FAmily Newsletter

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The FA Community Mourns

Unable are the loved to die. For love is immortality. —*Emily Dickinson*

Amy Frohnmayer Winn

1987 – 2016

"I hear a lot of words like 'unfair' or 'sorry.' But if you think about it, aren't these all just bonus years? Am I not just extraordinarily lucky? In this moment, sipping coffee and watching dawn paint downtown Portland in pastels, there is nowhere else I'd rather be." – Amy, mid-September

Amy Frohnmayer Winn died Sunday, October 2. In spite of losing two sisters, she considered herself lucky to have Fanconi anemia. For her it was a force that shaped her for the better. Without it she

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Chris Byrd

1982 – 2016

On September 8, the Fanconi anemia community and the world lost one of the brightest and kindest souls in Christopher Byrd. A dear friend and FARF board member, Chris passed away peacefully surrounded by love and support from family and friends across the world, after a year-long battle with head and neck cancer. Chris was well known in the FA community. He inspired hope, led by example, and showed everyone what it means to embrace life. The courage he showed this past year

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Ken Atkinson

1950 – 2016

Ken Atkinson, a father, husband, physician, and a dear friend of the Fanconi Anemia Research Fund, was killed on April 4. A pillar of his community, a physician dedicated to the patients he served, and a beloved family member, Ken was a hero is so many ways. He was tragically killed while trying to help an injured neighbor in his hometown of Centennial, Colorado. Showing his complete selflessness, Ken demonstrated his commitment to his community and his ability to give everything he had

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> “Like so many of you, we all feel deeply grateful that this unique spirit touched our lives so profoundly.”
>
> - Lynn Frohnmayer, about her daughter, Amy

Amy Frohnmayer Winn cont.

thought she might have been oblivious to the deep value of every moment of life. Instead, the knowledge that her time was “bonus time” filled her with gratitude for every day and for the love of family and friends. She found beauty everywhere—in nature, art, poetry, running--and she relished time with her adored husband, Alex. She was deeply committed to FA research and to her friends with FA, as well as to her goal to become a mental health counselor, working with the elderly and the chronically ill. For those who knew Amy—which includes many who read this newsletter—she will always be an inspiration, a mentor, and a source of joy.

Amy deeply admired the writer Mary Oliver. She always found special meaning in the last phrases of the poem “In Blackwater Woods”:

To live in this world you must be able
to do three things:
to love what is mortal;
to hold it against your bones knowing
your own life depends on it;
and, when the time comes to let it go,
to let it go.

“I am sure we won’t ever be able to ‘let Amy go’”, Lynn Frohnmayer, Amy’s mother, wrote. “Amy was our teacher, our guide, our inspiration, our love. Like so many of you, we all feel deeply grateful that this unique spirit touched our lives so profoundly. We are all determined to keep Amy forever in our hearts and try to embody, as best as we can, her love for nature, for cherished friends and family, and her enduring sense of gratitude for this far too short life she was given.”

Chris Byrd cont.

was not unlike the way he lived every day of his life. Chris served as a board member with FARF from February 2012 but was an important part the FA community for much longer. He was a role model for those with FA, sharing his story and offering advice based on his own experience. For parents, he was a source of hope, offering them a glimpse into a future as a happy, successful adult.

Born in 1982 in Virginia, Chris grew up in Winter Springs, Fla., where his sense of adventure, zest for life, and passion for the environment grew as he did. After graduating from the University of Central Florida, where he earned a double major in International Political Science and Legal Studies, he went on to obtain his Juris Doctor from Nova Southeastern University’s Shepard Broad Law Center. Christopher was a founding father of Sigma Nu, Mu Psi Chapter, and served as Vice Justice of Phi Alpha Delta Law Fraternity International while at UCF. He went on to become an advocate for the environment, spending five years with the Department of Environmental Protection (DEP). He then served on the Executive Council of the Environmental and Land Use Law Section of the Florida Bar and as the Community Service Committee Chair of the Orange County Bar Association’s Young Lawyers Section. Christopher started the Byrd Law Group, and for two consecutive years, was voted as one of Orlando’s Legal Elite by his peers. Chris was an accomplished but very humble person whose enthusiasm, dedication and optimism were felt by everyone who was fortunate enough to encounter him. His mission to improve the lives of others was evident in his involvement with the Fanconi Anemia Research Fund as a devoted board member and lifetime advocate. He was loved by many and will never be forgotten.

Ken Atkinson cont.

for others. Described by those who love him, Ken was a man of deep faith who loved and sought to serve.

Ken and his wife Jeanne started the Kendall & Taylor Atkinson Foundation (KATA) to honor their two children who died from Fanconi anemia. Over the past ten years, the generosity of the KATA Foundation and of Jeanne and Ken Atkinson personally have made an incredible and lasting impact on Fanconi anemia research. With donations and support exceeding

$1,730,000, the Foundation has enabled FARF to make exciting breakthroughs in gene identification and therapeutic discoveries, in addition to supporting FA families through education and scholarships for attendance at both FAmily Camp and the Adult Meeting. The KATA Foundation has significantly contributed to the success of the annual Scientific Symposium, and to the advancement of knowledge in the areas of research and clinical care. Specifically, KATA has supported critical research in squamous cell carcinoma (notably, head and neck cancer), screening for therapeutics, and advances in bone marrow transplantation.

Without the KATA Foundation and Jeanne and Ken Atkinson, the Fund would not be able to support the scientific community in making such significant progress in extending life expectancy and quality of life for those affected by FA. The Fanconi Anemia Research Fund and the entire FA community owes an enormous debt of gratitude to Jeanne and Ken Atkinson for their devotion and generosity, and to the KATA Foundation for its hard work and continued support to help find a cure and to support FAmilies.

Ken was a true hero to the entire FA community and remains an example to all of love, leadership, and a life of service.

New Initiatives to Accelerate Fanconi Anemia Research

The Fanconi Anemia Research Fund was founded on the principle that research is the key to solving Fanconi anemia. FARF catalyzes research through its highly successful grants program and scientific symposia. However, more needs to be done. In January, Dr. Brad Preston joined the Fund as the first Scientific Director to bring FA research to the next level.

Brad's primary goals are to accelerate FA research and to bring cutting-edge scientific discoveries into the FA clinic. As a first step, he is working with Dr. Ray Monnat (Chair of FARF's Scientific Advisory Board) and board members Dr. Rich Gelinas, Lynn Frohnmayer, and Kevin McQueen to critically assess FA research priorities and to identify opportunities to accelerate research. This dedicated panel of scientists and parents is the core of the Fund's new Council to Accelerate and Focus Research (CFAR, pronounced "see far"). The mission is to improve the clinical outcomes of FA individuals and to do so as fast as possible.

CFAR focuses on the prevention and early detection of disease, particularly bone marrow failure and cancer. CFAR members work with top-notch scientists and clinicians around the world to develop new promising areas of research. Examples include preclinical and clinical trials of drugs to prevent or delay bone marrow failure and cancer, CRISPR-based gene editing to correct FA mutations, and immunotherapies to suppress precancerous oral lesions. CFAR's next steps will be to identify specific projects for FARF funding and to leverage the newly established David B. Frohnmayer Research Fund and the Knight Fund to advance projects with the highest promise of improving clinical outcomes in FA individuals. In addition to these new "targeted" research grants, the Fund will continue its current investigator-initiated grants program, which seeks and funds the very best ideas from the very best scientists worldwide.

New Hope for Avoiding, Treating, and Curing Head and Neck Cancer

Bhuvanesh Singh, MD, PhD, Memorial Sloan Kettering Cancer Center
William William, MD, University of Texas MD Anderson Cancer Center

As the Fanconi Anemia Research Fund intensifies its efforts to support cutting-edge research, a major target is head and neck cancer. Two of the most exciting presentations at Camp Sunshine discussed potential new treatments that could be game-changers in this quest. It is well known that Fanconi anemia adults are at very high risk for this disease – 500 to 700 times more likely to get it – than the general population, at an average age of 33 years. If the cancer is caught early it can be cured surgically, but if it is not caught early, it is more lethal for the FA population than for others. This is because the regimens of chemotherapy and radiation that are needed to treat FA cancers can not be tolerated by people with FA. All this is about to change.

According to Dr. Bhuvanesh Singh, there are promising new therapies: right now, robotic surgeries can reach difficult areas of the head and neck previously unreachable; right now, proton radiation, which is precisely targeted, can be better tolerated by people with FA; and on the horizon are targeted drugs like the FDA-approved Erbitux, which allows doctors to achieve the same results with less chemotherapy and less radiation. According to Dr. Singh, Erbitux is not a cure-all, but it shows that a new class of drugs is emerging that can interfere with the pathways that cancer cells need to grow. As we wait for new drugs to emerge from clinical trials, Dr. Singh urges all people with FA to be vaccinated against the HPV virus, to shun smoking and alcohol, and to get frequent check-ups to detect these cancers early. He says, "FA is an inherited susceptibility, but it is not the cancer itself. Something else always causes it."

Dr. William William is also optimistic about future treatments for head and neck cancer. His presentation suggested that in the not too distant future immunotherapies may even be able to prevent this disease altogether. According to him, monoclonal antibodies now being tested can break through the shields that cancer cells erect to protect themselves from lymphocytes that fight them. Thus they harness a patient's immune system to wipe out cancer. In 2015, a Phase 1 clinical trial of Pembroluzimab reduced lesions in 56% of the subjects with head and neck cancers, and of those who responded, 71% experienced long-term benefit, with minimal side-effects. For Dr. William, this drug raises intriguing questions. Could it be taken by high-risk patients who have not yet developed head and neck cancer, to prevent it altogether? His group launched a clinical trial in August 2016 to try to answer this question. Yet there are also cautions. Might immunotherapy, which unleashes the immune system, increase the potential for graft-versus-host disease in FA patients post-transplant? More research will need to be done to answer this question.

