Outlook

Holidays Newsletter 2024

From BCM Families Foundation <info@bcmfamilies.org>
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To info@bcmfamilies.org <info@bcmfamilies.org>

BCM FAMILIES FOUNDATION
www.bcmfamilies.org

Dear Families, Dear Friends,

2024 has been a year full of many events. The journey towards the cure of BCM is continuing and we are collaborating with John Cavitt and Blue Gen Therapeutics Foundation who is looking for funds for the clinical trial.

BCMFF has achieved in 2024 the result of 14 years of clinical

studies at the University of Pennsylvania, as you will read below.
Moreover, we have expanded our diagnostic projects, we now have a free genetic testing project as you will read below and we continue, thanks to all of you, to collect data in the patient registry. I ask you to continue in 2025 to participate in these programs that are important for the entire community because they tell us which are the BCM causative mutations and gather the data in a single registry at www.BCMRegistry.org .
BCMFF has participated in the purchase of a machine for the Tübingen center, which will make the European center ready for clinical measurements. The fundraising program was done in collaboration with the Associazione Acromati Italiani.
Finally, we continue financing breathtaking research in the field of gene therapy vectors, thanks to Dr. Wentao Deng.
Here's to 2025! I'm excited to see what the new year brings.
Wishing you and your loved ones a joyous holiday season filled with warmth and happiness.

Renata Sarno, Ph.D.
President of the BCM Families Foundation

In this Newsletter:

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1. No-Cost Genetic Test Program for Blue Cone Monochromacy (BCM)

The BCM Families Foundation has launched a *No-Cost Genetic Testing Program* to provide accessible DNA testing for individuals with a clinical diagnosis of Blue Cone Monochromacy (BCM). Conducted by Dr. Bernd Wissinger's lab at the University of Tübingen, Germany, the program ensures high testing efficiency by identifying all known causative mutations of BCM and enabling differential diagnosis. This initiative eliminates cost barriers, fostering greater equity in accessing accurate genetic diagnosis. Find more information about the program here: https://www.blueconemonochromacy.org/no-cost-dna-test/ .
All patients with the genetic confirmation of Blue Cone Monochromacy are encouraged to enroll in the BCM Patient Registry at https://www.bcmregistry.org/ .

Join The Registry

Click on the image below to download the flyer:

No-Cost DNA Test Program for Blue Cone Monochromacy

BCM FAMILIES FOUNDATION

Universitätsklinikum Tübingen

Why get tested?

If you have a clinical diagnosis of Blue Cone Monochromacy, there are many reasons to test your DNA:

- to have a genetic confirmation of the clinical diagnosis, as clinical diagnosis is often very difficult to reach;
- to understand how the disease spreads within your own family and what are the chances of passing the disease to your children;
- to help scientific research to find all the possible genetic mutations that lead to the disease; this is of fundamental importance to improve the diagnostic tests themselves – to make them accurate and complete;
- for diseases such as Blue Cone Monochromacy, for which gene therapies are being developed, it is important for the patient to know his causative mutation, in order to know if he will be able to have access to that therapy.

The lack of an accurate diagnosis can have far-reaching consequences for patients and their families and for the entire BCM community. If you do not reach the true accurate diagnosis of a rare pathology such as Blue Cone Monochromacy, you cannot support the path toward the cure and identify your global community to achieve together the cure of the genetic disease, given that gene therapies can be different for each gene and also for each causative mutation.

Program Overview

The No-Cost Genetic Testing Program for Blue Cone Monochromacy provides no-cost genetic testing for individuals with a clinical diagnosis of Blue Cone Monochromacy. Targeted familial variant testing is also available to female relatives of individuals who receive a positive result through the program and meet certain criteria.

