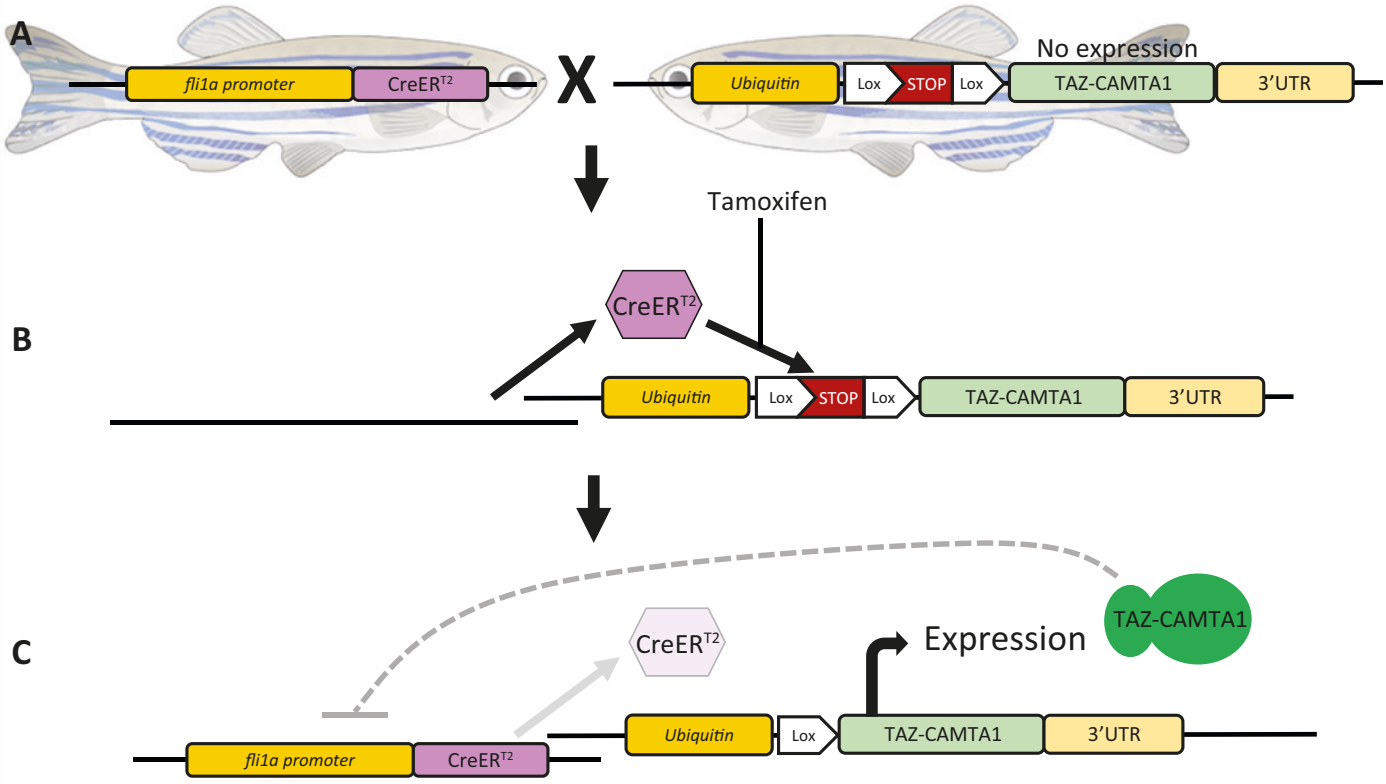
The EHE Foundation (USA)
The EHE Rare Cancer Charity (UK)
The EHE Rare Cancer Foundation (Australia)



Quarterly Newsletter for the EHE Group
January - March 2021

the pledge

Edition 24

Light Pillar photograph from Carl Dixon

Contents

Welcome

Amazingly, this is the 24th edition of **"The Pledge"**, our quarterly newsletter, covering the first quarter of 2021. We welcome all our readers, and hope that this edition finds you all well and still managing to cope with the dreaded COVID19 pandemic.

We hope that 2021 has also started well for you all. While the activities of the EHE Group were affected by COVID, it was fundraising that appeared to be hardest hit in the first quarter, with lock down once again imposed across much of Europe and the USA. But we are excited by the fundraising we see being planned and we hope that the second quarter and beyond will see a lot more activity.

But there is still much going on, so we hope that you enjoy the news and stories in this edition, and once again we want to say a huge thank you to all our supporters for their contributions. ***"Just Live".***

Highlights

The EHE360 Virtual Conference is a huge success

The EHE Foundation, on behalf of the EHE Group, was delighted to host the first international EHE conference in January, a virtual event held over two consecutive Fridays. With leading clinicians and researchers presenting and discussing their work, this was a truly inspiring event. We also extend huge thanks to the Chan Zuckerberg Initiative Rare As One Project for their generous support.

EHE foundation in Italy goes live

We were thrilled this quarter to see Italy's EHE foundation go live. Congratulations to Rosario and everybody who has made this happen. You are all awesome.

ESMO consensus paper on EHE is finalised

In the last edition of The Pledge we reported on the EHE consensus meeting chaired by Dr Silvia Stacchiotti under the auspices of ESMO. This quarter we can confirm that the consensus paper has been finalised, collating EHE expertise from over 90 specialists.

US EHE Biobank goes live

The collection of bio samples, both tissue and fluids, to support research is a major challenge for rare diseases. This quarter saw The EHE Foundation launch its own EHE biobank in the USA.

Fundraising is coming back up

After a difficult year of COVID lock downs, there were growing signs of people re-engaging with EHE fundraising while larger scale events are being planned for later in the year.

Dr Rubin publishes his mouse!

At the end of the quarter we were excited to see Dr Rubin publish his paper in *Genes and Development*, and so open up this amazing advance for wider use.

Further details on these stories, and much more, can be found in this edition

the pledge **Edition 24**

Just Live

01 Patient Support and Advocacy

The EHE Group's support is largely delivered through the Group's worldwide Facebook page which connects with over 2,000 people in over 70 countries across the globe.

That page continues to inspire and support our global EHE community largely thanks to the tireless energy and contribution of so many of our members, many of whom are EHE patients themselves. It is their collective contributions that allow us to support everybody diagnosed with EHE, wherever they may live, and which is a key goal of the EHE group, along with increasing awareness and understanding of EHE. Our patient support and advocacy activities are driven by these two key objectives which are passionately pursued by all the EHE foundations. We thank all our supporters who have contributed to this critical part of our activity, examples of which are provided in this section.

Italy goes live!

At the end of January we were absolutely thrilled to hear the news that the Italian EHE Foundation, organised and driven by our Italian EHE community, had gone live. Andrei Ivanescu posted the information:

> "I'm here to announce that the Italian EHE foundation has been officially created! We have worked a lot for its founding, and it has not been an easy process through this period with COVID, but finally we have reached our first goal. A big thank you to the leader of the Italian foundation, Rosario, and to all the people that made this first step possible. We really hope to start the collaboration with you all in order to keep on making progresses!"

We want to congratulate the Italian members of our EHE global community for this fantastic progress. We hope that this is just the first step as we continue to strive to develop a European-wide network of EHE patients and foundations, which is a core objective of the EHE Group. Hugh Leonard, Chair of The EHE Rare Cancer Charity (UK) explained:

> "We are so excited that Italy have made this first, and perhaps most critical, step of getting an EHE foundation up and running. We know how much work and energy it takes to do this, and so congratulate them on their success. We are also engaged in an initiative to build a network of EHE foundations, patient groups and individuals across Europe so that we can provide support to all and also access greater experience, data and information for our ongoing research. But it is one step at a time and that is why we are so thrilled to hear this fantastic news from Italy."