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Hand Differences in Fanconi Anemia

Scott Kozin, MD, Chief of Staff, Shriners Hospital for Children

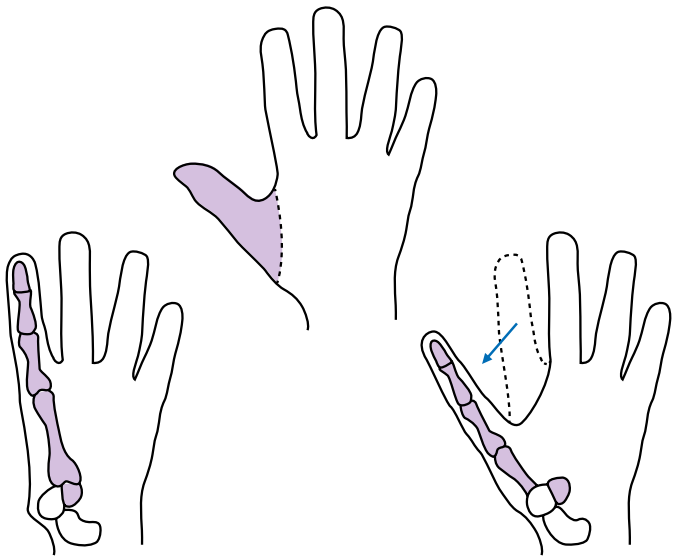
Skeletal anomalies are common in Fanconi anemia, particularly in the radius, thumb, and ulna (the long, thin bone in the forearm, opposite the thumb). The radius can be short or missing entirely, on either one side or both. Often when there is no radius, there is also no thumb, and the ulna is shorter, thicker, and bowed toward the absent radius.

Dr. Scott Kozin takes a holistic approach to treatment, looking at the full range of abilities and limitations of a particular person, and operating only when the benefits appear to outweigh the risks. He is particularly concerned with not *reducing* function. For example, it is common for those with radial deficiency to have a stiff index finger. Children adapt to this problem by approaching objects with their little fingers. If you straighten a child's hand, you can actually make things harder for him or her.

Radial deficiency treatment options include stretching and splinting, or centralization surgery. It's important to know that congenitally short bones don't lengthen or straighten as well, and recurrence is common. Surgery does improve appearance, but its effect on function is still unclear. Each person's case is different and needs to be evaluated individually.

Dr. Kozin classifies thumb anomalies by their severity and treats accordingly. Minor hypoplastic thumbs don't need treatment and thenar hypoplasia can be treated with reconstruction, while absent thumbs are candidates for pollicization (surgery in which a thumb is created from an existing finger).

Pollicization is often done at one year of age, based on the typical developmental change from ulnar grasp (with pinky and ring fingers) to radial grasp (thumb and index finger). However, there is no difference in the success rate of the surgery up to age three, so it's fine to wait if you're unsure about whether to do it, or if the child's function is unclear. Besides existing function, other aspects that can affect the choice whether or not to operate are general health and platelet counts.



> "Dr. Scott Kozin takes a holistic approach to treatment, looking at the full range of abilities and limitations of a particular person, and operating only when the benefits appear to outweigh the risks."

Gynecological Issues Facing Females with Fanconi Anemia

Pam Stratton, MD, Head, Gynecology Consult Service; Eunice Kennedy Shriver, NICHD, NIH

Girls and women with Fanconi anemia can experience multiple gynecological issues, including late onset of puberty, early onset of menopause, gynecological and breast cancers, reduced fertility and excessive menstrual bleeding.

Many different factors can contribute to menstrual cycle abnormalities, such as low body weight, chronic illness, low platelets, androgen therapy, transplant, and endocrine disorders.

Women who experience premature menopause may want to consider hormone replacement therapy. It provides some protection against bone loss, hot flashes and vaginal dryness. In the general population, it is unknown whether hormone replacement can increase risk of heart attack, stroke and thromboembolic disease, or slightly increase the risk of breast cancer in women after menopause. Other treatment options for osteoporosis include bisphosphonates, and vitamin D and calcium supplements.

Although women with FA often experience decreased ovarian function as well as a shorter timeframe for fertility, they can get pregnant, even post-transplant. Therefore, preventing pregnancy with birth control methods is an option.

Pregnancy in women with FA is considered high risk. Coordination of care between a maternal-fetal medicine specialist and hematologist enables monitoring and management of complications. Stopping androgens early in pregnancy helps avoid masculinization of the fetus. FA pregnancies also carry a higher risk of preeclampsia, eclampsia, miscarriage, and Cesarean section. Furthermore, hemoglobin and platelet counts can drop during pregnancy, necessitating transfusion.

Women who have been through transplant may have additional complications with both ovarian function and pregnancy, depending on the transplant regimen, the presence of graft-versus-host disease, age, and the relation between puberty and the time of transplant.

Some techniques may be available to preserve ovarian function prior to transplant. Embryos or eggs can be frozen (cryopreservation), which is the standard of care. Some specific hormones used to suppress menstruation may also protect the ovaries by turning them off. Currently this approach is experimental. Adoption and surrogacy are other options for becoming a parent.

Dr. Pam Stratton also discussed breast cancer and gynecological cancers, including genital, cervical, and vulvar squamous cell carcinoma. Like so many other cancers, these cancers tend to occur at a much younger age in those with FA. There is conflicting information about whether squamous cell carcinoma afflicting those with FA is associated with

> “Most importantly, women with FA benefit from screening for cervical and vulvar cancer and pre-cancer.”

HPV. However, Dr. Stratton recommends the 9 valent HPV vaccine for all FA teens, with re-vaccination after transplant.

Most importantly, women with FA benefit from screening for cervical and vulvar cancer and pre-cancer. Comprehensive screening should begin by age 18 and be performed at least annually, including cervical cytology screening, and vulvar and vaginal inspection. Unlike in the general population, for those with FA, HPV testing doesn't lengthen the interval between cytology screenings. Any suspicious lesions are biopsied because visual assessment isn't sufficient for diagnosis. Surgical excision of moderate or severe dysplasia is the optimal treatment to avoid a progression to cancer, which could necessitate chemotherapy or radiation. Anyone with genital tract cancer benefits from seeing a gynecologic oncologist immediately, because surgery is the best option for treatment, and an FA specialist needs to be consulted prior to administering chemotherapy or radiation.

While the number of cases of breast cancer in FA is low, the age at which it appears is considerably younger than in the general population, ranging from 20-45 years old. Given the sensitivity to radiation for those with FA, the risks of radiation exposure with mammography have to be weighed against the benefits of early detection. Breast MRIs may be a better option, although they have a high rate of false positives. Clinical breast exams 1-2 times per year and regular breast self-exams by those in their early 20s (or by eight years after transplant if TBI is used) are also important components of early detection. Any palpable mass should be biopsied immediately to enable early diagnosis.

Update on Cancer Screening Project

Because individuals with Fanconi anemia are at extremely high risk to develop cancer, early detection is key. The most common site of FA malignancies is the oral cavity. Dr. Eunike Velleuer of Heinrich Heine University, and Ralf Dietrich, Executive Director, German Fanconi Anemia Support Group, both from Düsseldorf, Germany, have seen over 800 individuals with FA all over the world as part of their FARF-funded project entitled *Reducing the Burden of Squamous Cell Carcinoma in Fanconi Anemia.* In June they attended FARF's FA Family Meeting at Camp Sunshine in Maine, where they examined the oral cavities of kids and adults with FA and took brush samples if they saw lesions. Those samples will subsequently be examined in Düsseldorf for any signs of concern. This is part of the effort to identify malignancies as early as possible, when intervention can successfully remove precancerous or cancerous lesions. Their work has been invaluable in early detection of cancer.

How to Perform an Oral Cancer Self-Exam

A self examination should be performed no more than once a month unless a lesion is found. Self examination should supplement, not replace examinations performed by qualified physicians or dentists.

1. Using your thumb and forefinger (finger on the inside of the lip, thumb on the outside), feel all around the inside and outside of your lips. Note any bumps, soreness, or any noticeable differences.
2. Pull your top lip up and away from the teeth and examine your upper gums. Look for any white or red patches, sores, bumps, or swelling. Check the lower gums in the same way, noting anything unusual.
3. Use your thumb and forefinger on each side of the mouth, pulling the cheeks away from the teeth to check the inside of the cheeks for red or white patches or anything unusual.
4. Gently pinching the area of the cheek between the thumb and forefinger, feel for any lumps or bumps. Do this on each side of the mouth.
5. Tilt your head back and say, "Aaaaahhh." Look at the roof of the mouth and note any white or red patches, any sores, any bumps, or anything that appears unusual.
6. To examine your tongue, grasp the end of the tongue using your fingers, gauze, or a washcloth. Gently pull the tongue from side to side, examining each surface for areas of discoloration, abrasion, or anything that appears to be unusual.
7. Reach the tip of your tongue to the roof of your mouth and look at the underside of the tongue, noting any red or white patches, any sores, or anything that appears unusual.
8. With your tongue still pointing upwards, run your finger along the floor of the mouth, feeling for any bumps or lumps.

FA Research & Clinical Trials: An Update

Richard Gelinas, PhD, Institute for Systems Biology; Scientific Advisory Board, Board of Directors, Fanconi Anemia Research Fund

At the FA Family Meeting, Dr. Richard Gelinas provided an exciting update on the research and clinical trials that the Fanconi Anemia Research Fund is currently sponsoring, including emerging anti-cancer therapies, improved methods to detect cancer early, and possibly the most exciting of all, genuine progress in gene therapy.