This testing Program is supported by the **BCM Families Foundation**, a nonprofit organization dedicated to find a cure for Blue Cone Monochromacy. The genetic testing is performed at **Dr. Bernd Wissinger's Lab, University of Tübingen, Germany.**

The efficiency of the test in this Program is very high, greater than 90%, because the Wissinger's Lab continuously updates the list of BCM causative mutations, is able to find all known BCM causative mutations and to perform differential diagnosis with other diseases showing similar clinical features, for example **Achromatopsia, Bornholm Eye Disease, Cone Dystrophy**. This efficiency is unique and is not found in other laboratories which on the contrary might not test for all BCM causative mutations and therefore could report a null response.

The aim of this program for the BCM Families Foundation is to enlarge inclusion and promote equity to the access to the genetic diagnosis of Blue Cone Monochromacy. The high cost of the test at the very few laboratories that offer it and the lack of information create barriers especially for the most socio-economically disadvantaged individuals, precluding inclusion and diversity in diagnosis.

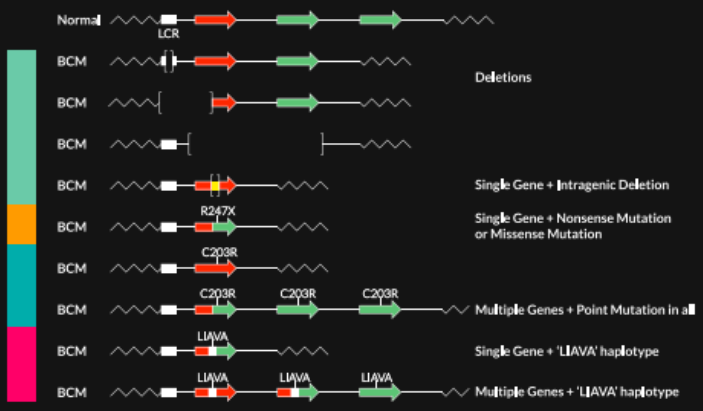
The only cost to patients is the cost of extracting blood samples and sending them to the laboratory.

Genes and Causative mutations

X-Chromosome: genes OPN1LW, OPN1MW and the upstream Locus Control Region (LCR).
BCM is a rare genetic disease of the retina caused by genetic mutations on **genes OPN1LW, OPN1MW and the upstream Locus Control Region (LCR).**

This picture was kindly provided by Prof. Bernd Wissinger, University of Tübingen, Germany and percentages come from 2019-2023 BCM Patient Registry aggregated data

Deletions - 55.1%
C203R - 37.9%
Other PT - 1.1%
Exon 3 - 5.9%



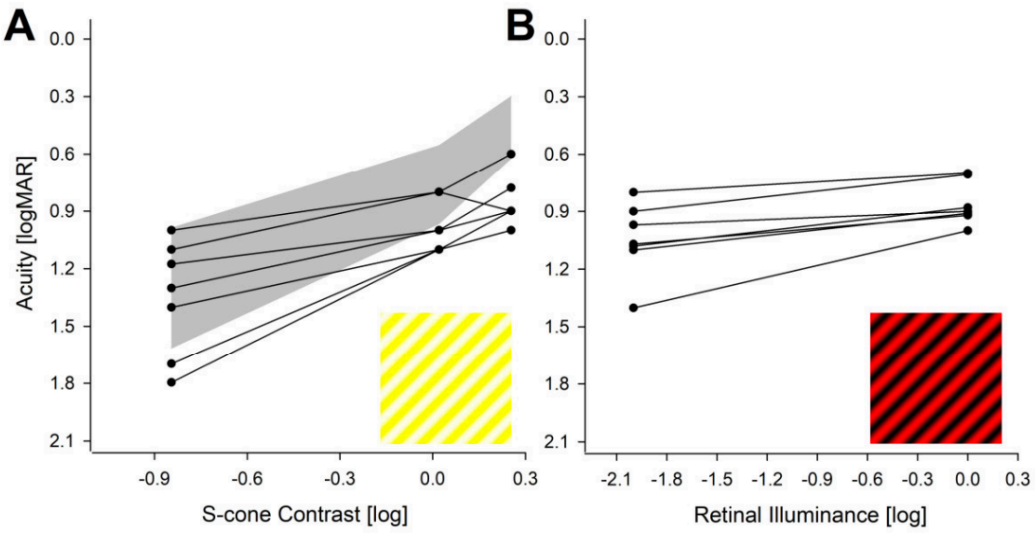
2. Gene Therapy Advances for Blue Cone Monochromacy (BCM)