Congratulazioni Italia. Siete tutti fantastici

New media sites launched

The New Year opened with exciting news in the UK as The EHE Rare Cancer Charity launched several new social media sites. This is part of a strategy to provide a more UK-focused platform for our UK and European members. Allana Parker, EHE patient and blogger is heading up this initiative, and was thrilled to share the news.

> "Today we excitedly went live with our new UK social media pages to promote EHE. Not only do we have a new open UK Facebook page, we also now have new Instagram and Twitter pages that I hope will help us spread awareness of EHE. We hope that all our members can support this initiative to spread the word about EHE by following and sharing these new sites with your friends all over the world."

The Charity also wanted to make clear that these new pages are not CLOSED sites so are open to the public. Contributors should not therefore post anything that they would not wish to share with everyone. The Charity also wanted to stress that the new sites in no way replace the global EHE Facebook page which is a closed group and where our global EHE community openly share information and experiences. Allana concluded:

> "We hope that these new tools for EHE awareness building will be a great success and that you will help us to spread the EHE word. And here are the links.."

Facebook page: (@eherarecanceruk)

Instagram: (@ehe_rcc_uk)

Twitter: (@ehe_uk)

Jane Gutkovich's Patient Briefing

At the start of March, Jane Gutkovich held the latest in her series of patient briefings. In these video conferences Jane leads a discussion with members of the EHE community on a particular aspect of EHE: research, clinical care, treatments or new ideas. Whatever the subject, Jane always provides brilliant explanations; she takes complex issues and explains them in ways that non-specialists can easily understand. On March 6th, she discussed two topics: common current systemic treatment regimens for EHE; and types and benefits of genetic testing. Global attendees agreed that it was another fantastic session. We thank Jane for her time in leading these discussions and encourage each of you to participate in upcoming sessions.

01 Patient Support and Advocacy

Mariana continues European engagement

Mariana Coutinho lives in Portugal and is a well-known member of our global EHE community because of her ongoing engagement and regular contributions. But Mariana is not only active within the EHE community. She is passionate about helping to contribute to not only EHE matters, but also broader rare cancer issues, across the European community.

In January Mariana was thrilled to update us when, during one of her European engagements, EHE was the focus of the discussion:

> **"I am attending a webinar provided by ESMO and Rare Cancers Europe and Dr Paolo Casali from Milan mentioned EHE and the meeting organised by ESMO one month ago that brought together many EHE experts from all over the world! He also mentioned that they will publish a consensus paper that will pull together the agreed views about EHE of these experts. Absolutely amazing that we and EHE are the subject of this meeting. It makes me hopeful that we are closer to achieving more clarity about our disease."**

The consensus meeting was organised and chaired by Dr Silvia Stacchiotti, who is well known to the EHE Group. We agree with Mariana that this consensus paper represents amazing progress in our battle against EHE, and are hugely grateful to Dr Stacchiotti, the experts who participated, and ESMO, for their invaluable contributions.

Later in January Mariana, through her membership of Youth Cancer Europe, also shared news of a webinar at the end of the month, entitled "Chemo Brain: Cancer & Mental Health". The webinar, including guest speakers and Q&A sessions, was addressing the important issues of the psychological impact of cancer, and sharing experiences. Mariana shared links and encouraged anybody who was interested to participate. The significant psychological impact caused by EHE was a key finding of the EHE patient-reported Quality of Life research conducted by the Radboud University Medical Centre in the Netherlands, so this type of discussion about mental health is likely to be of interest to many of our members. We thank Mariana for bringing this to the attention of the group.

Larnie Living, a great listen

Allana (Larnie) Parker was an active holistic therapist in the UK with her own business, delivering massage, reiki and Ayurvedic therapies, reflexology and other forms of treatment to her own patient community. In 2017 Allana sustained what she thought was an annoying gym injury, but as time went on the pain and effect on Allana's mobility was becoming worryingly severe. Then in June 2018 Allana was eventually diagnosed with EHE, predominantly bone related

Allana did not start her EHE journey with 'wait and watch', instead finding herself undergoing a round of radiation therapy to try and address the pain in her pelvis. Sadly, the radiation therapy led to Allana developing sepsis, which made her very weak, and

because the tumours and lesions began to grow in her bones, she found it hard to walk and so spent a lot of time in a wheelchair. Thankfully her treatments appear to have stabilised her EHE, and with physiotherapy she is now able to walk with a stick.

With all this taking place within her first year after diagnosis, it would have not been surprising to see Allana withdraw a little. But those who know Allana also know that she is not one to shy away from challenges, and she soon found comfort and inspiration from other sources, as she explains.

> "I found that even though I felt I was fighting my EHE physically, a lot of the battle was in my head, so I started to write, and the more I wrote the more I realised I wanted to help others. It might be people who have found themselves in similar situations, whether it is something non-cancer related like going from being mobile to a wheelchair, or becoming your own advocate for your care, or even just pointing people in the directions of what is out there to help them tolerate and cope with their cancer. So once I had watched a hundred YouTube videos on what equipment I would need, how to edit, and a few practice runs, I started the Larnie Living podcast and I love it, it is my new baby."

Allana loves the idea that her podcasts may be listened to by people anywhere in the world, and that they might find comfort and support from the content.

> "That's the thing about the whole Larnie Living concept, the social media, the website, the blogs and the podcasts; that they might help someone, somewhere feel less alone, because cancer is a lonely place."

So Allana started her podcast, Larnie Living, a place where she could keep friends up to date with what was happening in her life and also tell them about the things she was learning along the way. As more followers began to appear she decided to start her own Larnie Living website.

And in her latest podcast Allana was joined by Lois Slocombe, of Lois Slocombe Therapies, to talk about a whole range of complimentary therapies that can help people manage and live with cancer. Lois has been a Complimentary Therapist for fourteen years, after completing her three year complimentary therapy degree at the University of Westminster. It is a fascinating listen and we would encourage anybody who is interested in complimentary therapies to go to Allana's website at www.larnieliving.com where the podcasts can be found.

Well done Allana for creating the total Larnie Living concept, telling your EHE story through multiple platforms, spreading all important awareness of EHE, but most of all, for simply thinking of and trying to help others.

Larnie Living

A rare cancer thriver with EHE Sarcoma, just living ....

01 Patient Support and Advocacy

Inspirational thought

Sometimes patient support and community wellbeing can be fostered by positive thoughts and messages that lift the spirits. Messages don't need to be long and wordy. The First quarter saw several such messages posted, just three of which we wanted to include here. We hope that the positive messages and photographs may help uplift you, wherever you happen to live. Just Live:

A European strategy

The EHE Group have a common goal to reach out to EHE patients wherever they live and bring them into our global community. We hope that this will help in providing them with support and information as they embark of their own EHE patient journey. But there is also a broader and important goal. With such a rare disease, obtaining meaningful data is always a challenge, and so the greater the number of patients in our global community the greater our data pool will be.

To assist in this objective, the EHE Rare Cancer Charity has embarked on a European strategy. Hugh Leonard explains:

> **"We have many members in our global community from European countries, but at the moment many of these are engaging as individuals. As we begin to develop patient registries, undertake retrospective studies, encourage biobanking of bio samples, and collect other patient data, it would be wonderful to have patients within a country coordinated, and then linked in to a European-wide EHE network."**

To help develop this the UK charity has been evaluating the different sarcoma/rare cancer/ rare disease umbrella groups, and have identified what they believe are the three priority targets for this first stage of their European strategy. The three initial umbrella groups that the charity will be approaching are listed below:

1. **Sarcoma Patients EuroNet (SPAEN)**

Sarcoma Patients EuroNet

2 **Rare Diseases Europe (Eurordis)**

EURORDIS RARE DISEASES EUROPE

3 **European Cancer Patient Coalition (ECPC)**

European Cancer Patient Coalition

The target now is to reach out and join these three groups and then use their skills, experience and contacts to assist us in linking up the EHE communities across Europe. In doing this, the UK has already engaged with EHE patient Mariana Coutinho, who lives in Portugal and is an active member of several European cancer groups, to help build our European contacts. And of course we are also delighted to now have the EHE foundation in Italy up and running, who will be an integral part of this strategy. We look forward to further updates in future editions of The Pledge..