NAC & METFORMIN

Enough is known about how Fanconi anemia perturbs the body to realize that two drugs may benefit people with FA: n-acetyl cysteine (NAC) and metformin.

NAC is a building-block of glutathione, a key anti-oxidant inside every cell in the body; therefore, taking it could help reduce DNA damage in cells and could help correct for a missing FA pathway. NAC is quite safe, and emergency departments use it as an antidote to acetaminophen (Tylenol) overdose. Dr. Yigal Dror (yigal.dror@sickkids.ca), of The Hospital for Sick Children in Toronto, is about to open a clinical trial of NAC in FA patients.

Metformin (also called Glucophage) has been in use around the world for decades, since it helps control the symptoms of type 2 diabetes. In FA, metformin could be beneficial, because it can neutralize aldehydes which are naturally produced DNA-damaging chemicals. In FA mice, metformin shows a modest but measureable alleviation of some bone marrow defects, and it helps delay tumor formation. Contact the FARF office or go to clinicaltrials.gov for more information about clinical trials of metformin.

Both NAC and metformin are inexpensive and safe; we are still not sure how effective they will be in keeping the bone marrow healthy or delaying the emergence of cancer. However, some people take metformin in the hope that it will help them live longer!

IMMUNOTHERAPIES

Individuals with FA have an increased risk of developing aplastic anemia, leukemia, or some solid tumors such as head and neck cancer. A new class of anti-tumor drugs called immunotherapies or check-point inhibitors, which have resulted in dramatic remissions of some cancers such as melanoma and some lung cancers, are now being tested in typical head and neck cancer. These therapies work by enabling the body's own cancer-killing cells (anti-tumor lymphocytes) to attack tumors.

Early results with immunotherapy drugs from Merck or Bristol-Myers Squibb show these drugs can slow the progression of head and neck cancers, although complete remissions in this tumor type with the current drugs are rare. Immunotherapies can be combined with more conventional therapies, including surgery or other drugs for head and neck cancer, since their mechanisms of action are quite independent. FARF is following or supporting research on drugs that may improve bone marrow function, with potential to enter clinical trials within a year or two. The drugs include TGFß antagonists (lab of Dr. Alan D'Andrea) or drugs that may help restore the function of the FA pathway in certain patients by correcting mis-folded FA pathway proteins (HSP90 agonists; lab of Dr. Susan Lindquist).

GENE THERAPY AND GENE EDITING

Gene therapy is now an option for certain FA patients, and clinical trials are open on two continents: a program developed by Drs. Jennifer Adair, Hans-Peter Kiem, Pamela Becker and colleagues in Seattle, Wash. (http://research.fhcrc.org/adair/en/collaborations/gene-therapy.html) and a similar program developed by Drs. Paula Rio, Susana Navarro, Jordi Surrallés, and Juan Bueren and colleagues in Madrid, Spain (https://www.ncbi.nlm.nih.gov/pubmed/24859981). Both of these programs use a highly modified viral vector to add a normal FANC-A gene to the DNA of the bone marrow stem cells of a patient with a defective FANC-A gene. From both sites, about ten patients have been treated and results are encouraging.

FARF is also sponsoring research on pathways that limit the number of bone marrow stem cells. If a treatment can be devised that can safely expand the number of stem cells without causing them to differentiate right away, it could help conventional bone marrow transplantation methods, but also hasten the arrival of a new form of gene therapy: gene correction by gene editing. Many labs, including some that are supported by FARF, are learning how to correct the mutation in the DNA of an FA stem cell (sometimes just a single letter in the DNA code) that causes FA, by a method called gene editing, which was derived from bacteria. A key attraction of this approach is that it is a self-procedure: each patient is his or her own donor of cells to be corrected. Thus, graft-versus-host disease would be impossible. The mutation that causes sickle cell disease has been corrected in stem cells by gene editing, and this work is moving towards the clinic. These methods work in FA cells, and if pre-clinical studies show that they are safe and result in long-term benefits, the age of allogeneic bone marrow transplantation, developed in the last century, may come to an end.

Ear and Hearing Problems in Fanconi Anemia

H. Jeffrey Kim, MD, FACS, Otologist, Dept. of Otolaryngology-HNS, Georgetown University Hospital, Washington, DC and Staff Clinician, National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Dr. Jeffrey Kim shared updated information with families about hearing loss in Fanconi anemia. Hearing loss and congenital ear anomalies are much more common than previously reported. In the 31 people with FA seen at NIH for his study, 45% had hearing loss. Nearly two thirds of those had conductive hearing loss, and over half of those with hearing loss had only mild loss. Over half of those in the study had ear drum and/or middle ear abnormalities, but, interestingly, not everyone with abnormalities had hearing loss.

Mild to moderate hearing loss can be managed with hearing aids, FM assistive listening devices, ear surgery or implantable hearing devices, like Baha or Ponto. Those with absent ear canals do not usually benefit from traditional hearing aids, but they can use Baha or Ponto aids. They may also be able to undergo surgical ear canal reconstruction, if they have well developed ear structures. Those with profound sensorineural hearing loss can use CROS (contralateral routing of signals) hearing aids, and Baha or Ponto.

Dr. Kim also gave some practical communication tips for those with hearing loss: 1) make a habit of watching the speaker because visual cues aid in comprehension; 2) let speakers know when you need them to repeat something, and 3) reduce or move away from background noise.

Given the high rate of hearing loss in those with FA, individuals with FA should have a comprehensive exam by an ENT and audiologist, including a microscopic ear exam and audiologic evaluation. Follow-up audiograms should be conducted every 2-3 years, or more frequently if there is exposure to medications such as deferoximine, amincoglycosides and cisplatin, which can cause hearing loss.

Aldehydes and Bone Marrow Function in FA

Alan D'Andrea, MD, Dana-Farber Cancer Institute

In Dr. Alan D'Andrea once again visited Camp Sunshine and presented cutting-edge FA research in an easily understandable way. This year he talked about two subjects. The first was a summary of work from many laboratories about the role of aldehydes in FA. The second was an exciting presentation of work from Dr. D'Andrea's own lab on the role of TGFß in bone marrow failure and how this could be a new target for FA treatment.

The Role of Aldehydes in Fanconi Anemia

One big question in Fanconi anemia is what causes the bone marrow to fail? Laboratory Research shows that certain chemicals like mitomycin C and DEB damage the DNA of FA cells and that this damage causes the cells to die. However, mitomycin C and DEB do not occur naturally in our bodies, so for many years, scientists have asked which toxins play a role in Fanconi anemia.

A few years ago, Dr. KJ Patel and his colleagues at Cambridge University proposed that aldehydes are a likely source of DNA damage and cell killing in FA. Genetics studies in FA mice validated this hypothesis. So, what are aldehydes? These are small organic molecules with reactive atoms that can bind to DNA and cause blockage of cell replication. It is widely believed that this blockage is a cause of bone marrow failure in FA. Some aldehydes, like formaldehyde, are formed within our bodies (endogenous) during normal metabolism. Other aldehydes are agents that come from sources outside the body (exogenous). These include chemicals in our environment such as in automobile and cooking fumes, cigarette smoke, laboratory chemicals, cosmetics, perfumes and raw materials in factories. We also have dietary sources of aldehydes such as ripe fruits and vegetables, coffee, soy sauce and most notably, alcoholic beverages.

Acetaldehyde is formed from the breakdown of ethanol present in alcoholic beverages. Alcohol is converted to acetaldehyde by an enzyme called ADH, and the resultant acetaldehyde is toxic. This is why our bodies have deactivating enzymes that convert toxic acetaldehyde to non-toxic acetate. Acetaldehyde detoxifying enzymes (e.g., ALDH2) are of critical importance in people with FA.

Some people have a natural mutation in the ALDH2 gene. Approximately 1 billion people carry ALDH2 mutations, most commonly in Southeast Asia. These individuals develop Asian flushing syndrome, which is easily recognizable, because people who lack ALDH2 turn bright red in a matter of minutes after consuming a single alcoholic drink (or even just a few sips!). This is due to their inability to remove the toxic aldehydes generated from the alcohol in that drink. Early evidence suggests that low ALDH levels may increase the incidence of squamous cell carcinoma of the head and neck in Japanese populations and ALDH2 mutations have been shown to be associated with accelerated bone marrow failure in Japanese FA patients. This is consistent with studies in mice showing that FA mutant bone marrow is hypersensitive to acetaldehyde and that Alda-1, an

> "These research studies underscore the critical importance of understanding the role of aldehydes in FA and in developing ways to prevent unwanted aldehyde toxicity."

agent currently in development as a potential therapeutic for FA, increases acetaldehyde detoxification, protecting these bone marrow cells from destruction.

These research studies have important implications for FA patients. They underscore the critical importance of understanding the role of aldehydes in FA and in developing ways to prevent unwanted aldehyde toxicity. FA patients should limit alcohol consumption. Because alcohol and aldehydes can cross the placenta from mother to baby. Pregnant mothers carrying an FA fetus should also limit alcohol consumption.

TGFß Signaling: A Potential Target to Prevent Bone Marrow Failure in FA

Dr. D'Andrea also presented exciting studies that identify a new pathway involved in the failure of FA bone marrow cells, called the transforming growth factor beta (TGFß) pathway. Using a genome-wide screen in human FA cell lines, Dr. D'Andrea showed that genes in the TGF-ß pathway, such as SMAD3 and BMP2, could rescue the FA hypersensitivity to mitomycin C. They then discovered that FA mice exhibit a hyperactive TGFß pathway and that inhibition of this pathway promoted resistance to toxic agents (e.g., acetaldehyde) and partially corrected bone marrow stem cell function. Multiple genes in the TGFß pathway were shown to be up-regulated in FA patient cells, and inhibition of the pathway partially rescued the defects of bone marrow stem cells. Moreover, inhibition of the TGFß pathway partially restored normal DNA repair.

