



NEWSLETTER

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The Lowy Medical Research Institute Inc. MacTel Project Annual Meeting Summary

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OVERVIEW OF THE MACTEL PROJECT

The Lowy Medical Research Institute(LMRI)/MacTel Project is dedicated to determining the cause of Macular Telangiectasia Type 2 (MacTel), as well as developing possible treatments, preventions and/or a cure for this disease.

Currently, eight countries and 22 US states are represented by clinical, laboratory and imaging sites involved in the MacTel Project.

Purpose of the Meeting

The Annual Meeting for the MacTel Project was held at the University Club of New York in New York City, May 11-12, 2018. Just over one hundred people attended.

The primary purpose of this meeting is for the exchange of information and ideas between all stakeholders involved in Macular Telangiectasia Type 2 research, primarily work supported by LMRI. The meeting includes scientists and clinicians; members of the Board of Scientific Governors and Board of Directors; and the project Sponsors, the Lowy Family.



CLINICAL STUDIES

Natural History Observation and Registry Study (NHOR)

Worldwide over 2000 people affected with MacTel have been enrolled in NHOR at one of our 55 sites and over 1650 are still active. After an initial clinic visit where baseline data and images are obtained, the participants are contacted annually to check on their status and to be updated on the project's progress.

Occasionally, study members may be asked to participate in sub-studies at some of the clinical sites.

In addition, immediate family members of affected participants are welcomed to be screened.

The data we obtain at these visits are invaluable in working towards the Project's goals, especially the imaging and genetic data.

If you would like to enroll in the Registry, check for a nearby site on our website www.LMRI.net or contact us - info@lmri.net or (+011) 858-249-7109.

Clinical Trials

Encapsulated cell-based delivery of CNTF

The Lowy Medical Research Institute, in partnership with Neurotech Pharmaceuticals Inc, is testing the effectiveness of ciliary neurotrophic factor (CNTF) to slow the progression of Macular Telangiectasia Type 2. CNTF is a protein that has been shown to decrease photoreceptor (rods and cones) degeneration in the eye.

In the NT-501 CNTF trials, CNTF is delivered by an encapsulated cell technology implant, which continuously delivers CNTF into the vitreous (the gel that fills the posterior chamber, or back part, of the eye).

NT-501 CNTF Phase II Extension Study

The Phase II extension study is a follow-on to the two-year multi-center, sham-controlled study of the NT-501 CNTF device in MacTel. The study includes 67 participants. A preliminary analysis of the extension study (month 36) was presented. The data shows continued slowing of disease progression in the treated eyes. Reading speed at 36 months continues to show a trend to stabilization.

NT-501 CNTF Phase III Enrollment

Enrollment is open for the Phase III NT-501 CNTF clinical trial. Two identical studies will be enrolling 112 participants each; one eye per participant. There will be over 35 sites participating. This study is taking place in five countries.

Laser Study

A pilot study to test the use of non-damaging/subthreshold laser to treat MacTel is underway at the Medical College of Wisconsin. The study will include 10 participants, randomized to laser versus sham.

The rationale for this study is that the laser treatment may stimulate the retina to produce factors that have a protective or healing effect, which could benefit patients with MacTel.

If you are interested in participating in either of these clinical trials, please contact LMRI at (+011) 858-249-7109 or info@lmri.net.

METABOLOMIC STUDIES

Genetic Links between Low Serine/Glycine and MacTel

A genome wide association study (GWAS) that included MacTel patients and controls was done to see if any genetic variants are associated with MacTel. Variants are identified by their location on the chromosomes of DNA (locus). Five loci were found to be associated with MacTel. Four of those loci have been linked with serine and/or glycine metabolism in research published by other groups. The results of the GWAS in MacTel patients have been published and work is being done to extend these studies. Dr. Bahlo's group in Melbourne has entered into a collaboration to identify additional regions of the genome (DNA) associated with serine and/or glycine as well as other potential molecules associated with MacTel. LMRI has committed to extending this research by doing more genetic sequencing on MacTel patients. By increasing the number of MacTel patients who have their genome sequenced, LMRI researchers will have a better chance of identifying additional genetic variants (mutations) associated with MacTel.

Levels of Serine in Blood

Two independent studies analyzing blood metabolite levels found that MacTel patients have lower serine levels in their blood than control populations. These results were published as part of the GWAS. It should be noted that these studies involved a small number of participants, and that not all persons with MacTel have low serine. There was a range of serine levels measured in both the control population and in the MacTel population. These ranges overlap, but the average of the MacTel population was lower than the average of the control population.