Rare Disease Day celebrated

February 28th is international Rare Disease Day, and several of our global community wanted to remember this important day. While the EHE Group is of course focused on EHE, we also recognise that there are many other rare diseases in the world, some cancer-related, but many not, and people who face a diagnosis of one of those rare diseases will almost certainly face the same challenges that our community faces every day. So Rare Disease Day is a day where we can link arms with every rare disease patient in the world, and know that we are part of one huge community.

One person who absolutely wanted to recognise Rare Disease Day was Claire Anne Escoffey who, in her own words, summed up why this day is so special..

> "Today February 28th Feb is Rare Disease Day. So what? Because 1 in 20 people will live with a rare disease at some point in their life. Despite this, there is no cure for the majority of rare diseases and many go undiagnosed.
>
> It took Great Ormond Street Hospital two years to diagnose Isabelle... it took us a while to even pronounce its name Epithelioid Haemangioendothelioma (EHE). Then thrust into the unknown, we struggled to find scientific information, specialist knowledge, support... We tried the usual channels; Maggie's, Cancer Research, but only felt more isolated and helpless as to where to turn, until we finally found the EHE Rare Cancer Charity, which proved to be a beacon of light, in a what had overnight become our very scary obscure, insular world.
>
> The 300 million people living with a rare disease around the world and their families face common challenges in their daily lives. As a vulnerable and neglected population they are disproportionally affected by stigma, discrimination and social marginalisation, within their social environment as well as society at large.
>
> There are over 6000 rare diseases that are chronic, progressive, degenerative, disabling and frequently life threatening. Due to the rarity of each individual disease and scattered populations, expertise and information is scarce. In health and support systems designed for common diseases people living with a rare disease face inequities in accessing diagnosis, care and treatments."

And others also posted messages about this important day. The EHE Foundation in the US took the opportunity to send a simple but important message to the global EHE community:

> "Today is Rare Disease Day! We know that sarcomas are incredibly rare and EHE is one in a million. Guess what? SO ARE YOU!!"

02 EHE Research

We have been pleased to see the pace of research creeping back up after last year's COVID19 interruptions. We have also been pleased to see the continued delivery of really interesting results, while in Europe we were excited to see a new collaborative research project start, involving INT in Milan and the ICR in London. We hope that you will find the research articles in this edition both inspiring and exciting.

EHE360 Conference: a worldwide first

With the generous support from the Chan Zuckerberg Initiative Rare As One Project, The EHE Foundation in the USA, on behalf of the EHE Group and the global EHE patient community, hosted the first ever EHE-dedicated international scientific conference, called "EHE360" in January. The event was held in a virtual format over two consecutive Fridays, which allowed global participation by international researchers and clinicians and of course our EHE global community

The first session was dedicated to research, where we had nine world class researchers presenting their EHE research, and the exciting results they are seeing. They were also able to answer questions posted by the global audience. This also gave our speakers the chance to discuss the future of not only their research, but also EHE research as a whole, both from the perspective of the objectives and deliverables of such research, and also the challenges in delivering these programmes.

The second Friday was dedicated to clinical management of EHE, where we had nine clinical specialists, each an expert in their field, presenting different aspects of the diagnosis, treatments, and management of EHE. Question and answer sessions again followed each speaker's presentation and gave real insight to the clinical community's dedication and provided care, as well as the challenges they face in treating such a rare cancer.

We know from the post-event feedback that many of our EHE community found the conference uplifting, enlightening, encouraging and inspiring. Jennifer Mulligan summed up the feeling of many after session 1:

> "I was not sure I could attend the entire EHE conference part 1 today, but so thankful I did. The EHE Foundation did an amazing job and the presenters were brilliant and really committed to rare cancer work, especially EHE. I highly recommend coming to the 2nd part even if you cannot be part of it all. Just being left with a great feeling going into a long weekend!! So much exciting research and science going on."

Emily Gatzke also focused on the hope created by such an event:

> "Day one of the EHE conference was great. With a diagnosis that even many sarcoma experts know little about, it is so hopeful and meaningful to know there are brilliant scientists, experts and advocates working so hard to research and share their knowledge with us!"

We totally agree with those sentiments, but it was not just the researchers and clinicians who made the event special. At the heart of everything we do, including the EHE360 conference, is our global EHE patient community, and the inclusion of messages from our members ensured that this was not forgotten. Indeed, these simple messages helped remind all that EHE is not just a research target, or a clinical challenge, but is a rare cancer that can cut lives horribly short, devastate families, and cause unimaginable loss to those effected. Medha Deoras Sutliff summed up the views of many:

> "Not a dry eye in sight. Heartfelt thanks to Jane Biddlecombe, Sandy Meaders, Leah Heinrich, Delaney Wahl, Jono Granek, Fiona Ross, Maggie Cameron, Joe Mulligan, and Sarah Bright for providing the all-important patient voice."

Of course an event such as the EHE360 Conference does not just happen. Putting the conference together, organising the speakers, promoting the event and creating all the infrastructure and procedures to ensure the event is ultimately seamless and highly- professional, and reaches its target audiences, takes a huge amount of time, dedication and very hard work. We therefore want to thank all of those involved in delivering this world-first EHE conference, and give a special mention to Jenni Kovach who MC'ed the two days, Medha Deoras Sutliff and Denise Robinson for their dedicated focus and organization, and David Casimir for his faultless stewardship of the speaker sessions.

Finally, we want to again thank all our speakers, listed on the next page, for their brilliant contributions, and of course the Chan Zuckerberg Initiative Rare As One Project for their wonderful support both for this conference and our ongoing activities to defeat EHE.

Availability of presentations

We recognize that many people may not have been able to attend the EHE360 conference. For those who missed the conference, or would like to see any or all of the presentations again, these can be found on The EHE Foundation website at the address below, and will also be appearing on the individual websites of the EHE Group foundations.

https://fightehe.org/2021-ehe-360/

02 EHE Research

EHE360 Presenters

Denise Adams,
MD, Children's Hospital of Philadelphia

Cristina Antonescu,
MD, Memorial Sloan Kettering Cancer Center

James Chen,
MD, The James, OSU Comprehensive Cancer Center

Jordan Driskill,
UTSW Medical Center

Professor **Robin Jones**,
The Royal Marsden, UK

Professor **Valerie Kouskoff,**
The University of Manchester, UK

Govindarajan Narayanan,
MD, Miami Cancer Institute

John Lamar,
PhD, Albany Medical College

Albiruni Razak,
MD, Princess Margaret Cancer Center, Canada

Charles Rosen,
MD, Mayo Clinic

Brian Rubin,
MD PhD, Cleveland Clinic

Scott Schuetze,
MD PhD, Rogel Cancer Center, University of Michigan

Nathan D. Seligson,
PharmD, University of Florida

Silvia Stacchiotti,
MD, Fondazione IRCCS Istituto Nazionale Tumori, Italy

William Tap,
MD, Memorial Sloan Kettering Cancer Center

Professor **David Thomas**,
Garvan Institute of Medical Research, Australia

Marije Weidema,
Radboud University Medical Center, Netherlands

Breelyn Wilky,
MD, University of Colorado

Dr Rubin leads team that engineers EHE mouse model

Dr. Rubin used a novel approach to target the gene fusion that causes epithelioid hemgioendothelioma, engineering a novel, first-of-its-kind mouse model of the disease, which will help advance studies to identify new treatments.