These exciting studies lay the foundation for testing TGFß inhibitors as therapeutic agents for FA. Dr. D'Andrea is pursuing this opportunity with drug companies. He discussed a possible partnership with FARF to accelerate clinical trials of TGFß inhibitors.

Markus Grompe, MD,
Oregon Health & Sciences University

NIH National Heart, Lung, and Blood Institute

$9.9 Million Fanconi Anemia Research Project Funded

New drug treatments may be right around the corner for individuals affected by FA. In August of 2016, researchers at the Oregon Health & Sciences University were awarded a $9.9 million grant from the National Heart, Lung, and Blood Institute at the National Institutes of Health to study in humans novel drug therapies that have shown promise in FA animal models.

Dr. Markus Grompe is the principal investigator on the awarded grant and director of the Oregon Stem Cell Center at OHSU and Papé Family Pediatric Research Institute at the OHSU Doernbecher Children's Hospital. The five-year grant is composed of three interrelated projects focused on the pathophysiology and treatment of Fanconi anemia. The projects will use animal models and human cells to test the efficacy of potential drug compounds that will then be used in a human clinical trial. The interdisciplinary projects bring together experts in pediatrics, hematology, oncology, and medical genetics. Co-investigators on the study include Drs. Alan D'Andrea, MD, and Akiko Shimamura, MD, of Harvard University and William H. Fleming, MD, PhD, of OHSU.

This research study is an essential next step in using targeted therapies to fight FA. It is anticipated that results from this research will have the capacity to create a major paradigm shift in FA treatment and bring hope to patients and families affected by the deleterious effects of this disease. "This important work has the potential to be life-altering for those suffering from FA," said Kevin McQueen, president of the Fanconi Anemia Research Fund Board and father of 17-year-old Sean, who was diagnosed with FA in 2000. "The forthcoming research will lay the groundwork for developing new interventions for FA that could dramatically improve and extend lives. Most importantly, it provides hope of a brighter future for FA families."






25 Years of FA Family Camp

The Fanconi Anemia Research Fund's 25th annual Family Meeting brought together 51 families from four countries for a week of bonding, fun activities, medical presentations, and research opportunities. Fifty-two children and adults with Fanconi anemia (ranging in age from 1 to 40) attended Camp Sunshine in Casco, Maine, with their parents, siblings and other family members. One parent shared the important value of meeting adults with FA: "I love having adults (with FA) at Camp to represent what we are all striving for. They give us so much hope for the future!"

In a series of educational presentations, 19 speakers presented on a range of topics. Medical and science topics included stem cell transplantation, nutrition, head and neck cancer treatment, aldehydes, and overall updates in FA research. In addition, members of the FARF Philanthropy Council gave an inspiring and helpful presentation on how families can increase their fundraising efforts. Participants commented that the presentations were not only informative, but hopeful and inspiring.

Researchers representing three distinct studies were on site at Camp Sunshine to collect data and samples from FA individuals and their family members. Scientists appreciated the opportunity to gather data from so many people with FA in one place, and participants were able to directly help move FA research forward. One research participant remarked: "Hopefully all of us together can make a difference!"

Another key piece of the Camp Sunshine experience involves the support groups with Psychosocial Director, Nancy Cincotta, MSW, MPhil. Throughout the week, Nancy met with parents, siblings, and kids and adults with FA, addressing common issues unique to each group. "It is so great to be in a place with people who share the same fears and concerns. Nancy is a fantastic facilitator!" one parent commented.

51
families

19
presentation speakers

4
countries

52
children and adults with FA

Some of the most memorable moments occurred during social activities, such as the adult banquet and karaoke night, the overnight campout for the kids, the night swim for the adults with FA, and of course, the annual talent show. This year, the talent show included a surprise performance via video by Amy (Frohnmayer) Winn, who was in Minnesota going through transplant. Although Amy was not physically at Camp, her spirit was present all week, especially during the viewing of the amazing music video Amy created with friends and family, appropriately set to Taylor Swift's song, "Bad Blood." The video, which captured the unwavering strength of Amy and her crew, was undeniably the highlight of the evening.

> "We love Camp Sunshine. It is the only time when everyone around us truly understands what we are going through. It's so comforting to make those connections." –FA parent

Thanks to the speakers, researchers, staff, volunteers, and, of course, the families, this year's Family Meeting inspired, educated and encouraged all participants. As one person eloquently stated: "It was so informative and valuable. I am so grateful that we had the opportunity to attend. The presentations gave us access to specialists in FA from all over the world, which was an opportunity that we would not otherwise have had. The connections we made with other FAmilies were truly amazing. It was a safe place where everyone else either had been or was in the exact same boat as us."

We look forward to seeing you all again next year!

Science Snapshots

The Fanconi Anemia Research Fund, in partnership with Fanconi Canada, is proud to announce a new series of FA-related videos entitled "Science Snapshots". The videos, less than five minutes each, feature FA researchers and clinicians sharing their research and work. Filmed at the 2015 FA Scientific Symposium in Toronto, the videos were generously produced by Wil Noack and RTA Productions and are available on FARF's Facebook and YouTube pages (visit facebook.com or youtube.com and search "Fanconi Anemia Research Fund").

Calix, Chloe, Jesse, and Lenny at Family Camp

Life After Diagnosis

By Chloe Eminger

In the 16 months since my son Calix was diagnosed with Fanconi anemia, our world has changed in many ways. This nightmare disease, whose name I had never heard before that fateful morning, has pulled seemingly endless tears down my cheeks, forced my precious son to endure countless painful procedures, and has shaken our once blissfully ignorant family to its core. However, with these trials and tribulations also comes newfound strength, perspective and a realization that there IS life after an FA diagnosis.

In the winter of 2015, I had this ugly feeling in my gut. It picked at all of my happy moments and filled my heart with anxiety. That feeling was that something was wrong with my son. At the urging of my partner Jesse (who always seems to know exactly what to say to calm my anxieties), I made an appointment with Calix's doctor, mostly just so that she could tell me that everything was fine and to stop worrying. At the appointment, his pediatrician noted that he had lost a little bit of weight, but said it wasn't too concerning and that we'd just "keep an eye on it." As she was wrapping up the visit, I suddenly blurted out "I need you to run some bloodwork." I still don't know where it came from, or why I said it, but thankfully she took me seriously and ordered the CBC.

That same night, about an hour after putting my kids to bed, I received a call from the doctor's personal cell phone. I can't tell you what she said, all I remember were the words "take him to the ER right now," and then "possible malignancies." I fell to the floor and started hysterically crying. Jesse woke up both kids, and carried each of us to the car, including me. I was absolutely frozen with fear.

The next few months were mostly a blur. Calix had to endure weekly bloodwork, which gave him intense anxiety. It was truly awful to watch and even more awful to have to force him to continue when it didn't seem to be getting us anywhere. Weeks went by and we were told that it was simply "viral suppression," which meant he had an unknown virus and it brought all of his blood counts down. Two months went by without improvement and my gut started nagging again. I decided I had enough of the waiting game and pushed hard for the doctors to do something more. With that extra push, the doctors agreed to send out a DNA panel.

On May 26, 2015 I strolled into the Tomorrow Fund clinic at Hasbro Children's Hospital for Calix's weekly bloodwork, unaware of what was about to occur. I was met by a social worker who told me she would take my kids

> "...with these trials and tribulations also comes newfound strength, perspective and a realization that there IS life after an FA diagnosis."

while I spoke to the doctor. For almost all of the other appointments, Jesse, and/or Calix's father, Craig, had joined us at the hospital, but in an awful twist of fate, I was alone with both of my children at this visit. Before the doctor ever said a word, I knew it was terrible.

Finding Purpose

By Matt Farrow

When you are faced with your own mortality, especially at a very young age, it brings a lot of anxiety and you may struggle with finding your purpose in life. Some people may not discover their purpose within their lifetime. This has been a huge burden on me throughout my life: not knowing why I have this horrible disease, not understanding why I'm still here when my friends are not, not knowing how long I will be able to be there for my family.

As hard as it is, everyone is different, and this is the path God has for me. I have to choose on a daily basis to be thankful. Sometimes I fail miserably at this and spend way too much time paralyzed by fear instead of enjoying what is right in front of me. Sometimes, when I'm focused on the right things, I am truly thankful for the opportunities that FA has given me. I'm thankful that I can inspire others with FA and offer them hope, thankful that I can guide others facing transplant, thankful that I can make others smile when I know they haven't smiled in a while.

That is my purpose in life and just knowing that gives me comfort. I may have to remind myself of it over and over again, but I know this is what I need to do. It makes my heart happy when I can support those who are going through what I did.

> "No matter where you are in your journey, you must remember there is hope. Don't wait for anything. Chase your dreams and keep living."

Randi, Elijah, and Matt Farrow

As an adult with FA, I can be an example for the kids who worry about the future and hopefully relieve a little stress by showing them that it is possible. It's okay to plan for the future. You can have a family, a great job where you get to help others, and a purpose in your life. No matter where you are in your journey, you must remember there is hope. Don't wait for anything. Chase your dreams and keep living.

My head was spinning and my heart was in my throat. The conference room he had led me to felt both huge and insanely claustrophobic all at once, and it was right then and there that our entire world changed forever. I have no idea how I got home.

