundraise to bring even greater meaning to these angels' lives by honoring what their struggle has taught the researchers and doctors, which in turn will be used to benefit our FA loved ones who continue to fight.

There will never be a perfect time to fundraise. You will never know all that is needed to do the task without falter. However, you will never regret taking action, knowing that something else was far more important than your fears: *hope* for those with Fanconi anemia. ■

## In Loving Memory

*“For some moments in life there are no words.”*

*Sophia Sitzerman..... 2/28/07 - 12/7/12*

*Luke Monaghan ..... 6/17/89 - 1/11/13*

*Robert Haroldsen..... 7/31/97 - 12/8/12*

*Austin Jaros-Riley..... 2/28/96 - 2/3/13*

*Brian Kerr ..... 2/24/02 - 12/8/12*

## FA Family Meeting at Camp Sunshine

Casco, Maine • June 28 - July 3



Questions or need financial assistance for travel?  
Please contact Teresa Kennedy at [teresa@fanconi.org](mailto:teresa@fanconi.org) or 1-888-FANCONI.

## FARF Can Help You Fundraise

More than 90% of the Fanconi Anemia Research Fund’s annual budget comes from family fundraising. We’re here to help make your events a success. We can:

- Provide sample fundraising letters and help you edit your letter
- Use your photos to personalize your letter, event invitation or brochure
- Use your mailing list to send your letter or invitation from our office
- Provide ideas, information and display materials for events
- Provide a PowerPoint or video presentation to use at your events
- List your event on our website
- Send a thank-you letter and tax receipt to your donors

We ask that all fundraising events be covered by liability insurance. Insurance for a one-time event is often available through a family’s homeowner’s insurance policy as a relatively inexpensive insurance rider. Please contact the Fund if you need assistance obtaining or paying for this required insurance.

Please ask your donors to make checks payable to the Fanconi Anemia Research Fund. When a donation is received, we’ll generate a letter of thanks with a tax receipt, and we’ll notify you that a donation has been made in your name.

We appreciate all your efforts to raise funds for FA research and family support. You are making a difference! ■

## Fund Claims First Place in Online Contest!



Allstate Insurance Company announced the Fanconi Anemia Research Fund as the first-place winner in its Cash for Your Community program in

November. The program was a three-week campaign during which people voted for their non-profit of choice in the Eugene, Ore. area. Cash awards were given to the top three charities.

Long-time Fund supporter and fundraising “Shining Star” Sharon Schuman (see our 2011 *Donor Newsletter*, page 11) spotted this contest. Sharon quickly brought the contest to the attention of FA parent Peg Padden, who promoted the opportunity on the family e-group. With simply one vote per household, Peg wrote, “there is no

easier way to raise money than this.” The FA community again rallied, and raise money they did. Despite entering the contest a week after it opened, the Fund received the highest number of votes and was awarded the top prize of \$35,000!

The small but determined FA community is truly amazing. As many recall, we won the \$50,000 top prize, plus an additional \$65,000 in donations, in Parade Magazine’s Giving Challenge in 2008. Next, we won \$25,000 in Chase Bank’s Community Giving program in 2011. Peg ended her call-to-action email with an apt quote by Margaret Mead: “Never doubt that a small group of thoughtful, committed citizens can change the world. Indeed, it’s the only thing that ever has.” Thank you all. ■

## FA Parent’s Fundraising Surpasses \$1 Million!

Peg Padden’s sons Jake and Spencer were diagnosed with Fanconi anemia in 2003. Sadly, Jake died later that year due to complications from a bone marrow transplant. In response to the diagnoses and tragedy in her family, Peg began tirelessly campaigning to raise money for FA research. In less than ten years, Peg’s amazing efforts have earned more than \$1 million in donations to the Fanconi Anemia Research Fund!

One of Peg’s fundraisers is an annual Valentine Fanconi Anemia Run/Walk in Portland, Ore. After nine years, many avid runners see the race as the unofficial kick-

off to the running season. Readers of *The Oregonian* overwhelmingly voted this year’s race the Best February Race in the state. The race added 21 new donors to the National Bone Marrow Registry and raised \$35,000.

In addition to the Valentine FA Run, Peg also organizes an annual golf tournament, BBQ, and raffle, among other efforts. Peg is an enthusiastic, inspirational, and resourceful fundraiser for FA research, fully understanding that every dollar can make a difference. Thank you, Peg, for your many efforts! ■

### SCC Fact Sheets Available

Regular screenings for oral cancer are critically important for FA patients. The Fund produced fact sheets about squamous cell carcinoma to share with your dentist and ear, nose and throat doctor (ENT). **FA patients and families are encouraged to take a fact sheet to every dentist and ENT visit.** Fact sheets—in English, Spanish, Afrikaans, Dutch, French, German, Hebrew and Italian—are available on our website or by calling our office.