According to new study findings published in Genes & Development, Department of Cancer Biology researchers have engineered a novel mouse model of epithelioid hemangioendothelioma (EHE), a rare vascular cancer that grows from the cells that line the inside of blood vessels.

Led by Brian Rubin, MD, PhD, the team's animal model was proven indistinguishable from how EHE presents in patients.

Dr. Rubin, who also chairs the Robert J. Tomsich Pathology & Laboratory Medicine Institute, explains:

> **"While EHE is rare, it is highly lethal and there is unfortunately no standard treatment for the disease. One of the main factors that has limited advances in treatment options is the lack of reliable preclinical disease models for study."**

Model points towards EHE drug targets to explore

Importantly, the researchers also determined that TAZ-CAMTA1—the protein fusion encoded by WWTR1-CAMTA1—is sufficient to drive EHE development and progression independent of other genetic factors.

The gene fusion acts as an over-activated form of the TAZ protein. Under normal conditions, TAZ regulates several characteristics of the cells that line blood vessels. When its activity is increased, TAZ contributes to the growth and spread of tumors. Dr Rubin went on:

> **"Taken together, this suggests that TAZ-CAMTA1 and related signalling pathways are a promising target for treating EHE. We are excited to continue exploring this line of investigation, and hope the studies for new EHE treatments by others in the field will also be advanced by our new mouse model."**

Caleb N. Seavey, MD, a general surgery resident in the Digestive Disease & Surgery Institute, is first author on the study, which was funded in part by the CRAVAT Foundation, the EHE Foundation, the EHE Rare Cancer Charity UK, the EHE Rare Cancer Foundation Australia, the Margie and Robert E. Petersen Foundation and VeloSano, Cleveland Clinic's flagship fundraising initiative for cancer research. Dr. Seavey is also a member of Cleveland Clinic's physician-scientist training program called PRISM (Physician Researchers Innovating in Science and Medicine), which allows residents and fellows to pursue a PhD in molecular medicine.

> **"This article appeared on the Cleveland Clinic website following publication of the associated paper in Genes & Development)."**

Targeting a disease-driving gene fusion

While genetic analyses and in vitro studies are important, in vivo studies are critical to uncover disease pathology and drug targets.

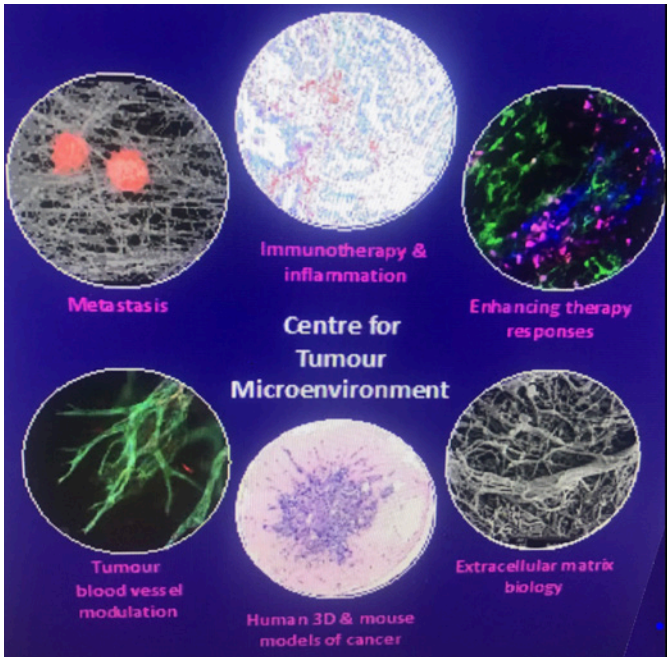
In more than 90 percent of cases, EHE patients have a gene fusion—when two previously separate genes get rearranged as a result of chromosomal changes to become one hybrid gene. In EHE, the WWTR1 and CAMTA1 genes fuse together, a seminal discovery previously made by Dr. Rubin. In about 45 percent of EHE patients, the WWTR1-CAMTA1 gene fusion is the only genetic abnormality present.

Here, Dr. Rubin and his team used a novel approach to target this gene fusion to engineer their mouse model. Their model very closely mirrors EHE in patients, including its clinical, histological, immunohistochemical and genetic manifestations.

Dr. Brian Rubin

02 EHE Research

Barts Cancer Centre open day



Last year the EHE Rare Cancer Charity was delighted to announce that Dr Oliver Pearce had joined its Board of Trustees. Dr Pearce is the cousin of one of our UK patient members, and heads up one of the labs at the Barts Cancer Institute in London, as part of the wider Centre for Tumour Microenvironment, and where his key focus is extracellular matrix biology, and in particular its impact on the immune system's response to cancer.

On 5th March the Centre held it's Industry Partnership Day where it presented an overview of the work that it was conducting, with presentations and discussion under six key themes, namely:

1. **Metastasis;**
2. **Immunotherapy and inflammation;**
3. **Enhancing therapy responses;**
4. **Extracellular matrix biology;**
5. **Human 3D and mouse models of cancer;**
6. **Tumour blood vessel modulation.**

Hugh Leonard and Liz Milligan, Trustees of the UK charity, attended the virtual event, and were very impressed and excited by the combined capabilities of the Centre, as Hugh explained.

We want to thanks Barts for inviting the UK charity to the open day, and for presenting the impressive research that is taking place in their labs.

> **"The Barts team presented an overall integrated approach to understanding the tumour microenvironment, and how the different elements of their programme are combined in the overall research programme. Emphasis was of course placed on the need for tumour tissue, and/or a good quality animal model. In light of Dr Rubin's success with the EHE mouse we asked if they would be able to apply their research programme to a rare sarcoma if a good mouse model was available. The answer was yes, which is quite an exciting possibility, and one that we will be exploring further."**

ESMO EHE Consensus paper is completed

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Last December we reported on the exciting news that the European Society for Medical Oncology (ESMO), as part of their strategy for the development of consensus-based clinical practice guidelines, held a virtual workshop on epithelioid haemangioendothelioma, chaired by Dr Silvia Stacchiotti. The meeting included around ninety clinical specialists from all over Europe, representing all major specialisms involved with the clinical treatment of EHE. In addition, invited groups from Japan and America also participated.

But the consensus meeting was just the start. Reviewing the consensus paper, prepared by the Dr Stacchiotti's team prior to the meeting, all comments then needed to be incorporated into a second draft and circulated for final review. That was completed and we are now waiting for the final consensus paper to be published.

Of course we understand that with such a rare disease, there are still many areas of uncertainty associated with the clinical care and treatment of EHE. It was never intended that this paper would answer all questions. But it is certainly a great step forward to see the clinical knowledge that does exist pulled together in such a comprehensive way. This paper will also assist us in developing retrospective and prospective studies, as well as formulating our patient registry questionnaires, as we strive to fill the gaps in the clinical understanding of EHE.

We certainly want to thank Dr Stacchiotti, all her team, and all the specialists who attended the meeting and have given their time to reviewing and commenting on the final paper. On behalf of our global EHE community, we want to express our gratitude for your ongoing care and dedication to cancer care, treatment, and patient care.

Italian retrospective study provides indicators of possible worse prognosis

In March, Jane Gutkovich posted news of another important paper involving several cancer centres in Italy who had undertaken a retrospective study of 67 EHE patients who had stable disease at the time of their diagnosis. The aim of the study was to try and identify factors during the period of stability that could be viewed as predicting a worse prognosis. As always there are limitations in such a study with relatively small numbers, but it identified with reasonable statistical confidence some factors predicting worse prognosis in patients with stable scans. These factors associated with a worse prognosis are:

a) Tumour-related pain at the time of diagnosis;

b) Development of pain during the follow-up period;

c) Fever at the time of diagnosis; and

d) Development of fatigue during follow-up.