We've had many ups and downs since that moment, the worst of which were the late nights spent in the emergency room with terrible fevers and low counts, and the best of which were finding out that Calix has 15 perfect matches on the bone marrow registry, and meeting so many amazing FA families at Camp Sunshine this summer! Our family was so happy there and we felt so welcomed and supported. We can't wait to go back again next year! Through all of this, Calix has blossomed into such a brave boy who no longer panics about bloodwork or IVs and who takes each ER trip and procedure in stride. He is truly our hero, and he is only seven years old! We know he is going to live a long life and do amazing things in this world, and I'm going to make sure of it.

While we wait for the next step with FA, we are making the most of our time by seeking out the best possible center for Calix's upcoming transplant. We are also focused on raising awareness and as much money as we can for research so that he and other amazing children and adults with FA can live the long, healthy, amazing lives they deserve. We will once again be participating in the Pell Bridge Run in Newport, R.I., where last year our family raised $5,000 for the Fanconi Anemia Research Fund (Team FARF as a whole raised 10,000!). We are proud of what we've been able to do so far and will continue to push ourselves to reach higher goals each year.

Fanconi anemia is the worst thing that has ever happened to our family, but it is also somehow one of the best. We are different, better people now and we know we have a giant FAmily with us every step of the way, and for that we thank you from the bottom of our hearts.

James Graham

Loving A Dying Child

What it is Teaching Me About Happiness and Humanity

By Jessica Grady

From the moment I became pregnant with James, it was obvious that something wasn't right. At five weeks my ultrasound showed no fetal pole, and the doctors assured me I would miscarry. Miraculously, I didn't. Little James appeared at my next scan, severely behind in growth. At 22 weeks, an ultrasound showed a missing kidney, deformed brain, and missing bones in the arms. I was referred to a specialty clinic at Sacred Heart hospital. I was told over and over not to get my hopes up; James could be born stillborn, or die shortly after labor. His brain could be too defected to tell him to breathe.

Let me rewind a bit and tell you a little bit about myself. You see, I have severe anxiety. Growing up, one of my biggest fears was death. The uncertainty of it all was so terrifying. I could not, for the life of me, wrap my head around nothingness. The universe, or God, or whatever higher power you fancy, has given me an experience that has changed my soul from the inside out.

Fast forward to James's birth, which was a C-Section of course, to protect his brain. They showed me my little angel and then took him to the NICU and wheeled me off to recovery. Adamant to see my child out of fear he would die, I refused pain medication and sedation after surgery. I forced the nurses to put me in a wheelchair and take me to the NICU. I made it there long enough to look at his perfect face before I fainted. Over the next three days, my husband would go up to the NICU, and every time he came back there was worse news. 'He has five holes in his heart. He has no anus. His GI tract is blocked in several places. He is deaf. He is blind (or so we think, he won't open his eyes). His brain is basically water.'

We were offered comfort care, also known as hospice. In the midst of considering it, my husband kissed James' cheek, and he smiled. That was all I needed.

Lesson one: Quality of life is subjective. Blind, deaf, and presumably dumb, James, at days old, felt joy. We were brought into the genetics room weeks later for a conference and were told the most heartbreaking news I've ever received. We were told that our son has a genetic disease called Fanconi anemia. It's a death sentence for kids like James. Because of his defects, transplant would likely kill him.

After months in the NICU, surgeries, ventilators, IV nutrition, James opened his eyes. I had been having dreams that he would.

Lesson two: There IS a reality outside of our five senses. Whether you want to call it intuition, or spiritual guidance, or psychic ability, it's there. It is the reality that exists beyond what we perceive. It's the reality of love, hope, fate, and the power of will.

Along this road we have had pneumonia, multiple organ failures, more tubes than you have fingers, and many brushes with death. Yet, James, with all of his pain and struggles, was the happiest person I have ever encountered in my entire time on this earth. I like to make the joke that James could get poked six times and still smile at the nurses and coo at them, while my daughter Alice would have an hour long meltdown if she scraped her knee! My nights of endless

> "Death is not final. Our loved ones with FA live on in the way they have changed our hearts, minds, and souls."

research, my hundreds of phone calls and doctors' visits, our family's dedication to his development did not go in vain. My daughter, at just three years old, learned how to operate a food pump and oxygen. Where he is weak, we are strong. More importantly, she learned to treasure every moment she had with James, before he went to live in the sky.

Lesson three: When someone is incapable of being strong, you can be strong for them. When my son was dying and I fought for him endlessly and held him until my arms hurt, I

had the "will to live" for him. This child, who was assumed to die at birth, who had a death sentence encoded in his DNA, could babble, sit up, see, grab, laugh, and pull down his eye for better vision. He loved to be cuddled, but didn't cry when you put him down or left the room. He could turn red and gag and vomit for an hour, but still find the joy to laugh from the depths of his belly when you tickled him.

Lesson four: Happiness and love in their purest forms require nothing. They don't require a functioning body. They don't require money. They don't even require thumbs (James was born without). Love doesn't require anything. It is something you give. And the more you give, the more you have.

Now let me tell you what James has taught me about the human race.

Along this journey, we were introduced to a community of people with Fanconi anemia or who have loved ones with FA. The Fanconi Anemia Research Fund, founded by parents of three FA children, brought together the families to form a support group. They also all meet up once a year at Camp Sunshine. We call them our FAmily. These people, who have FA or love someone with it, *they know*. They operate on this level of reality which we are all aware of, and live in, together. Too many FAmily members have died this year. When one goes, the whole FAmily feels it. Through some sick twist of genetic fate, we are all related. The FA kids and adults all have one thing in common that isn't FA-related: their spirit. When you look into their eyes, you see and feel it. They are everything you are afraid of. They represent how fragile and unsure life is. They live, with one foot in death, and one in life. And they are happier than you.

We the FAmily are all in this together. We face the same things. Feel the same loss. Have the same genetic issues. We operate daily with the reality that life is short. Too short. And death is always at our door. And we are better for it. We live like we are dying. We donate thousands of dollars to research. We walk miles upon miles for our kids in 5K races everywhere. Those affected with FA are there for each other every step of the way. Kids and adults, and even those whose FAmily member has long passed.

How would you live if you were dying? Would you worry so much about money or pride? Would you do more to help others, and less to help yourself? Death is not final. Our loved ones with FA live on in the way they have changed our hearts, minds, and souls. Being aware of death has made my life so much more valuable.

Dr. Farid Boulad with Dylan Hessels

Our Experience Living Through Bone Marrow Transplant

By Rutger Boerema

With the diagnosis of Fanconi anemia comes the knowledge that your FA child or children will most likely need a bone marrow transplant (BMT) in the future. The question is "when?" and that question is always in the background. With every new blood count you wonder whether you are closer to the date of admission. Dylan and his sister Joy were diagnosed with FA in January 2013. Between that date and the actual BMT admission date of March 25, 2015, Dylan had numerous blood counts; often weekly.

When we discussed a BMT date with Dr. Boulad (Memorial Sloan Kettering Cancer Centre), I compared preparing for a BMT with preparing for the delivery of a baby. You read about it, you talk about it, you visualize it and try to absorb as much information as possible, but when the contractions start, you have no idea what is going to happen. Will it be long or will it be short? Will it be painful? If so, can they control the pain? Will there be complications and/or unexpected events? Having gone through a BMT with Dylan, I can tell you this is a good comparison. Dylan's transplant time in the hospital was long: 77 days in total and double the time doctors were expecting before he was admitted. It was very painful (C diff, BK virus and CMV virus) and they did have difficulties controlling his pain. There were complications due to the BK virus, and he developed hemorrhagic cystitis in the bladder. The most unexpected event was an accident with the cord blood of Dylan's brother, Ryan. Because of this, the cord blood was not sterile and could not be used for the transplant. They had taken Ryan's bone marrow the day before the transplant, so instead of having a combination of cord blood and bone marrow we ended up only using bone marrow.

> "Will [the BMT] be long or will it be short? Will it be painful? If so, can they control the pain? Will there be complications and/or unexpected events?"

At the end of a pregnancy, you are ready to deliver the baby. In our case, we were also ready for the BMT. Dylan was not responding to Danazol anymore, and his blood counts were close to or below critical levels. In consultation with Dr. Boulad, we decided to start a BMT after the flu season. This way, Dylan's brother Ryan would be older than a year and would be able to be his donor, and we would avoid the risk of catching the flu while being immune suppressed.

Our initial admission date was March 5. However, first Ryan got sick and then infected Dylan with the Rhino virus. After that, Dylan got the RSV virus and then the whooping cough! Our transplant date got delayed, then further delayed. Everyone in the family was vaccinated and Joy was not attending school in order to protect Dylan, but the viruses kept coming into our apartment.

A BMT is team work. Andre was able to take time off work, and we took

turns in the hospital. We lived only eight streets away from MSKCC, which made it easier to maintain some daily routine at home with Joy and Ryan. Also, both my parents and Andre's parents came over to help out. That created peace at home. A BMT requires a lot of energy. Andre and I continued running during the BMT to get some relaxation. Fortunately, after Dylan was discharged from the hospital and we got into the routine of giving (IV) medications, changing fluids and do dressing changes, everything calmed down.

A final comparison for me between delivering a baby and going through a BMT is that while you never forget the experience, you forget details very quickly. I think that is a good thing, as it helps us to move on. We've already noticed that Dylan

> "Going through a BMT... you forget details very quickly. I think that is a good thing, as it helps us to move on."

has forgotten parts of his BMT; however, there were some very painful episodes he will never forget. Dylan will repeat third grade, and we hope that he will have more afterschool activities than he had before. We hope he can attend school as soon as possible, as he has been out of school for eight months now. In September he had his first karate lesson, which he really enjoyed. We know that some time in the future Joy will have to have a BMT and that we have to go through a similar but different journey again. For now, we can only hope it will be at least a couple of years away.