On October 2, 2024, the *International Journal of Visual Sciences* published a study titled "Evaluation of Retinal Structure and Visual Function in Blue Cone Monochromacy to Develop Clinical Endpoints for L-opsin Gene Therapy". This landmark research, representing 15 years of clinical investigation primarily conducted by the University of Pennsylvania, focuses on patients with Blue Cone Monochromacy (BCM).

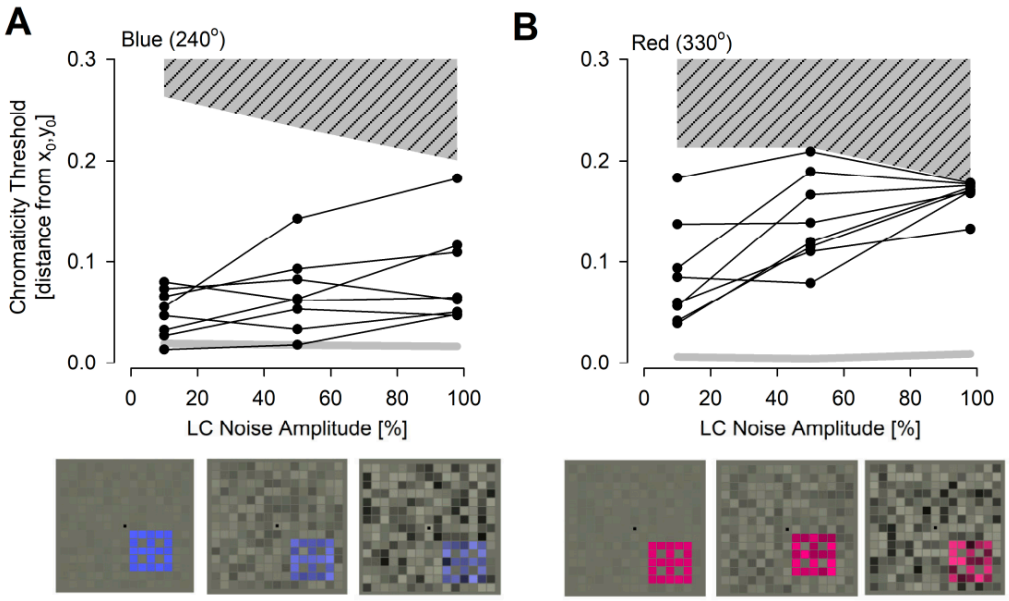
This publication in the International Journal of Visual Sciences collects the results of 15 years of clinical studies, carried out mainly by the University of Pennsylvania, on patients affected by Blue Cone Monochromatism (BCM).

The clinical center was once led by one of the world's leading experts in retinal diseases, Prof. Samuel G. Jacobson, and is now, after Jacobson's passing, in the hands of Drs. Artur Cideciyan and Tomas Aleman.

Several dozen patients with BCM have been examined. The aim was to concentrate the data on the clinical characteristics of our rare disease in a single clinical center and, based on this data, to design the clinical trial for the administration of gene therapy to humans. The fundamental elements of a clinical trial were thus obtained: the definition of the so-called endpoints; and the study protocol. The endpoints are output values that answer the question: how do we measure the changes that occur between before and after the administration of gene therapy? For example, will individuals see colors after gene therapy? Will their visual acuity improve, and if so, by how much? The protocol instead collects all the patient selection criteria for the clinical trial, the dosages of the therapies and the measures to be taken to ensure safety and to verify the efficacy. Doctors at the University of Pennsylvania have developed a series of endpoints specifically designed for BCM, such as the yellow-on-white and red-on-black colored grids to measure chromatic visual acuity that you can see in the Figure 4 of the publication:



and computerized color tests. In Figure 5 of UPenn publication, you can see colored stimuli on a screen that are made increasingly more difficult to see and that will serve as a color vision test, to understand if there are improvements and if they are progressive.