### Online Fundraising Tools Available

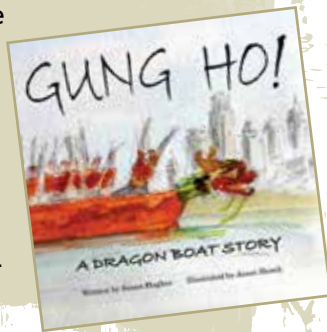
Qgiv and Hobnob are online fundraising tools available through the Fanconi Anemia Research Fund. Through Qgiv, we can accept online donations directly on our website. Hobnob offers people a customizable fundraising page for events, enabling online registrations and donations in advance and at the event. Contact FARF for details on how Qgiv and Hobnob can enhance your fundraising!



## Gung Ho for Fundraising

*Gung Ho! A Dragon Boat Story* is now on the shelves. This children's book tells the story of the "Gung Ho!" dragon boat team as they prepare for a race. The team works so well together that they are taken on a fantastic flight through Philadelphia, arriving at the finish line just in time to win the race.

Susan Hughes, a friend of the Himmelreich family, wrote the book. All proceeds from the book sales will be donated to the FA Research Fund in honor of Megan Himmelreich. You can purchase the book at [www.createpace.com/4125442](http://www.createpace.com/4125442).



## Kicking Things Up

For the third annual KICK FA kickball tournament last year, Matt Pearl, 16, FA, decided to "kick" things up a notch by raffling off his dirt bike as a prize. The raffle sales netted \$1,150 in addition to the more than \$10,000 raised by the KICK FA tournament. The event raises money for FA research in honor of Matt and his sister, Alexandra, 18.

"I want to help find a cure for FA and have hope for Alex and me to live longer, successful lives," says Matt. "We will work hard to raise money and continue awareness every possible year we can."

## Brave Hearts Hoot 'N' Holler

Attendees and volunteers kicked up their heels and raised \$162,000 at the 2012 Brave Hearts Hoot 'n' Holler held in November. The Kendall and Taylor Atkinson Foundation and the Atkinson and Nash families organize this annual event. Molly Nash, 18, shared her insight about living with FA and encouraged people to help fund research for a cure. "I have many dreams that I'd like to accomplish," Molly said. "All of these things are not out of my reach. I just need time."

Alan D'Andrea, MD, Dana-Farber Cancer Institute, Boston, and long-time FA researcher, was an inspiring volunteer guest speaker. "The spirit of this meeting tonight just gives me a great feeling about what I do," he said.

Guests bid on silent auction items, participated in a "Virtual Cow Plop," and bought numbered wine corks corresponding to a bottle on the "Wall of Wine." This foot-stomping event certainly put the "fun" in fundraising!



Alan D'Andrea, MD addresses Hoot 'n' Holler attendees

## Triathlon Runners raise \$46,000

Steve and Jen Klimkiewicz raised \$46,000 in honor of their son, Wyatt, with the help of a group of other racers at the 2012 Sandman Triathlon in Virginia Beach, Va. It was the largest fundraising total since they started racing for Wyatt, 8, about five years ago.

"We have a great support system with our friends and family," Jen said of this year's fundraising.

The runners had sponsors from as far away as Pennsylvania and Delaware, including friends whose children set up benefit lemonade stands.

"This is an awesome cause and an awesome event for an awesome little kid," said one of the racers who helped raise funds. "We set a big high goal from last year and broke that."





Derek Persson, aka Batman

## Monster Dash with Batman

Running a half-marathon is no easy task—much less running in a full Batman costume. Derek Persson did just that at last fall's Chicago Monster Dash, and all for a good cause. Attached to the back of his costume, Derek wore a sign reading "I run in memory of my daughter Diamond to help raise funds for the Fanconi Anemia Research Fund." Diamond died nine years ago, at one and a half years of age, from Fanconi anemia.

"I had several people come up and want to take pictures with me," Derek said. "I also had many people give me support throughout the race after seeing the fundraising sign on my back."

Derek completed the race in just over two hours, finishing 1,004<sup>th</sup> out of a total of more than 2,500 runners. He recently ran the Lexington Bluegrass Half-Marathon, and finds the "I Am Athlete" website a great way to raise funds. He adds, "I have found that my friends and family are more willing to donate since I am willing to work for it by running a half-marathon."