Catch 4 a Cure

By Daniel Kold, FA adult and member of the Danish FA-association

In January 2015, Kirstine & Tue from our Danish Fanconi anemia association came up with a great idea for a fundraising campaign: "Catch 4 a Cure". They didn't have the ability to run with the idea back then, but when they introduced the idea to the rest of the Danish FA-association earlier this year, we were excited to make a move!

The idea is to make several "Catch 4 a Cure" videos and share them on social media. Short homemade video clips will show people from all around the world tossing and catching various objects: a ball, a teddy bear, a cake, a bottle, or whatever creative object people choose. From a person with FA, to a person without FA, from an adult to a child, these short clips are then made into videos and shared on YouTube, Facebook and other social media platforms. Each video will end with a person with FA stating "I hope they find a cure" or something similar. The videos will also include a call to action button where we ask for donations to the Fanconi Anemia Research Fund.

How can you get involved?

We need people to make small video clips in landscape mode and send them to this email address: **catch4acure@gmail.com**. You can watch the first video on the Catch 4 a Cure Facebook page: https://www.facebook.com/catch4acurefanconi

But most important: We need you all to spread and share the videos as much as you can and ask your family and friends to do the same. Hopefully people who watch it will donate to a good cause, and of course, it will create a great deal of awareness. We ask you all to help us spread the word and the videos. Thank you!

Our Superhero, Blake

By Emily Robison

Blake Robert was born on November 2, 2011. My husband, Neil, came from visiting him in the NICU and said, "he has 11 fingers." I thought he was joking, but soon found out that Blake really did have an extra thumb. We later discovered that Blake also had mild unilateral hearing loss in one ear. We continued to live our lives and didn't really think much of these things that the doctors kept telling us were actually pretty normal.

Almost two years later, on September 9, 2013, our lives were forever changed. Blake, at 21 months old, was diagnosed with Fanconi anemia. We were living in Alaska and we received a phone call from Blake's geneticist in Seattle. I remember writing down random words and phrases on my notepad. I wrote in big letters, FANCONI ANEMIA and possible bone marrow failure.

I called Neil at work and I don't even remember what I told him. I didn't even fully understand what I had just been told, but I had to turn around and explain it to him. He came home immediately. I remember sobbing on the floor in Blake's room while we searched the internet for Fanconi anemia. We read of all the horrible things that could happen to people with FA and saw many different life expectancies: 12, 25, 33. We had no idea what we were facing. I hugged my little boy so tight that day.

We were lost until we found the Fanconi Anemia Research Fund. FARF was like a ray of light in our darkest hour. We were instantly connected with a network of families who were willing to share their experiences with us. The most important thing we learned in the beginning is that most of the information online is outdated. Research has come so far! Many FA patients are now surviving a bone marrow transplant and living longer. It's so much better than it was 20 years ago, but to me, it's still unacceptable. I'm 28 years old. I can't imagine my life ending now or in the near future. It kills me to consider the possibility that my four-year-old might not live longer than the age I am now.

After finding FARF and learning about all of the good that they do, we immediately knew that we needed to help them, we needed to fundraise. At that time, Blake was pretty stable and there was nothing, except monitoring, that we could do for him, so we decided we needed to take action.

> "We hope that 20 years from now we will look back on today and say, "look how far we have come!"

Since Blake's diagnosis we have put on multiple fundraisers, from small lemonade stands raising a few dollars, making and selling cupcakes, and our annual 5k run that brings in over $10,000. I know that every penny counts for FARF.

We are not doctors, scientists or researchers. We have hope because of FARF. Our kids are living longer and into adulthood. With that comes a whole new set of problems for our children. We have hope that, just like the advancements made in the last 10 to 20 years, there will be even more advancements made as we head into the future. We hope that 20 years from now we will look back on today and say, "look how far we have come!"

We don't just wish that these advancements will be made. We tirelessly fundraise so that FARF, the doctors and researchers will be able to help our children live better, longer lives.

Keep Climbing Higher in Life and on the Mountain

By The McCoreys

In the pre-dawn hours of August 16, 2007, Bill McCorey fell into a crevasse at 12,500 feet while attempting to summit Mount Rainier. He dangled by rope for twenty-five minutes in complete darkness while his Rope Team, who had been complete strangers just two days before, worked desperately to rescue him. If it weren't for their strength and courage, he would not have survived.

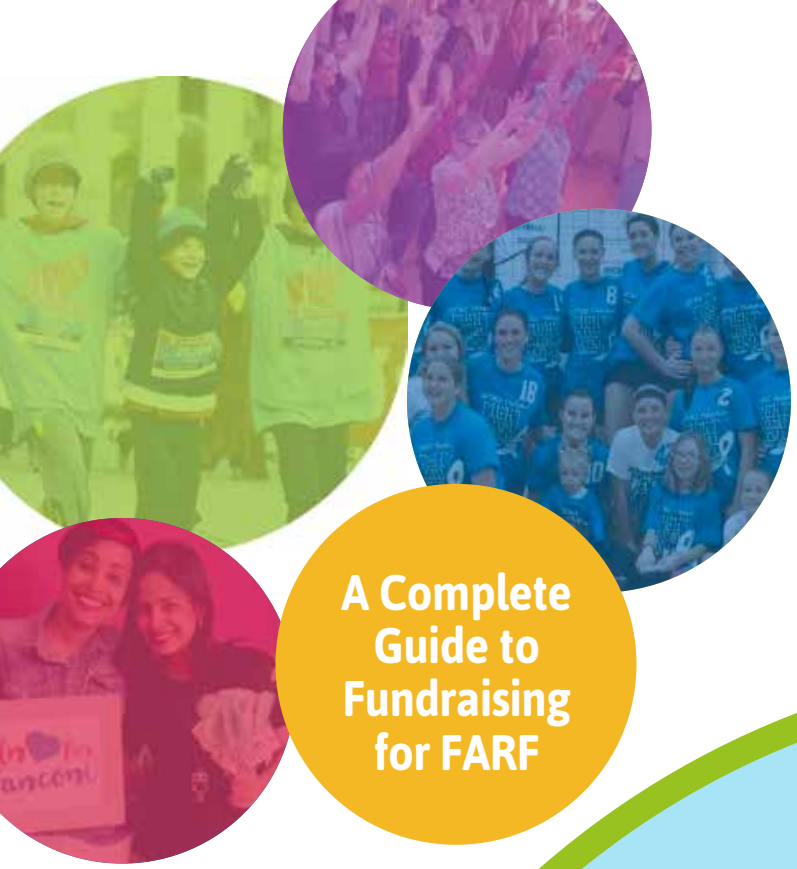
Inspired by how his rope team saved his life, Bill decided to form "Your Rope Team" to help save the lives of others whose lives are at risk. The new rope team returned to Mount Rainier a year later and successfully made it the top. This time, however, Bill decided to devote his effort to a special boy named Sean McQueen, who has Fanconi anemia (FA).

> "Many would have given up after one or even two attempts but this team would not stop until the goal was reached, much like the children and families with FA who never give up."

The Fanconi Anemia Rope Team (Bill, Bill III and Drew) made the summit on Mt. Rainier on July 20, 2016 after attempts in 2014 and 2015 where the team had to turn back due to high winds and avalanche conditions. The climbing McCoreys would not take no for an answer and have continued to climb higher each year to raise money for FA research. Many would have given up after one or even two attempts but this team would not stop until the goal was reached, much like the children and families with FA who never give up.

This year's climb marks eight times that the Rope Team has scaled a mountain for FA, and over these eight years, they have raised more than $150,000 and brought greater attention to the cause. Bill McCorey says, "I am so proud of the team, my sons and all the supporters over the years who have not stopped with their continued support, thoughts and prayers. For me personally, this all started with that fall on Mt. Rainier... I knew soon after that I was saved for more important work, and climbing for FA was a way for me to give back, raise awareness and create a kindred spirit in my sons and other friends who have climbed with me. I am also fortunate to be able to share my story and raise awareness for FA via speeches around the world and have done so well over 100 times. I will keep climbing higher for FA and hope that you will join me on the FA Rope Team in some way."

The next climb will take place in 2017. To follow Your Rope Team's story and adventures, visit www.yourropeteam.com.



FARF Amps up Fundraising

A Complete Guide to Fundraising for FARF

FUNDRAISING TOOLKIT

1

Fundraising Toolkit

For the past several months, the Fanconi Anemia Research Fund has focused on improving and increasing fundraising efforts to better push forward the organization's mission. In Spring 2016, we launched a new, easy-to-follow Fundraising Toolkit to better support families in their fundraising efforts. The toolkit is complete with event ideas, frequently asked questions, useful spreadsheets and worksheets, as well as step-by-step guides to planning fundraisers. It is available on our website www.fanconi.org or by request by emailing info@fanconi.org. We are happy to send hard copies upon request.

2

Philanthropy Council

In June 2016, a group of about 15 people met at Camp Sunshine for the inaugural Philanthropy Council meeting. This group is comprised of seasoned fundraisers, Fund board members and staff, with the overall goal to build the fundraising foundation for the future. The group meets quarterly to exchange and promote ideas to strengthen fundraising efforts, including focusing on FA Day, getting new families involved, expanding FARF's reach, helping families with their fundraisers, and providing materials and messages to make events more effective.

3

New fundraising materials

We want your events to be a success! It's important to remind your donors about the cause they are supporting. That's why FARF provides materials for your fundraisers, including: pens, tote bags, tablets, display boards, pop-up banners, hanging banners, brochures, frequently asked questions, and fact sheets. To view samples of materials available, visit the fundraising page at www.fanconi.org

Ideas

Which activities do you enjoy doing? Crafting, exercising, cooking, listening to music? Adding a fundraising component to your favorite activity is a great place to start.