To understand which photoreceptors have been activated by gene therapy, in what position of the retina they are, for example if they are in the most sensitive part, the fovea, or are extra-foveal, it is necessary to have measurements that allow sending a light signal

of a particular color, localized in a point of the retina, and recording whether the patient has seen that signal. In this case scientists have envisaged the use of machines that perform a microperimetry of the retina.
We are truly proud to have supported this clinical research! Thank you to all those who sent donations and those who participated in the clinical studies.

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3. **A Heartfelt Thank You to Our 2024 Giving Tuesday Supporters**

We are deeply grateful to everyone who contributed to our Giving Tuesday 2024 campaign. Particularly we thank people who created a Facebook fundraiser: Amanda Whelan, Renata Sarno, Kay McCrary, Donna J. Bigelow-Taylor, and Laura Beth and thanks to all people who sent donations.
With Blue Cone Monochromacy affecting only about 1 in 100,000 people, raising funds for research and treatments can be a significant challenge.
Your generous support plays a vital role in driving our mission forward and bringing us closer to achieving a #Cure4BCM.

Donate

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4. **Understanding Colors** An Article by Dean Monthei

I have been involved in photography for 50 years giving me a lot of insight into how color works. All of photography, including the screen you are reading now, is based on mixing red, green and blue light in various amounts to make you “perceive a color”. The photos below show the spectrum of white light from the sun reflected off a white card and the spectrum from an iPhone 12 displaying an all-white screen. People perceive both as white but they are actually very different mixes of wavelengths. If people could directly sense wavelengths of light, the 2 whites should look very different.

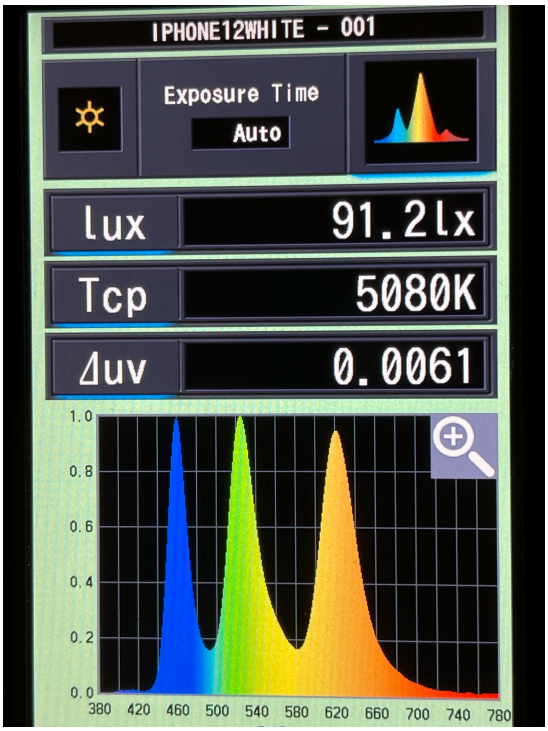
As an example, purple is not a specific wavelength of light. It is always a mix of short wavelengths and long wavelengths (some blue and some red). This is true for natural items like a purple berry or purple being displayed on a computer.