## Casual for a Cause

Teachers and staff at Midway Elementary School, Church Road, Va., raised money for FA research by wearing jeans. Midway Elementary started a "Casual for a Cause" fundraiser late last year, allowing teachers and staff to wear jeans on Fridays if they made a donation. Students also donated, bringing the total donations from students, faculty, and staff to more than \$3,500. Wearing jeans for FA research? It's a win-win combination!



## Team BrAvery Crosses Florida



Orion Marx is often challenged by his father-in-law, Charlie Scott, to participate in athletic events around the country. The challenge last year was to mountainbike across Florida on 235 miles of dirt trails and back roads in the first Cross Florida Individual Time Trial. Their effort also was to raise funds for FA research as Team brAvery, named after Orion's daughter and Charlie's granddaughter, Avery. Avery survived a bone marrow transplant two years ago, and is now 9 years old. Orion said, "Although the events we are participating in are difficult, they are nothing compared to the challenges facing children and adults with FA." Team brAvery's miles totaled more than \$3,800 for FA research!

## A 5-Spot for Eli

Birthdays are usually a time to receive gifts, but for Eli Lana, it was a chance to give back. For his 8<sup>th</sup> birthday, Eli hosted a "5-spot" party, where guests bring a \$5 donation instead of a gift with the total donations split between the birthday child and a charity of choice. Eli chose three charities, including the FA Research Fund, hoping to send them each \$500. With the help of an online fundraising page, he doubled that goal, giving each charity more than \$1,000!

"He's a hero every day," Eli's mother, Mary Ann says. "He takes on challenges no kid should have to face and he perseveres."

With Eli's help, we're a step closer to making sure no kid has to take on the challenge of FA.



Eli Lana  
Bone Marrow Transplant Survivor

## Fund Welcomes New Executive Director



The Fanconi Anemia Research Fund is delighted to announce that Laura Hays, PhD, has been hired as executive director effective May 1. Laura succeeds Beverly Mayhew who resigned in January.

Laura has an extensive scientific background and has worked in Fanconi anemia research for the past 10 years. She received her bachelor of science from the University of Washington, Seattle, in cell and molecular biology, and her PhD in oncological sciences (cancer genetics) from the University of Utah, Salt Lake City. After postdoctoral research at the University of Washington and Oregon Health

& Science University (OHSU), Portland, Ore., Laura became a faculty member in the OHSU Department of Hematology and Medical Oncology in 2007. She has been highly active in the FA scientific community and has attended numerous FARE-sponsored meetings including the past ten Scientific Symposia, three FA squamous cell carcinoma meetings, the recent small molecule meeting, and Meeting for Adults with FA. In addition to her scientific background, she has significant experience in both fundraising and community outreach as a member of the Knight Cancer Institute at OHSU.

Laura says “I look forward to meeting all the members of this wonderful community and hope to apply my scientific, medical, and outreach skills to help fulfill the mission of the Fund to both find a cure and provide support for those living with FA.” Laura can be reached by calling the Fund or writing her at [laura@fanconi.org](mailto:laura@fanconi.org). ■

## Board of Directors: Comings and Goings



*Amy Frohnmayr, MA*



*Peter Pless, MD*

The Fanconi Anemia Research Fund welcomed Amy Frohnmayr, MA, and Peter Pless, MD, to the board of directors early this year.

As a young adult with Fanconi anemia, Amy has attended numerous FA Family Meetings, the Meeting for Adults with FA, and several Scientific Symposia. Along with board member Christopher Byrd, she serves on the US Food and Drug Administration’s Patient

Representative Program. In joining the board, Amy says “I am delighted to participate as a board member, and hope to be as helpful to the FA community as possible in this capacity.”

Peter Pless is an FA parent and practicing dermatologist in Pennsylvania. He and his wife, Janice, have two daughters—Julia, 16, who has FA, and Victoria, 21. Peter has attended several Scientific Symposia, and the Pless family regularly attends the Fund’s Family Meetings at Camp Sunshine.

The Fund and board of directors bid fond and grateful farewells in January to two board members, each of whom gave many years of service to the Fund. Ruby Brockett joined the board in 1998 and served as its secretary/treasurer. Ruby’s business experience was a benefit to the board, most recently in her role on the board’s financial investment committee. Bob Sacks served faithfully for 13 years. He continues to be a tireless advocate for FA patients and families. Our great thanks to Ruby and Bob for their efforts and commitment to the Fund’s mission. ■

# Your FA Research Dollars at Work in 2012

During 2012, the Fanconi Anemia Research Fund awarded \$1,572,608 in research grants to the following projects:

**Investigator:** David Wong, DMD, DMS, UCLA School of Medicine, Los Angeles; Abu Nazmul-Hassain, DDS, PhD

**Title:** *Salivary Biomarkers for Oral Cancer Detection in FA*; **Amount:** \$193,588

**Investigator:** Madeleine Carreau, PhD, Laval University, Quebec, Canada

**Title:** *Exploring the Role of FANCC in the Development of Cell Death*; **Amount:** \$93,644

**Investigator:** Ruud Brakenhoff, PhD, Free University, Amsterdam, Netherlands

**Title:** *Targeted Treatment of Oral Cancer and Pre-cancer in FA Patients*; **Amount:** \$324,000

**Investigator:** Michael Spiotto, MD, PhD, University of Chicago, Chicago

**Title:** *Non-genotoxic Inhibitors for HPV-induced HNSCC in FA*; **Amount:** \$198,910

**Investigator:** Dong Zhang, PhD, University of South Dakota, Vermillion, S.D.

**Title:** *Investigate the Molecular Mechanisms of How FANCI Regulates Centrosome Cycle*; **Amount:** \$186,545

**Investigator:** Robert Sclafani, PhD, University of Colorado, Denver

**Title:** *Potential Therapeutic Use of Resveratrol for Head and Neck Carcinogenesis in FA*; **Amount:** \$100,000

**Investigator:** Parinda Mehta, MD, Cincinnati Children's Hospital Medical Center, Cincinnati

**Title:** *Serology Biomarker for Immune Response to HPV Vaccination & Exposure in FA*; **Amount:** \$40,000

**Investigator:** Rachel Katzenellenbogen, MD, Seattle Children's Research Institute, University of Washington, Seattle

**Title:** *HPV Infection and Serology in FA Patients*; **Amount:** \$69,028

**Investigator:** Hebiest Berhane and Joel Greenberger, MD, University of Pittsburgh Medical Center, Pittsburgh

**Title:** *GS-Nitroxide (JP4-039)/F15 Liposome Oral Radioprotective Therapy for FA Patients Requiring Chemoradiotherapy for HNSCC*; **Amount:** \$33,045

**Investigator:** Farid Boulad, MD, Memorial Sloan-Kettering Cancer Center, New York

**Title:** *Multicenter Pilot Trial of HSCT Lacking a Genotype Identical Donor*; **Amount:** \$101,531

**Investigator:** Markus Grompe, MD, Oregon Health & Science University, Portland, Ore.

**Title:** *Testing Clinically Relevant Compounds in FA*; **Amount:** \$83,817

**Investigator:** Johannes Walter, PhD, Harvard Medical School, Cambridge, Mass.

**Title:** *FA and the Repair of DNA Protein Crosslinks*; **Amount:** \$148,500 ■

## Consensus Conference Held to Develop New Guidelines Book



Fifty physicians, researchers, and representatives from the international Fanconi anemia community gathered for a day-and-a-half meeting near Washington, D.C. in April to discuss updates and additions to a new edition of the Fanconi Anemia Research Fund's handbook, *Fanconi Anemia: Guidelines for Diagnosis and Management*. The busy agenda invited lively debate on presentations

based on current and proposed new chapter topics. Eva Guinan, MD, Dana-Farber Cancer Institute, Boston, and member of the Fund's Scientific Advisory Board, facilitated the conference and organized advance web-based meetings for topic-specific committee groups. We are grateful for Dr. Guinan's hard work.

The book provides critical and potentially life-saving information for patients, families, and physicians. The current third edition of *Fanconi Anemia: Guidelines for Diagnosis and Management* is available free of charge in English or Spanish as a book or on CD from the Fund. It can also be downloaded on the Fund's website. Look for the new fourth edition in English by early 2014; a Spanish edition will follow.

**Mission: To find effective treatments and a cure for Fanconi anemia and to provide education and support services to affected families worldwide.**

### Use of Logo

A reminder to our families with FA: Please use our logo or letterhead only after you have consulted staff at the Fanconi Anemia Research Fund and received approval. This step is necessary to be sure our messages are accurate and consistent and it helps avoid legal complications. We are happy to collaborate on fundraisers and mailings.

### 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.*

## HOW YOU CAN HELP

**Donations Online:** You can donate via the heart button on the Fund's website ([www.fanconi.org](http://www.fanconi.org)) or through [www.networkforgood.org](http://www.networkforgood.org) or [www.paypal.com](http://www.paypal.com)

**Donations by Phone:** Call us at 541-687-4658 or toll free at 888-FANCONI (888-326-2664) (USA only)

**Donations by Mail:** 1801 Willamette St., Suite 200, Eugene, OR 97401  
*Please go to [www.fanconi.org](http://www.fanconi.org) to learn about other ways to donate.*

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