Tip: Start Small!

Fundraising can seem intimidating, but it doesn't have to be! It doesn't even have to take a lot of time. One of the best ways to raise funds is by sending out a letter to your family and friends. Find an example letter in this toolkit. FARF can even handle the printing and mailing for you!

Events

- Mystery dinner theater
- Dodge ball tourney
- Baking/cooking competition
- Bowling competition
- Car wash
- Trivia night
- Talent show or Dance for a cure
- BBQ or block party
- Potluck
- Casino night
- 5K run/walk
- Golf tournament
- Dessert dash

Sales & Auctions

- Bake sale
- Raffles
- Art sale
- Totes/tees
- Basket auction
- Dinner & dessert auction
- Yard sale
- Craft sale
- Lemonade stand

Creative Asks

- Envelopes (at church or any group gathering)
- Gameshow
- The un-fundraiser
- Scavenger hunt
- Xbox challenge
- Flamingo flocking

Abbey Franzen, OH, sells her artwork to raise funds

FAMILY FUNDRAISING EFFORTS

From January 1 through August 31, 2016, Fanconi anemia families raised an amazing $931,153 for the Fanconi Anemia Research Fund. Almost 85 cents of every dollar donated goes directly to research and family support to make a difference in the lives of individuals and families affected by FA. Thank you for your outstanding fundraising efforts so far this year!

January through August

$290,000
Lynn and Amy Frohnmayer

$171,000
Kendall & Taylor Atkinson Foundation with the Nash and Atkinson Families

$52,000 - $62,000
Kevin and Lorraine McQueen
Gerard and Cynthia Vandermeys

$22,000 - $30,000
Kerrie Cazzari
Mark De Groot and Hanneke Takkenberg
Tim and Mary Ann Lana
Todd and Kristin Levine

$10,000 – $20,000
Rachel Altmann and Tyler Morrison
Mark and Linda Baumiller
Chris and Susan Collins
Charles and Katy Hull
Steve and Jennifer Klimkiewicz
Ian and Tricia Mitchell
Emily and Neil Robison
Nigel and Ann Walker

$4,000 – $9,999
Michael and Jennifer Aggabao
Jimmy and Jenny Armentrout
Andrew Coons and Valeen Gonzales
Antonino and Marie Di Mercurio
John and Martina Hartmann
Brian Horrigan and Amy Levine
Nancy Nunes
Peter and Janice Pless
Peg Padden

$1,000 – $3,999
Juanita and Ron Arroyo
Israel and Mary Jo Becerra
Jeffrey and Donna Boggs
Chris and Jennifer Branov
Anita Casani
David and Kim Chew
Colin and Ashley Chorneyko
Ana Concha
John and Kim Connelly
Justin and Britteny Ferrin
David and Mary Ann Fiaschetti
Andrew and Jennifer Gough
Alan and Rachel Grossman
Owen Hall and Margaret Kasting

The Levine Family held the 2016 Coley's Cause Memorial Golf Tournament in Lakeville, Mass.

Andre Hessels and Rutger Boerema
Stan and Michelle Kalemba
Mark and Angela Lamm
Gregory and Lynnette Lowrimore
The Family of Kelly Muschlitz-Taylor
Mark and Diane Pearl
Rose and David Pennell
Joshua and Crystal Pepper
Michael and Joanna Peros
Mark Ritchie and Lisa Mingo
Rick and Lynn Sablosky
Bob and Andrea Sacks
Bill and Connie Schenone
Bryan and Karen Siebenthal
Sean and Kristin Young

Up to $999
Dorian and Kelly Adams
Jeanne Atkinson
Adam and Marissa Becker
Jasmine Bennetsen
Tracy Biby
Richard and Tena Boson
Michael and Diane Bradley
Sean and Allison Breininger
Ryan and Becky Brinkmann
Donald and Danielle Burkin
Chris Byrd
Robert and Barbara Capone
Michael Christian
Tyler and Teresa Clifton
Daniel and Melinda Coleman
Darrel and Kalani DeHaan
Egil Dennerline and Nanna Storm
Rob and Dawn Desmond
Scottie and Jessica Dill
Pat and Mary DiMarino
Brian and Jennifer Dorman
Sharon Ellis
Chloe Eminger
Billy Jo and Debbie Estep
Ezat and Laila Faizyar
Fanconi Canada
Nancy and Scott Finnegan
Daryn & Carol Franzen
Liz Funk
Mitch and Erin Furr
Susan and Skip Gannon-Longstaff
Gary and Melody Ganz
Kevin Gatzlaff and Rachael Alaniz
Brian and Lisa Gillott
Ben and Stephanie Griggs
Abdul Hameed
Eric and Elisabeth Haroldsen
Bob and Victoria Hathcock
Greg and Diane Hayes

Shawn Huff
Jeff and Beth Janock
Steve and Cheryl Janowiak
Lester and Nancy Jansen
Dan Klug and Elizabeth Bertrandt-Klug
Martin Lamo
Robert and Darla Lindenmayer
Tanner and Jessica Lindsay
Deane Marchbein and Stuart Cohen
Orion and Lisa Marx
Dan and Nikki McCarthy
Kevin and Barbara McKee
Catherine McKeon
Jeremy and Stacey Mefford
Gianna and Lauren Megna
Sydney and Betsy Moore
Ashleigh and Tim Pinion
Kenny and Lisa Myhan
Louis and Virginia Napoles
Jack and Lisa Nash
Jack and Tammy Neal
Philip Nelson and Candy Lindsey
David A Neumann
Robert and Mary Nori
Ron and Fredi Norris
Anne Park
Stacia Pattison
John and Dianne Ploetz
Lynn and Shirley Quilici
Joel and Jennifer Ramirez
Dov Rom
Stanley and Lisa Routh
Sam Hoffman Medical Fund
Steven B. Sample
Richard and Dolores Satterlee
Sharon Saunders
William Schaecher
Lorne Shelson and Annette Waxberg
Jim and Carol Siniawski
Kevin and Joanne Smith
Adam and Jennifer Stewart
Charles and Jennifer Sumrall
Jan and Ken Sysak
Mary Tanner
Bruce and Loreen Timperley
Mark and Susan Trager
Steve and Melissa Turner
Mike and Beth Vangel
Louis and Theresa Viola
Joe and Wendy Vitiritto
Joseph and Natalie Vitrano
Joel Walker
Anthony and Elisa Walsh
Marc Weiner
Cecelia Zurhellen

RAISE $ FOR FA RESEARCH SIMPLY BY WRITING A LETTER

Asking for donations can be a very intimidating task, whether you're asking friends, family, or strangers. Yet to continue to make significant progress in research and family services, everyone must continue fundraising efforts. One of the easiest ways for you to reach out to donors is by sending a compelling, personal letter – and FARF will do almost all of the work! Write a letter about the status of the FA individual in your life and share a joyful accomplishment or a challenge you are facing. It is important to remind your friends and families what their contributions have accomplished and what they could mean for the future. That's why highlights from 2016 can be found on our website, www.fanconi.org (click on fundraising). The FARF team is here to help you with editing, printing, paying for postage and mailing your letters, or any portion of this process. Contact us at 541-687-4658 or info@fanconi.org.

In Loving Memory

Anastasia Volynkina	6.29.10 – 3.9.16
Piyush Khatri	4.22.05 – 3.13.16
Melissa Burgos	2.11.81 – 6.23.16
James Graham	6.9.14 – 8.18.16
Mason Lee	3.13.12 – 8.23.16
Christopher Byrd	7.12.82 – 9.8.16
Amy Frohnmayer Winn	2.25.87 – 10.2.16

FUNDRAISING SCRAPBOOK

Nina's Starry Night

Rachel Altmann is always looking for new, creative and fun ways to raise funds for the Fanconi Anemia Research Fund (FARF). This year, to kick off the International Fanconi Anemia Day fundraising season, she organized a festive Bollywood-themed event called Nina's Starry Night, in memory of her daughter, Nina. On April 2 in Portland, Ore., dozens gathered to experience Bollywood dancing, Indian food and henna, all to raise funds to support the Fund's mission. The FARF team even joined the festivities! Altogether, Rachel and her team raised $6,000! Thank you!

Strike Away FA

Inspired by other FA Day fundraisers, Valeen Gonzales felt motivated to hold her own event to raise funds for FARF. She gathered her family and together they decided to put on a bowl-a-thon in honor of her son, Teddy, who has FA. Strike Away FA with Teddy took place May 15 in Upland, Calif. After a fun-filled afternoon at the bowling alley, Valeen and her family had raised over $3,000 for FARF. Thank you, Team Teddy! To learn more about Teddy and his family's fundraisers, visit www.teamteddyfa.org.

Un ♥ por Fanconi

For the second year in a row, Alejandra Tabar Concha, an adult with FA, held a fundraiser for FARF in support of International FA Day. Alejandra and her friends, who live in the Dominican Republic, sold artisan lollipops to raise funds. They also educated the public about what Fanconi anemia is and how they can help. At the end of the day, Alejandra raised $1,000 to support FA research and family services. Gracias, Alejandra!

Emily's Drive for a Cure

This year, the Mitchell Family wanted to make a splash for International FA Day, so they organized Emily's Drive for a Cure, a golf tournament in honor of eight-year-old golf enthusiast, Emily, who has FA. The community in Wahiawa, Hawaii came out in numbers to support Emily and FARF. Emily and her mom, Tricia, even appeared on local television to talk about FA, the tournament, and how it will help support FARF's mission. By the end of the tournament, the Mitchell family raised nearly $8,000! Way to go!

