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BCM FAMILIES FOUNDATION

Toward the cure of Blue Cone Monochromacy

PO Box 7711 - Jupiter FL 33468-7711 USA

Dear Families,

We hope you enjoyed a wonderful and relaxing summer holiday and are ready to get back to work and to start children's school and activities.

At BCMFF we have continued working on our path toward a cure. Specifically, our main goal at the moment is to work with biotech companies which are necessary sponsors of clinical trials.

Moreover, our BCM Registry received the approval of the WIRB, an external ethical committee reviewing projects that involve humans.
We want to remind all of you to submit a DNA test if you want to participate in the BCM Registry.

The DNA test report is a necessary document in the registration process. Due to a longstanding collaboration between BCMFF and Dr. Wissinger you can test your DNA by shipping your samples to University of Tubingen, with no costs for DNA examination.

In this newsletter you will learn about:

- **Dr. Samuel G. Jacobson, Director of the Center for Hereditary Retinal Degenerations, and Professor of Ophthalmology at the University of Pennsylvania;**
- **How to test your DNA;**
- **A trip to the Micronesia island of Pingelap , the Oliver Sacks "Island of the colorblind";**
- **60sec with: Dean Monthei.**

A warm hug to all of you,

Renata Sarno, President,
and the Board of Directors of the BCM Families Foundation

Dr. Samuel G. Jacobson, Professor of Ophthalmology at the University of Pennsylvania

For those who know me well, I have never been a self-promoter. Patients tend to find out about our Center for Hereditary Retinal Degenerations (CHRD) from other patients or by referral from colleagues. No advertising; no websites. However, Renata asked me to contribute to the Newsletter because it would serve to introduce me to the wider group of BCM families that are now part of the BCMFF – "…many of them don't know you. I think it will be important to write something." she said.

Let me introduce myself then. Born in Norfolk, Virginia, USA, and schooled in Chicago, Illinois, London, UK, and Boston, Massachusetts. As I was told by a colleague recently, I am a 'double doctor' – M.D. and Ph.D. My clinical training was in Ophthalmology (eye doctoring) and I emerged from this background with a full commitment to work with patients with inherited retinal disorders. When this mission started for me (in the 1980's), there were no treatments or cures for these conditions. Very few of us were committed to this ophthalmological sub-specialty. With no treatment tools available in my 'double doctor' lab coat, the doctoring was all about increasing understanding of the retinal disorders so we could push the field forward to treatment. Ideas were plentiful but detailed understanding of the 'how and why' patients developed such visual losses was not as clear.

As many families with BCM experienced in the past, there were initial visits to specialists who were not sure of the exact diagnosis of the family member with visual problems. Names like cone dystrophy or achromatopsia or macular degeneration or myopia or optic nerve dysfunction or other diagnoses could be given and would lead to some level of confusion. For those specializing in inherited retinal disorders, however, making a correct clinical diagnosis was not an issue. Knowing the cause, however, was needed and this step toward

treatment occurred when gene changes on the X-chromosome leading to BCM were discovered by Dr. Jeremy Nathans and colleagues in the late 1980's and further clarified by Dr. Susanne Kohl and Dr. Bernd Wissinger and many luminaries in the field of molecular genetics to the present day.

Thanks to Dr. Renata Sarno and BCMFF we are all in a better position to consider novel ways to approach (and eventually treat) BCM. Over the years, she brought together scientists and medical doctors to 'brainstorm' and then do the relevant work to try to take smart steps toward greater understanding of BCM and even plan for therapies. My colleagues and I at the CHRD in Philadelphia, Pennsylvania, are specialists in diagnostics and monitoring of patients. In the current era, we have transformed into a group that conducts evaluations relevant to therapy – such as gene therapy – and designs treatment trials. We were one of several groups of scientists and doctors who conducted the first gene therapy trials in those with a childhood blindness that was made better (to our joy) with one form of gene therapy. Now we are involved in other such clinical trials or the preparation for such. When I say my colleagues at CHRD, I am referring to: Artur V. Cideciyan, Ph.D., Alexander Sumaroka, Ph.D., Alexandra V. Garafalo, M.S.Eng., and Alejandro J. Roman, M.Sc. Surrounded by these engineer-scientists (very dedicated and kind people, as well), we evaluate families with BCM using sensitive vision tests and imaging of the retina to ask questions like: "Is BCM a condition that may be amenable to a gene therapy?" "How would we be able to determine if a treatment is successful – i.e. which quantitative evaluations would be key to knowing if the treatment has been (to some degree) helpful to the patient?" "Are there differences between BCM families with different types of gene changes causing the condition (note: the gene changes are not all the same and do not have the exact same effect on vision)?"