The investigators suggest that doctors might consider starting treatment in this patient population even if the scans are stable. Jane has copy of the paper and is happy to share it with anybody who wishes to have a copy.

EHE Biobank launched

In February, The EHE Foundation (US) formally opened their centralized EHE Biobank. This is critically important as our researchers need donated biospecimens (tissue, blood and fluids), from EHE patients to advance research and improve treatment. Medha Deoras-Sutliff explained:

02 EHE Research

> "That's why this news is so exciting, to actually launch a centralized EHE BIOBANK. All of us here at The EHE Foundation have been working tirelessly to centralize and streamline the tissue donation process to make this as easy as possible for our patients AND to ensure critical donated biospecimens get to the right researchers. We are grateful to every patient who considers tissue donation to support EHE research."

What is the EHE Biobank?

An ongoing collection of tissue samples and other biospecimens, including blood and bodily fluids donated by people with EHE to advance research.

Your Participation is Important

Tissue and body fluids are important to rare cancer research and the search for EHE treatments and cures.

Imminent surgery or procedures?

If you have upcoming surgery or procedures, and want to find out how you can donate your tissue or fluid please visit:

https://fightehe.org/ehe-biobank

To learn more, please visit The EHE Foundation's biobank webpage above. The Foundation's Biobank coordinator can also be contacted at **biobank@fightehe.org** if you or someone you know has any questions or needs help with donating tissue. We hope that every EHE patient will engage in this critical process by helping to ensure their biospecimens are captured for research.

Leah Heinrich Participates on Scientific Peer Review Panel

The Congressionally Directed Medical Research Programs' (CDMRP), Rare Cancers Research Program (RCRP) consumer advocate Leah Heinrich recently participated in the evaluation of research applications submitted to the RCRP. Leah was nominated for participation in the program by The EHE Foundation, Hobart, WI. As a consumer reviewer, she was a full voting member, (along with prominent scientists) at meetings to help determine how the $7.5 million appropriated by Congress for Fiscal Year 2020 will be spent on RCRP research.

Consumer reviewers are asked to represent the collective view of patients by preparing comments on the impact of the research on issues such as diagnosis, treatment, and quality of life. When commenting on serving as a consumer reviewer, Leah said:

> "It is an honor to be a part of such an important program and represent the rare cancer patient voice. It's exciting and humbling to see brilliant minds at work developing innovative ideas that could one day make a huge difference in the lives of rare cancer patients."

The U.S. Congress established the Rare Cancers Research Program in the FY20 Department of Defense appropriation. With this new program, consumer advocates and scientists work together in this unique partnership to evaluate the scientific merit of research applications. COL Sarah B. Goldman, Director of the CDMRP, expressed her appreciation for the consumer advocates' hard work.

> **"Integrating consumer perspectives into our decision-making process brings energy and focus to our research programs. Patients, caregivers, family members, and advocates help us keep our efforts centered around what is truly important to those impacted. We very much value this critical input from our consumers who help ensure that CDMRP's work remains critical and relevant."**

Scientists applying propose to greatly improve outcomes for people with rare cancers through discovery, community building, and expansion of knowledge across the cancer landscape. The RCRP fills important gaps not addressed by other funding agencies by supporting ground-breaking research while encouraging out-of-the-box thinking.

We also want to thank Leah Heinrich for representing the voice of those with rare cancers.

Zebrafish – one more year?

Over the last two years, a small team in Sheffield have been working hard, trying to generate an EHE zebrafish model. A zebrafish model would be a wonderful addition to EHE research as these fish are far cheaper and far quicker to produce, and therefore far lower costs, than mice. However, the project has proved difficult with TAZ-CAMTA1 expression not presenting in endothelial cells. This was surprising as a parallel construct using GFP (green florescent protein) had been successfully introduced.

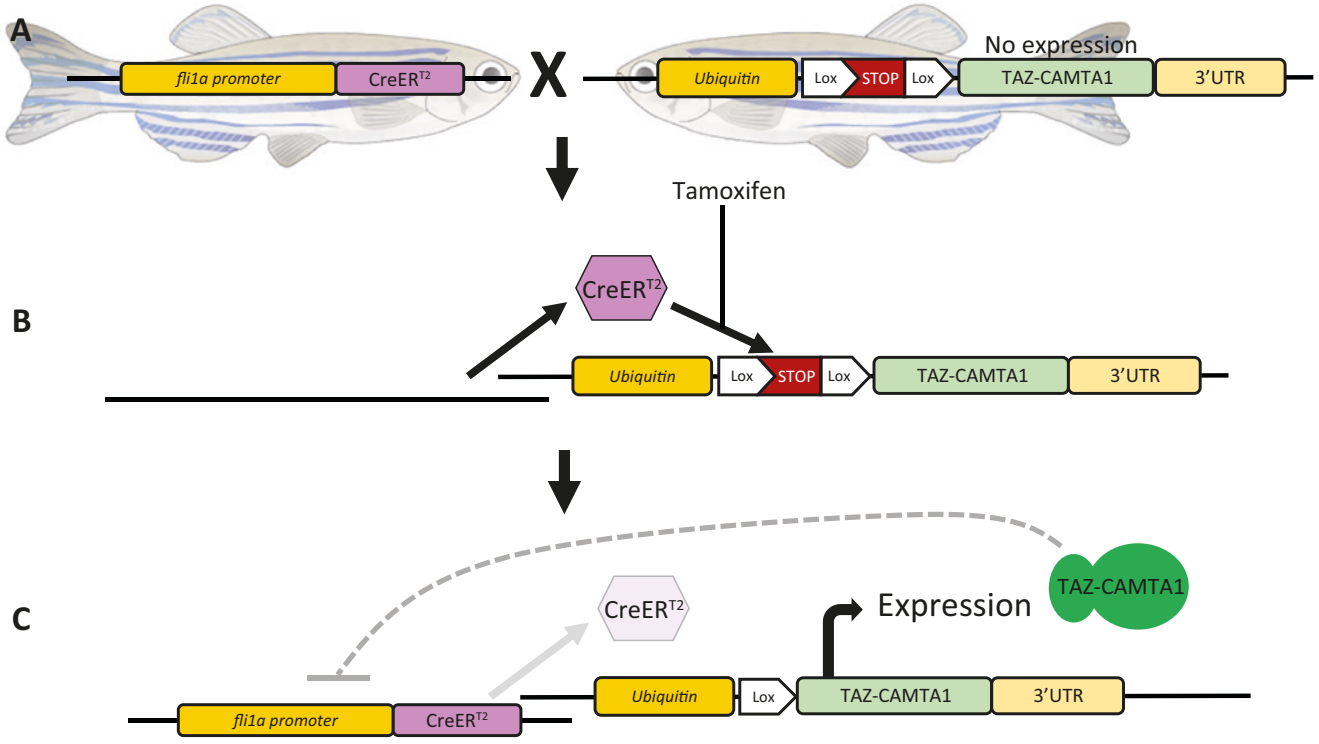
Dr Fredericus van Eeden, the PI for the project, believes that a number of possible causes for this failure to achieve TAZ-CAMTA1 expression can be hypothesised. There could, for example, be sequence elements in the construct that lead to repression of expression. Codon optimisation was used to try and address this issue but does not change the sequence completely and although the team used two different approaches, it may not have "hit" the relevant bases. If the mechanism of this repression can be identified and understood, the team also hope that it might perhaps be therapeutically exploited in EHE tumours in humans. A detailed understanding of this mechanism is therefore warranted. In addition, understanding of the precise reasons may allow us to relieve this repression and gain epithelial expression.