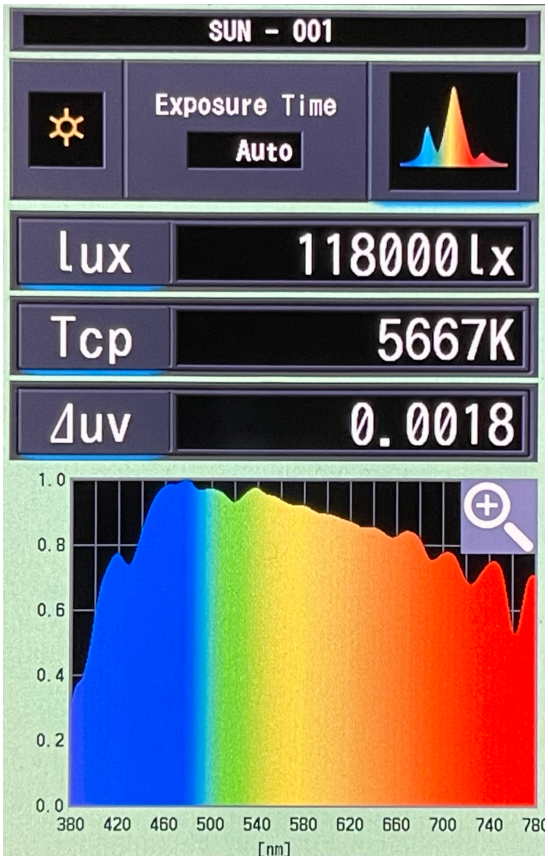
Unlike purple, yellow can be produced by a single wavelength of light but whenever you see yellow on a computer screen or TV it is being produced by mixing green and red light of many wavelengths (never a single wavelength). You see both as yellow but in fact they are very different.

Human color perception is only very loosely related to light wavelengths. It is like a piano with only 3 keys. You can press the 3 keys softer or harder for more or less loudness (corresponding to brightness) and you can press multiple keys to mix 3 tones (equating to red, green and blue). With hearing on the other hand, you can sense a large number of different tones (sound

wavelengths).

BCM is like a 2-key piano analogy. We can sense blue with our S-cones and medium wavelengths of light with our rods. For normally sighted people, rod signals are suppressed by the vision system in brighter light. With BCM rods continue to signal vision under conditions normally associated with daylight vision. With BCM rods sense medium wavelengths while blues are sensed by S-cones giving me something similar to a 2-color blue-greenish color system with very little sensitivity to red (rods don't sense much long wavelength red). For more details, read the last section (Appendix 3) of my writeup on BCM simulation glasses at: BCM Demo Glasses | BCM Families Foundation





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5. 60 seconds with Nolan… An Interview by Trudi Dawson

Name: Nolan Arve Kroll

Age: 7 and a half

Where do you live? Monticello, MN

How many relatives do you have with BCM?
I know my Papa *(maternal grandfather)* does and his

cousin and my mom's cousin so that's three. *(Note by the family: Nolan is actually the first in our family to be officially diagnosed and we have been tracing it back now through our family tree. We have identified at least 7 males going back to Nolan's grandpa's grandfather and great uncle who almost certainly had it - 4 are still living. Nolan's grandpa is having genetic testing done now.)*

What is your job/would you like your job to be?
Right now, helping Daddy and Papa with yard work and stuff. When I grow up, I want to be a police officer, like my Dad.

What are your hobbies?
Swimming, playing outside with my friends, and building forts.

What is your most useful BCM tip?
Try different colored lenses and see which color can help you see best. I like red the best!

What would you tell younger BCM boys/your younger self?
Don't be afraid to ask for help if you need it.

Greatest achievement/proudest moment so far…
Learning how to ride a bike with no training wheels in about 5 minutes last summer.

Not many people know this about me but…
I've been to Florida 3 times and I have a really cool collection of shells that I've found there.

Nolan (right of picture) with siblings Jack and Ruthie.

We are looking for volunteers to join our ‘60 Seconds Community’. If you would like to feature here please contact trudidawson@yahoo.co.uk, a list of questions will be sent to you and we'll do the rest.

Donate

Our mailing address is:

info@bcmfamilies.org

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