We have already determined that BCM has the potential to benefit from a gene therapy – in other words, the cells to signal vision are there and waiting for the wake-up call (*reference 1*). We then decided on what type of visual tests would be most informative to monitor BCM when there is a clinical trial of treatment (*reference 2*). We even devised a specialized method to measure small amounts of red-green vision to use in a BCM trial (*reference 3*). And recently, we are seeking the answer to the important question of whether different families with different gene changes are different enough to warrant a modified approach to treatment (*reference 4*).

So, we started with a known clinical vision problem with an unknown cause;

we moved to a clear cause at the level of the gene and mutation; and now we are trying to edge closer but cautiously to therapy. We appreciate your patience and participation in all of this – we at the CHRD look forward to meeting those of you we have not yet had the pleasure to meet.

References:

1) Cideciyan AV, Hufnagel RB, Carroll J, Sumaroka A, Luo X, Schwartz SB, Dubra A, Land M, Michaelides M, Gardner JC, Hardcastle AJ, Moore AT, Sisk RA, Ahmed ZM, Kohl S, Wissinger B, Jacobson SG. Human cone visual pigment deletions spare sufficient photoreceptors to warrant gene therapy. Hum Gene Ther. 2013 Dec;24(12):993-1006.

2) Luo X, Cideciyan AV, Iannaccone A, Roman AJ, Ditta LC, Jennings BJ, Yatsenko SA, Sheplock R, Sumaroka A, Swider M, Schwartz SB, Wissinger B, Kohl S, Jacobson SG. Blue cone monochromacy: visual function and efficacy outcome measures for clinical trials. PLoS One. 2015 Apr 24;10(4):e0125700.

3) Cideciyan AV, Roman AJ, Jacobson SG, Yan B, Pascolini M, Charng J, Pajaro S, Nirenberg S. Developing an outcome measure with high luminance for optogenetics treatment of severe retinal degenerations and for gene therapy of cone diseases. Invest Ophthalmol Vis Sci. 2016 Jun 1;57(7):3211-21.

4) Sumaroka A, Garafalo AV, Cideciyan AV, Charng J, Roman AJ, Choi W, Saxena S, Aksianiuk V, Kohl S, Wissinger B, Jacobson SG. Blue cone monochromacy caused by the C203R missense mutation or large deletion mutations. Invest Ophthalmol Vis Sci. 2018 Dec 3;59(15):5762-5772.

"The first time I met Dr. Samuel G. Jacobson was in 2010, when I went to Philadelphia with my 3 children with BCM, who were 5, 8 and 11 years old. It was a very important experience and I was struck by the professionalism and passion with which Dr. Jacobson and his group work on hereditary retinal diseases. I am happy and proud that my children and my brother have been able to contribute to advancing the search for a BCM cure".

Renata Sarno

The importance of having your DNA tested

We have always underlined the importance of having your DNA tested and the numerous reasons why this is essential for rare diseases patients. If you have a clinical diagnosis of BCM, the DNA Test would give you a genetic confirmation of the diagnosis, it would help scientific research to find all the possible genetic mutations that lead to disease, and know the possible experimental therapies that often depend on the particular genetic mutation that you have.

The genetic confirmation is important because a patient with BCM needs to understand how the disease spreads within his own family and what are the chances of passing the disease to his children.

You can have your DNA tested for free thanks to the University of Tubingen, with which the BCMFF has an ongoing long-term professional relationship.

You can read more here.

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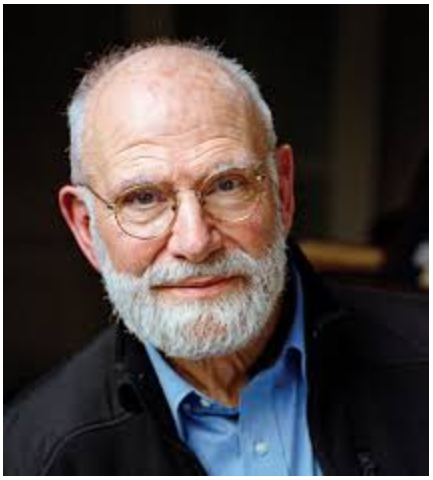
A trip to Pingelap

We are happy to have been one of the sponsors of the trip organized by the Italian Achromatopsia Association (IAA) to Pingelap, a remote Micronesian atoll in the South Pacific known as the "Island of the Colorblind" because of the high incidence of Achromatopsia among its population (between 10 and 30 percent). Here you can find the event press release.

The trip was strongly desired and organized by IAA President, Elisabetta Luchetta, in honor and memory of two great Scientists, friends of the Association. Twenty-five years ago, the neurologist Oliver Sacks, together with the psychologist Knut Nordby went to Pingelap to study the condition and how the population adapted to it. The experience was then reported in Sack's 1996 book "The Island of the Colorblind", which helped create awareness on Achromatopsia worldwide.