The first approach will be to examine if there are sequence elements in the construct that prevent expression under control of the fli1a promoter that has been used. We will systematically add in parts of the TAZ-CAMTA1 coding sequence, and use these to create a set of destination vectors. These will be used to evaluate whether they allow expression in endothelial regions. As a potentially faster assay/alternative the team plan to use these constructs to transfect coronary artery endothelial cells or HUVECs. In these endothelial cells, expression of GFP can again be used as a readout of expression levels. The researchers have collaborators in Sheffield who have a lot of experience with these cells and so have cell culture facilities available. For example, the team will clone either the TAZ or CAMTA1 part of the oncogene behind GFP and see which of the two may block expression. Once they have found which sequence is responsible for a block, they will further subdivide the sequence to home in on potential sequence elements that prevent expression. If a small inhibitory element can be identified, they will collaborate with their bioinformatics core to identify potential binding of proteins or miRNAs that might be responsible for the suppression of the expression.

Zebrafish (continued)

The second approach has arisen following dialogue with Dr Valerie Kouskoff in Manchester who is also working on EHE. Importantly, Dr Kouskoff found that in embryonic stem cells the TAZ-CAMTA1 expression can lead to downregulation of endothelial markers including fli1 expression (the mammalian equivalent of fli1a). This could therefore explain the negative results as well. In this case, switching to an alternative endothelial promoter (e.g. flt1 or VE-cadherin) is unlikely to solve the problem. To best model the disease, the same promoter should be used as is actively driving TAZ-CAMTA1 in the human condition. It is in all likelihood the TAZ promoter that drives expression. The TAZ promoter has been somewhat characterised in humans and the team have requested this promoter from Dr Kapus. In addition, the team will clone a similar element from the zebrafish and test both of these for driving expression in zebrafish and endothelial cells using GFP initially as a reporter.

Another issue with the use of a TAZ driver is that this will still lead to expression in regions outside the endothelium, as TAZ is rather widely expressed in zebrafish. A parallel and perhaps most important approach will therefore be to combine an appropriate promoter and STOP cassette to the TAZ-CAMTA1 coding sequence, to prevent unwanted expression. The STOP cassette can then be removed, specifically in endothelial cells, and drive expression from this generic promoter at a chosen time, by activation using tamoxifen.



"Figure: Strategy for driving TAZ-CAMTA1 in endothelial cells. Fish containing a fli1a driven CreERT2 and a silenced TAZ-CAMTA1 expression construct are crossed together (A), the resulting larvae containing both constructs express an inactive form of Cre in the endothelial cells -when activated with tamoxifen the Cre will remove the stop cassette (B) and lead to expression of TAZ-CAMTA1 under the control of a constitutive ubiquitin promoter. If subsequent feedback of TAZ-CAMTA1 leads to downregulation of the fli1a promoter activity and CRE production, this is irrelevant, as removal of the stop cassette is permanent (C)."

The third element of this year's work will address the issue faced with previous assays where the team only established that lines were not behaving as expected after creating a line, which takes a significant amount of time (3-4 months). Normally this is fine, because gene expression is not an issue when using well-established promoters like fli1a. However, it is clear from the team's previous attempts that TAZ-CAMTA1 requires more checks. Therefore, they will also do in vitro experiments before progressing with transgenesis in fish. They will establish a cell-culture system to evaluate the constructs they produce in vitro, in endothelial cells. The plan is to transfect human endothelial cells (arterial and venous) with the relevant constructs, and assess mRNA and protein expression levels. In addition, they will also evaluate some of the previously generated controls to check for expression of the relevant proteins. The team will also evaluate endogenous human fli expression with collaborators in Sheffield who have a wealth of experience with human endothelial cells in vitro, and who have cell culture facilities available within the research department. In addition, they will collaborate further with Dr Kouskoff, and will test some crucial constructs in mouse embryonic stem cells, as Dr Kouskoff has extensive experience with expressing this protein and studying its effects on endothelial differentiation.

The final and fourth element of the year's work will be to take the learnings of the above assays, and introduce these to the zebrafish, assuming of course that the results are positive. Only when the team are convinced from their in vivo and in vitro experiments that the construct is working as expected, will they progress and raise transgenic lines. If successful, the team hope that with these lines they will be able to: (i) identify the correct expression pattern; (ii) perform a preliminary phenotypic analysis; (iii) verify that the lines activate the TAZ signalling pathway; and (iv) determine the expression levels of TAZ target genes. If successful they will then establish lines from the best performing transmitters, for further analysis.

We thank Dr Van Eeden and his colleagues for their dedicated and detailed analysis to date, and of course wish them every success for the coming year's work. We are also delighted to see that this project is benefitting from wide collaboration, including with Dr Kouskoff in Manchester and Dr Rubin in Ohio, two other researchers whose EHE research is being funded by the EHE group.

YAP-TFE3 focus

Two mutually exclusive gene fusions define EHE. The TAZ-CAMTA1 fusion affects 85-90% of all EHE patients, while the YAP-TFE3 affects approximately 10-15% of patients. In the last edition of The Pledge, we reported on the successful fundraising campaign being coordinated by Lael Bellamy and Lynne Hechman. They are raising substantial funding for Dr Rubin to help develop a second EHE mouse model, which is focused on the YAP-TFE3 mutation.

While this fundraising initiative is ongoing, focus has now turned to coordinating the patient community and the collection of appropriate information and possible samples. Jane Gutkovich shared the importance for those who have the YAP-TFE3 version of EHE:

> **"Dr Rubin at the Cleveland Clinic is rolling out a large project to study this subtype of EHE. Thanks to the amazing efforts of several members of our community he has funds now to look closer at this rarer version of the disease. He needs your information and, maybe in some cases, tissue. So if you have this EHE subtype, please contact me."**

02 EHE Research

Jane went on to provide further explanation:

> **"Many of you have had either a genetic analysis done or a special staining to diagnose EHE. These tests should in most cases be able to tell the subtype of your EHE. Why is it important? Because it is likely that different drugs may be more effective in different subtypes of EHE. That is what several scientists studying EHE are looking for, and if it is proved to be the case, you will definitely want to know! Current cancer research is all about precise, targeted therapies. We hope that sooner rather than later, we will have effective drugs for each subtype of EHE so that if you ever need treatment, you will be able to get the right drug for you."**

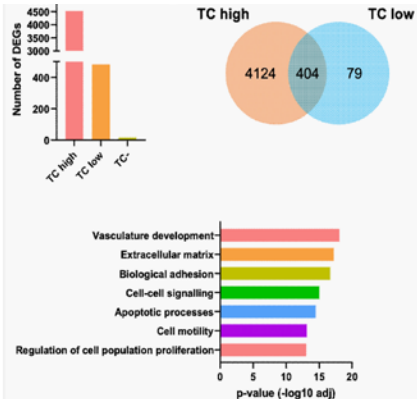
So if you know that you have the YAP -TFE3 subtype, please let Jane know. If you don't know then please ask your oncologist. If your tissue has never been tested, ask them to order an appropriate test. In addition, the NCI MyPART program in the USA (see below) may also be able to provide appropriate genetic testing for those who are eligible.

PhD continues to generate interesting results

The PhD being funded by the EHE Rare Cancer Charity at the University of Manchester is continuing to produce interesting results, and as we hoped, further questions. Last quarter we reported that Emily Neal, the PhD student, was beginning to produce samples for RNA sequencing with the aim of uncovering differences in the transcriptional landscape between endothelial cells with different levels of TAZ-CAMTA1 expression.

The results have identified 404 genes that are differentially expressed when comparing cells with high and low TAZ-CAMTA1 expression, despite the fusion protein only being induced for 24 hours. Gene ontology analysis was used to reveal the biological areas in which gene enrichment had occurred. Significant enrichment was observed in terms relating to angiogenesis (blood vessel development and cell motility), as well as cell proliferation and apoptosis (cell death). Emily is now engaged in further analysis to identify specific genes that are involved, and also to understand how TAZ-CAMTA1 causes such large changes in the transcriptional output of endothelial cells in such a short period of time (see figure 1).