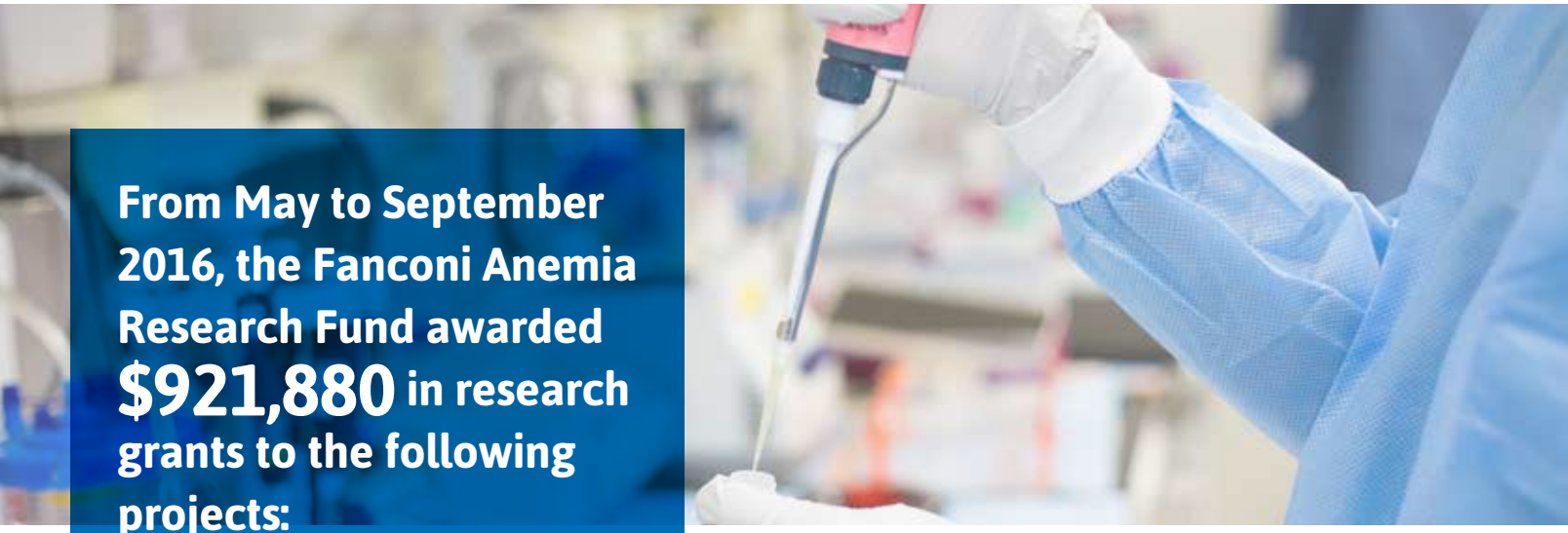
2nd Annual 5K for FA

The 2nd Annual 5K for FA took place May 7 in Hilton, N.Y. The Lana Family expanded on the success of their first run in 2015 to draw in even more participants and sponsors. Mary Ann and her son, Eli, who has FA, went on local news and radio programs to spread the word. Two other families affected by FA, the Fiaschetti's and the Eminger's, also joined in the race. By the time all runners crossed the finish line, the Lana's had nearly doubled what the raised last year, bringing in $22,000 to support FARF! Thanks, Lana Family! Next year's race is scheduled for May 6, 2017. Learn more at www.5kforfa.com.

Century Ride

Rachel Altmann, who lost her daughter Nina to FA, asked Sharon Schuman of the FARF board to join her for the 100-mile Portland Century bike ride on August 6, 2016. It seemed impossible! Nonetheless, they both spent the summer stretching out their weekend rides longer and longer. August 6 arrived, and there was no turning back. Sharon had talked her bike-crazy husband David into riding, and one of Rachel's co-workers at the Multnomah County Library also joined the team. It was a gorgeous day, and by the time they hit the strawberry short cake at the 90-mile mark, they knew they had it made. Rachel's original goal was $1,000 in sponsorship. They raised $7,400!

YOUR FA RESEARCH DOLLARS AT WORK



From May to September 2016, the Fanconi Anemia Research Fund awarded $921,880 in research grants to the following projects:

Investigators:
Andrew Deans, PhD; Wayne Crismani, PhD, St Vincent's Institute, Fitzroy, Australia

Title:
Detection and characterization of ubiquitinated FANCD2 and FANCI

Amount:
$182,967

Investigators:
Wei Tong, PhD; Roger A. Greenberg, MD, PhD, The Children's Hospital of Philadelphia, Philadelphia, Penn.

Title:
Targeting LNK(SH2B3) to ameliorate hematopoietic stem/progenitor defects in Fanconi Anemia

Amount:
$204,593

Investigators:
Josephine Dorsman, PhD; Patrick May, PhD, Dept. of Clinical Genetics, VU Medical Center, Amsterdam, The Netherlands

Title:
Towards improved clinical management of FA-related cancer via a novel functional genomics approach

Amount:
$234,320

Investigators:
Blanche P. Alter, MD, MPH; Philip S. Rosenberg, PhD, National Cancer Institute, Bethesda, Md.

Title:
Cancer in Heterozygote Carriers of Fanconi Anemia

Amount:
$300,000

The Fund is committed to supporting research to further our mission of finding new treatments and a cure for Fanconi anemia. Over our 27-year history, we have funded 216 research grants and one service grant to over 110 investigators worldwide. The total amount of research dollars awarded is over $19 million!

STAFF UPDATE

The Fund is pleased to welcome Cynthia Pappas as Interim Executive Director. The Board of Directors is confident that Cynthia will provide strong leadership through this time of organizational transition following the departure of Pam Norr. FARF is deeply grateful to Pam for her pivotal role at FARF and wishes her success in her future endeavors.

Cynthia comes to FARF with more than 30 years of leadership and development experience in nonprofit organizations and city government. Her history of managing organizational transitions includes serving as President and CEO of Planned Parenthood of Southwestern Oregon, as Board President of community-based organization Food for Lane County, and as City Manager for the City of Springfield. Cynthia has two adult sons and lives on a farm with her husband and two dogs. Her daughter-in-law recently went through a bone marrow transplant, giving the family some understanding and appreciation of what FA families experience.

Cynthia will work closely with the Board to ensure a smooth transition and lay the foundation for success of the new Executive Director. She will also oversee staff and organizational operations. FARF's commitment is to FAmilies and remains devoted to the mission during this time of transition. Please don't hesitate to reach out to Cynthia with any comments or questions at 541.687.4658 or cynthia@fanconi.org.

BOARD OF DIRECTORS UPDATE

The Fanconi Anemia Research Fund would like to recognize the contributions of Annette Waxberg, MBA, Chris Byrd, Esq., and Amy Frohnmayer Winn, MA, for their service on the FARF Board of Directors.

Annette served from Spring 2012 - Spring 2016, providing astute financial insight throughout her tenure and serving as treasurer. She represented Fanconi Canada and was instrumental in the success of the 2015 Scientific Symposium in Toronto and the larger, ongoing commitment to Fanconi anemia research and affected families. Annette and her husband, Lorne, continue to run Fanconi Canada.

Chris and Amy served on the board for four and three years, respectively. As adults with Fanconi anemia, they brought a unique and distinctly valuable perspective to the board. They were both passionate about the mission of the Fund and worked hard to carry it forward. Their presence at scientific and family meetings was evident in the way researchers and family members alike looked to them for guidance and inspiration.

The Fund thanks Annette, Chris and Amy for their steadfast service to advancing the mission of the organization.

NEW LOGO

FANCONI ANEMIA RESEARCH FUND
Advancing Research. Supporting Families.

The Fanconi Anemia Research Fund is proud to announce its new logo and look, officially in use since September 2016.

The new logo is a dynamic design with more color, vibrancy, movement and a human aspect, while still maintaining FARF's identifying helix. If you would like to use the new logo for fundraising purposes, files can be found at www.fanconi.org or by emailing info@fanconi.org.

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Sharon Schuman, PhD
Sherri Van Ravenhorst, MA

The Fanconi anemia community spans the entire globe, with events in several different sites. The Fund encourages everyone to participate in FA fundraisers. Check this list to see upcoming fundraisers near you! Visit FARF's website to see more events and follow links to find out more information. Do you know of an upcoming fundraiser? Contact us as 541-687-4658 or info@fanconi.org.

UPCOMING FUNDRAISERS

Nov. 6, 2016

Thumbs Up for Katrina and Jared

Online, New York Marathon

The Aggabao Family

Nov. 12, 2016

KATA Brave Hearts Hoot n' Holler

Parker, Colorado

The Atkinson Family

Nov. 1-Dec. 5, 2016

Faces of FA Calendar Sale

Worldwide (online)

The Gonzales-Coons Family

Dec. 11, 2016

Journey with Jacob

Skokie, Illinois

The Grossman Family

April 1, 2017

Band, Brew & BBQ

Richmond, Virginia

The McQueen & Vandermeys Families

May 1, 2017

8th International FA Day

Worldwide

All FAmilies!

May 7, 2017

5K for FA

Hilton, New York

The Lana Family

Spring 2017

FARF Benefit Concert

Eugene, Oregon

Sharon Schuman

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.*

FANCONI ANEMIA RESEARCH FUND
Advancing Research. Supporting Families.

1801 Willamette St, Suite 200
Eugene, Oregon 97401

RETURN SERVICE REQUESTED

Our mission is to find effective treatments and a cure for Fanconi anemia and to provide education and support services to affected families worldwide.

HOW YOU CAN HELP

Donations Online:
Donate via the heart button on the Fund's website (www.fanconi.org) or through www.networkforgood.org or 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

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