Dietary Amino Acid Supplementation

The publication of the GWAS and supporting metabolomics research suggests an association between serine, glycine, and MacTel. LMRI is aware that patients are interested in knowing if dietary supplements could help their eye disease, and physicians attending the meeting asked about possible trials to investigate whether oral dietary supplementation could help MacTel. While LMRI will consider such trials in the future, more research is required to properly design the trial. **LMRI cannot advise for or against taking dietary supplements at this time. LMRI posted its position on serine/glycine supplementation to its website.**

LABORATORY INVESTIGATIONS

The Lowy Medical Research Institute funds and coordinates research between nine extramural laboratories. LMRI also has its own laboratory facility at its California headquarters, dedicated to the study of MacTel. These research groups are highly collaborative, which has been key to LMRI's progress.

The laboratory research program is following up the leads generated by the genetics program, continuing to search through metabolic data and pursuing fundamental studies involving parts of the eye known to be affected by MacTel including blood vessels, neurons and glia. Groups are also studying what makes the "MacTel zone," or the specific region of the retina that is affected by MacTel, unique or susceptible to disease. This is accomplished through cell-based research and histology. Eyes donated through the **MacTel Eye Donor Program** have been critical to this research. LMRI is also following up on genetic leads outside the serine/glycine pathway.

UK Biobank Studies. The vast majority of patient-based MacTel research carried out by LMRI relies on participation in the Natural History Observation Study and Registry. This is an unparalleled resource for MacTel research. LMRI-affiliated researchers were recently granted access to the UK Biobank, which expands our opportunities for patient-based research.

The UK Biobank is a major national and international health resource. The study includes 500,000 people, aged between 40-69 years old, who will be followed for 20 years. They undergo extensive medical exams, the results of which are included in the UK Biobank. One of the first projects the LMRI-affiliated researchers undertook was to screen for MacTel in the UK Biobank population. This provided an opportunity to assess the prevalence of MacTel in this population. It is also an opportunity to develop and test models that can be used identify or predict MacTel.

IMAGING CLINICAL INVESTIGATIONS

FLIO Fluorescence lifetime imaging ophthalmoscopy (FLIO) is an imaging technology that can be used to investigate the presence and distribution of specific molecules in the back of the eye. FLIO images are captured using a prototype device developed by Heidelberg Engineering. Within the MacTel research community, there is one device in Utah, USA and one in Bern, Switzerland. It has been observed that MacTel patients have a signature FLIO pattern that is not seen in other retinal diseases; this finding was published. Research is being done to test this imaging technique in very early MacTel cases.

By developing a test, such as FLIO, that can detect MacTel before patients become symptomatic, it is hoped that treatment can be initiated before irreversible damage has occurred.

PARTICIPANT PRESENTATION

We were fortunate to have one of our Natural History Registry participants (who also happens to be an optometrist), Dr. N,* speak to the attendees of the annual meeting. Dr. N was able to provide both a patient and practitioner perspective to the group. (**Our guest speaker chooses to remain anonymous.*)

Although our clinicians are in contact with their patients daily, the healthcare system does not always allow for the in-depth conversations that portray the impact that a visual disorder has on a person's emotional as well as physical well-being. Dr. N eloquently shared her personal experiences.

The take home messages she left the group with were an expression of gratitude towards the MacTel Project for carrying out its mission, and the advice to always offer patients some ray of hope.

Last year's guest speaker, Dr. Pete Kellett, has published a book on his experiences with MacTel. Titled Patienthood and Communication – A Personal Narrative of Eye Disease and Vision Loss, the book is available through the publisher, <https://www.peterlang.com>.

TEAMWORK – THANK YOU!

Following up on Dr. N's words, we sincerely want to express our appreciation to our Sponsors, the Lowy Family and all our collaborators in the MacTel Project. Most importantly, we thank our participants and their families for allowing us to collect data, endure the procedures and wait patiently as we work towards our common goal. We are open to input on ways we could better serve you. Feel free to contact us at any time at 858-249-7109 or info@lmri.net.

Research, unfortunately, usually takes a significant amount of time before direct benefits are available to help patients. Each bit of information that is amassed in our project, gets us that much closer to the goal.

So, Thank You, Merci, Danke, Gracias, Dank Je to everyone who contributes information to this project; the patients, their doctors, the investigators and our sponsors.

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