Figure 1. RNA sequencing analysis of TAZ-CAMTA1 expressing endothelial cells. (A) Graph showing the number of significantly differentially expressed genes (DEGs) in TAZ-CAMTA1 high, TAZ-CAMTA1 low and TAZ-CAMTA1 negative populations when compared to uninduced controls. Genes were considered differentially expressed if the fold change was <-1 to 1< and p<0.01. (B) Venn diagram showing the number of significantly differentially expressed genes which are common to TAZ-CAMTA1 high and TAZ-CAMTA1 low populations, when compared to uninduced controls. (C) Graph showing gene ontology (GO) terms enriched for in the significantly differentially expressed genes common to TAZ-CAMTA1 high and TAZ-CAMTA1 low populations, when compared to uninduced controls.



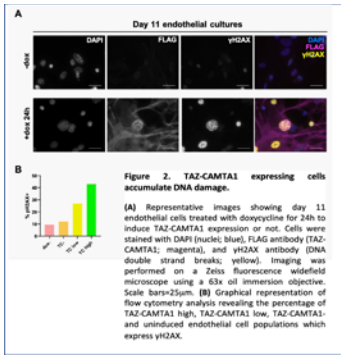
Last quarter we also reported that Emily's research had identified that cells expressing TAZ-CAMTA1 had a significantly larger proportion of cells in the S phase of the cell cycle (where cell DNA is replicated in preparation for cell division) than in the G1/G2 growth phases of the cell cycle, when compared to normal endothelial cells.

This quarter has focused therefore on trying to understand if the TAZ-CAMTA1 cells are proliferating more quickly or are just being arrested in the S phase.

This is done by labelling cells with CellTrace Violet, a dye that stains the cell membrane, the intensity of which halves with each cell division. Using flow cytometry, Emily was able to show that the TAZ-CAMTA1 cells are in fact proliferating at a lower rate when compared to normal cells, and the accumulation of cells in the S Phase is due to them being arrested at this point

Further experiments using a double thymidine block were carried out to analyse the cell cycle expression. In line with previous experiments, TAZ-CAMTA1 expressing cells had a higher proportion of cells in S phase at earlier time points than TAZ-CAMTA1 negative and uninduced cell populations, indicating faster entry into S phase after release from the block. However, at 10 hours post thymidine release, TAZ-CAMTA1 -expressing cells had an increasing number of cells in late S phase, with decreasing G1 and G2 populations. In TAZ-CAMTA1 negative and uninduced populations, the proportion of late S phase cells remained similar or decreased at the 10-hour time point, respectively. This suggests that TAZ-CAMTA1 expressing endothelial cells become arrested in late S phase, whereas TAZ-CAMTA1 negative cells progress through the cell cycle as expected.

Towards the end of the quarter, Emily had begun some experiments to investigate DNA damage in TAZ-CAMTA1 expressing endothelial cells. The presence of DNA damage is known to arrest cells in S and G2 phases of the cell cycle which allows initiation of DNA repair mechanisms and stops mutations from being passed on to daughter cells. Therefore, this could provide a mechanism behind why TAZ-CAMTA1 expressing endothelial cells become blocked in S phase. Phosphorylation of H2AX, a histone H2A family variant, to generate H2AX is an early event in the DNA damage response, and its presence marks sites of DNA double strand breaks. Hence, fluorescence microscopy and flow cytometry techniques were used to determine differences in H2AX expression between endothelial cells expressing TAZ-CAMTA1 or not. Imaging revealed that TAZ-CAMTA1 expressing cells had higher amounts of H2AX than uninduced controls, 24 hours after induction, and that this effect was dose dependent, with TAZ-CAMTA1 high endothelial cells expressing more H2AX than TAZ-CAMTA1 low populations, whereas TAZ-CAMTA1 negative and uninduced populations had similar, lower amounts (see Figure 2). This suggests that TAZ-CAMTA1 expression may result in increased DNA damage, and could explain why TAZ-CAMTA1 expressing cells become arrested in S phase. Further investigation is required to determine if the accumulation of DNA damage is directly mediated by TAZ-CAMTA1 itself, or due to TAZ-CAMTA1 influencing the activity of another pathway. These results are fascinating as they begin to shed further light on the actually biology of EHE cells. Well done Emily for continuing to deliver this important research in an environment that remains restricted by COVID19. We look forward to your next report.



National Cancer Institute's MyPART program

The EHE Foundation (US) is a partner advocacy organization with the MyPART network of NCI's Rare Tumors Initiative, which focuses on accelerating the development of potential new therapies for rare tumors by bringing together patients, clinicians, researchers, and patient advocates. Here's news on several key points:

- The turnaround for genetic testing is now 2-3 weeks! In some cases it might take longer if the tissue sample is too small, but they will significantly expedite the process.
- If you are eligible, you will get a free genetic analysis done in a relatively short period of time.
- This will contribute tremendously to our overall EHE research.

Patients are encouraged to visit the MyPART website for further information:

https://www.cancer.gov/pediatric-adult-rare-tumor/

03 EHE Fundraising

In the fourth quarter of 2020, we were pleased to see some of our wonderful supporters re-engaging in EHE fundraising activities. But that initial progress was quickly extinguished by the reimposition of lock down over many countries. But while the first quarter of 2021 has seen fundraising activity drop off again, we are excited by the plans we see being made for Q2 and beyond. We find the determination of our EHE fundraising warriors inspiring, but as they will tell you, EHE never stops or relaxes, and so they won't either. We hope you enjoy the articles below.

In memory of Leo

Taryn Nicole decided in March that she wanted to fundraise for the EHE Foundation in memory of her husband, Leo Hansen. Taryn explained,

> "For my birthday this year, I'm asking for donations to The EHE Foundation in memory of my husband, Leo Hansen. He battled bravely against this cancer but had we more info perhaps we could have stolen more years for ourselves. I've chosen The EHE Foundation because their mission means a lot to me, and I hope you'll consider contributing as a way to celebrate him with me. Every little bit will help me reach my goal."

Taryn was amazed at the support she got and the wonderfully generous donations that flooded in, including a donation of $2,500 from Leo's company, MBFS.

Taryn's continued support for The EHE Foundation, in memory of Leo, is inspirational. Her love for not just Leo, but for the whole EHE community shines brightly! She stated:

> "This is truly unbelievable and I'm so proud of my husband and his courage as well as all the wonderful people battling EHE and their families. I'm just waking up to the best birthday gift I could ask for...hope for others and a beautiful testament to my husband's reach. I love you all and this is for you Leo Hansen, my love."

Thank you, Taryn, for thinking of those battling EHE during this most difficult time. We are grateful for the generosity of everyone who loved Leo.

Saving the 'shrapnel' for research

Fundraising comes in many shapes and sizes. It's not always about running miles, climbing mountains, or rowing oceans. Equally important are the quiet, far smaller events, that all add up. One idea posted a few years ago was to set up an EHE jar at home in which all your lose change that drives you mad could be collected. We called them Jessie Jars after Jessie Hayman who championed the concept and introduced it throughout her school friends, family, neighbours and anybody else she knew.

Hugh and Sally in Kingston Upon Thames have kept their jar going for over four years now, donating the cash to the charity each time the jar fills up. Sally explained:

> "This is the third time we have filled it and it amazes us each time how much we have collected. There will be well over £100 in loose change, which we've collected by adding a few coins every day for well over a year. It's a great way to save funds because it's the perfect example of how a 'little and often' soon adds up."