The BCMFF supported this beautiful initiative, due to our longstanding collaboration with all achromats patients' organization. BCM is also known as X-linked Achromatopsia. Elisabetta Luchetta was travelling together with two Achromats and two representatives of the BCMFF.



Oliver Sacks

Knut Norbdy

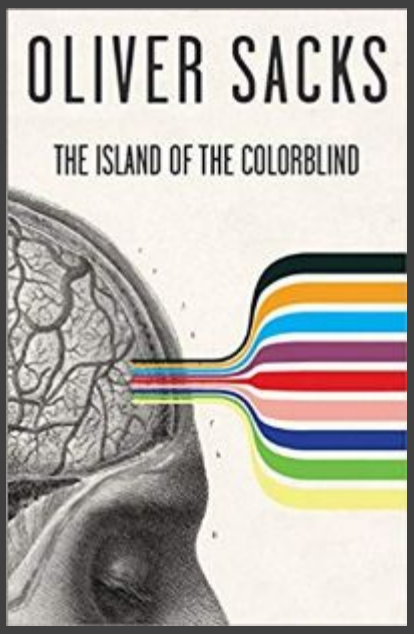
Ferdinando, one of the representatives from the BCMFFF, has shared with us some of the memories he brought back with him.

"It has been a thrilling experience for me and I was really happy to represent BCMFF in this important trip to create awareness about our rare diseases".

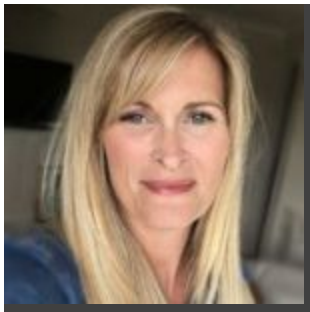
Ferdinando

Elisabetta Luchetta gifting sunglasses to children in Pingelap

IAA and BCMFF representatives

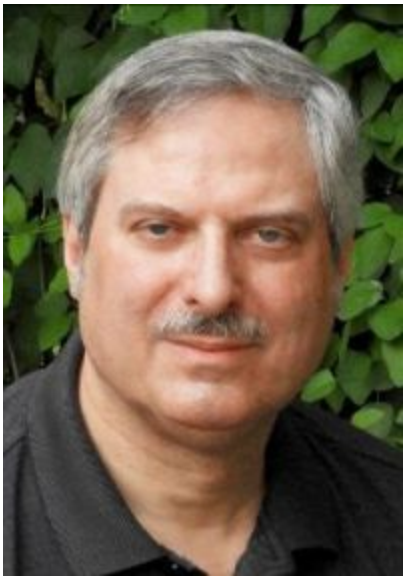


You can discover all about Oliver Sack's Journey to the Island of the Colorblind by purchasing his book on Amazon Smile. Using this link, you can donate to BCMFF while shopping online!



60 Seconds with...

By Trudi Dawson



Name:
Dean Monthei

Age:
61

Where do you live?
Portland Oregon - USA

How many relatives do you have with BCM?
I have two older brothers, a cousin, and a grandfather.

What is your job?
I am retired now but worked as a materials engineer specializing in electronics packaging for 35 years. I worked for Tektronix, Intel, and QORVO. Most of my career has been working on cell phone power amplifiers (the part that sends the signal from your phone to a cell tower). I traveled extensively to Europe and Asia for work.

What is your most useful BCM tip?
Get familiar with magnifiers, monoculars, accessibility features of cell phones and the magnifying software for computers (Windows built in accessibility magnifier and Zoomtext). I use a bunch of magnifiers of various powers for various purposes. These will let you read anything. Search on YouTube, Amazon and Google for "low vision" and "accessibility" to find useful info. I have also found photography to be a great hobby since I can see so much more detail in the photos when I get home than when I was there taking the photo.

What would you suggest to young boys with BCM?

Don't let false concerns get in your way of trying things or doing what you want. We have some true limitations but for most items in life it is just figuring out the right tool to use (in our case mostly magnifiers or software solutions). Just like a carpenter needs a hammer to pound nails we need magnifiers or other tools to get our jobs done.

Greatest achievement/proudest moment so far…

My greatest achievement was writing a technical book about my work. Only one other person at my company out of several thousand employees had written a book My proudest moment was when I was asked by one of my company's customers if I would sign copies of my book for him and he told me that they were using my book for training at his company (Ericson in Europe).

Not many people know this about me but…

One odd thing that very few people know about me (even close friends) is that there are very rare instances where I can see better than a person with normal vision. This only happened a few times, all at work, where I could clearly make out a pattern that people with normal vision could not see at all. This was always related to color combinations where there was so much red that looked bright to normally sighted people that they could not see some subtle other color on top of the sea of red. The other people and I were both astonished when this happened, especially because for me it was not subtle at all. I could see it clearly and they could not.

Our mailing address is:
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