In honour of Kristen Leigh

Supporters of EHE patient, Kristen Leigh, have come together to raise money for EHE research while enjoying a little friendly competition as part of the 2021 March Madness NCAA tournament, Participants filled out their brackets, not only for bragging rights and to be titled the 2021 champion, but also to raise money for The EHE Foundation in honor of Kristen. Thanks to this group for finding a creative way to support our mission and fight EHE. For those not familiar with basketball, LeeAnn Conner explained what 'brackets' are:

> "March Madness is college basketball (NCAA), not the professional league (NBA).Brackets are used for people to guess which teams are going to win in each round. It is a pretty common term here and it essentially shows the path basketball teams follow to get to The Final Four and then the championship game. Many people participate in this event and often it is the non-basketball experts who predict the winners."

03 EHE Fundraising

Nicola is preparing to walk!

Almost exactly two years ago, UK EHE patient Nicola Henderson underwent a liver transplant due to her progressive EHE. That was the start of what has been a two-year-long intense psychological and emotional rollercoaster that only organ transplant recipients will be able to comprehend.

But it is not just the transplant process that Nicola has had to contend with. Being a relatively new transplant patient, Nicola was high on the at-risk register for COVID19, with the result that rather than being able to go out and enjoy herself and get her life back on track, Nicola has faced an extended period isolating at home.

But those who know Nicola also know that she is one courageous fighter. So while she of course faced dark days where she did not feel full of life, she has also battled on, spurred on by her fantastic husband and wonderful son.

So we were not surprised when Nicola posted news in late March that she was taking on a new challenge, and at the same time, raising funds for EHE research.

> “I have decided to do a personal challenge and hopefully raise a few ££ for EHE research.
>
> *1st April till 7th May is 37 days. 7th of May 2021 is my 37th birthday. I want to walk 370,000 steps during those 37 days*
>
> It’s only 10,000 a day. Not a huge amount for most people but for me to get up and out and do this every day will be a big deal. Lockdown has been very hard, (as I’m sure so many can relate) a big part of my post-transplant recovery for me should have been ‘living life’ that hasn’t happened in the way I planned and it really set me back. I’ve had enough, I have spent way too long in my house feeling down and low. I feel up to doing this now, I want to get out and about more, I want to get my fitness back and I need the outside world!! I feel a shell of my former self if I’m honest. I need to do something for me and this just feels a good starting point. I know my amazing donor would be cheering me on and I want to do this for them also. 14th April marks 2 years post-transplant. I really am so lucky. Let’s do this! 💪
>
> It would be great if anyone would like to donate a couple of ££ to help fund research into EHE whilst I do this, every little donation helps. Thank you.”

What a fantastic plan, and what great drive and determination. We can totally understand why this is so important to her. Go Nicola, and we are guessing that you may have just one to two friends who may join you as you stride out each day.

https://www.justgiving.com/fundraising/nicola-henderson31

Just Walk and Just Live

London Landmarks Half Marathon is back on!

Last year the EHE Rare Cancer Charity had 52 runners ready to run in the London Landmarks Half Marathon at the end of March. Then after five months of training, the race was cancelled due to COVID19. The EHE team were totally gutted. Hugh Leonard summed it up:

> **"I got back from my final four hour session running and cycling in the gym, only to be told that the race was cancelled. Like everybody else I was just totally deflated. The only good thing was that all of our original 40 places were carried over to 2021."**

The reality is that EHE of course never relents or gives up, and we have to fight it with the same relentless energy and drive. So as soon as the 2021 race was announced the EHE Rare Cancer Charity went out with a call for volunteers.

> **"By August this year the UK will have rolled out a huge amount of COVID vaccine. We will once again be allowed out! The weather will be perfect. The only thing missing from this idyllic picture is a half marathon to run in! But don't be down-hearted. We can help. We have 40 places in the London Landmarks Half Marathon in August. 15 of our brilliant runners from last year's cancelled race are running this year. But we need 25 more. So dust off your running shoes. Get out the shirts and shorts. It will be brilliant."**

Once again we got a wonderful response and soon had filled the 40 places with brilliant runners, in a team called the **EHEAwesome40!** The training is underway, running shirts are being ordered, and fundraising pages are live. We cannot thank everybody who is taking part enough for their wonderful support.

03 EHE Fundraising

Raise the funds - drive the research - find the cure

The EHE Rare Cancer Foundation Australia has launched its latest 10,000 steps challenge to raise funds for EHE research and at the same time help people get fit. The challenge is about promoting the importance of keeping active across the whole day, not just organised sports and events. Jane Biddlecombe, Director of the EHE-RCFA, explained:

> "By signing up to the 10,000 Steps Challenge and incorporating regular physical activity into your daily activities you benefit from increased energy and improved fitness which increases concentration, productivity, self-esteem, and improved sleep. Then there are the benefits you can't see such as strengthening your bones, boosting your immune system all whilst sweating out toxins which boosts oxygen and blood flow. It is also a great way to get out and connect with friends and family, improving those relationships."

Jonathan Granek, a fellow Director, explained how the fundraising will help:

> "For the EHE-RCFA we benefit by your fundraising efforts of which 100% is donated to frontline research, but more important, you help us raise awareness of the EHE Rare Cancer Foundation and the research and advocacy work we do."

We want to thank the 30 individuals and groups who are taking part in the event this year. We wish them every success and hope that they end the month fitter, stronger, and feeling really good about what they have contributed to the fight against EHE.

Birthday gifts of enormous value

Many supporters continue to create and share Facebook Fundraisers to celebrate milestones, such as birthdays, while benefiting The EHE Foundation. These campaigns are often created by patients, family members, friends, or co-workers who share heartfelt stories or photos. These remarkable people are not only supporting our mission monetarily, but creating much needed EHE awareness on social media. We are thankful that Facebook has no fees for donations to non-profits. Thank you to **Olivia Wahl**, **Kelsey Green Williford**, **James Forgione**, **Patricia Ruth Hoover**, **Taryn Nicole**, **Maudi Alvarado-Robles**, **Lisa Broman**, **Heidi Littlefield**, **Icy-Jamie Miller**, **Alexandra Lydy**, **Kathryn Noel**, **Diana Donohoo**, **Andrea Cohen Brenick**, **Tina Martiniello Vert**, **Todd Young**, **Amber Donohoo**, **Cinthia Williams**, **Tomera Sheets**, and **Taylor Muillins**, for raising over $13,000 on Facebook Fundraisers this quarter. We are grateful for your kindness! Olivia Wahl said:

> **“I created a Facebook fundraiser for my birthday to support The EHE Foundation in honor of my sister and others who fight this rare cancer. It was easy to set up and family and friends are always happy to help with such a great cause.” Supporters can create a fundraiser in just a few minutes using this link: ”**

https://www.facebook.com/fund/Ehefoundation/”

04 And in other news...

Photo Therapy

Carl Dickson is a regular contributor to our EHE support group, and this quarter was no different. He posted this photo in January with a slightly different take on having EHE:

"You gotta love cancer! Even at 17 degrees and 8,000ft elevation you stay hot, thank God for little favors."

Photo Therapy

Dr Robinson Ortiz is another regular contributor of support for our EHE community.

"Leave your worries by the shore line,
And run your bare feet through the sand,
Let the water be a soft bed,
When you can longer bear to stand,
Make friends with flying seagulls,
And hold the sun up on your palm,
Take a dive beneath the water,
Where the world is forgiving and calm,
Let the water hold your sadness,
And wash it right out to sea,
So like a message in a bottle,
All your worries are set free."

~ Erin Hanson

The EHE Foundation (USA)
www.fightehe.org

The EHE Rare Cancer Charity (UK)
www.ehercc.org.uk

The EHE Rare Cancer Foundation (Australia)
www.ehefoundation.com.au