

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



Quarterly Newsletter
for the EHE Group
October - December 2020

the pledge

Edition 23



Light Pillar photograph from Carl Dixon

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Welcome

We wish everybody a warm welcome to the 23rd edition of **“The Pledge”**, our quarterly newsletter, covering the final quarter of 2020.

We hope that all our readers were able to enjoy the festive season, and that you all had a great New Year, despite the worldwide pandemic. The extreme situation due to COVID19 continues, although I am sure we all hope that the new vaccines will improve the situation in 2021. While the activities of the EHE Group were again curtailed, we did see a continuation of the growth we saw in all our areas in the third quarter, once again driven by our wonderful supporters.

As always, 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

Major EHE Conference in Europe organised by ESMO

We are delighted to be able to report that ESMO's 'Development of the Consensus and Guidelines for EHE Treatment' conference took place in December. EHE patients were represented by Hugh Leonard from the UK and Medha Deoras Sutliff and Jane Gutkovich from the USA. See our Patient Support and Advocacy Section for more details.

New European EHE research project funded

The EHE Rare Cancer Charity UK is delighted to report that it has concluded agreements for a new collaborative research project to be carried out by Dr Stacchiotti at INT in Milan and Dr Paul Huang at the ICR in London. The project, funded jointly by the EHERCC and The EHE Foundation in the USA, is looking to identify possible cytokine and hormone biomarkers for EHE.

Giving Tuesday campaigns raise substantial funds again!

Giving Tuesday has become a major annual fundraising opportunity in the USA, with their brilliant supporters offering matched funding to increase all sums raised. 2020 was no exception with over \$80,000 raised on the day.

UK Charity reaches out to all UK sarcoma centres

Spreading awareness is sometimes just about reaching out and maintaining contact. In the UK, the EHE Rare Cancer Charity sent its annual report, and a 2021 wall calendar, to every sarcoma unit in the UK.

Anna's 2021 Wall Calendar an amazing success

Anna Wydro's vision was to organise an EHE Wall Calendar that would bring the EHE worldwide community together in its development, raise funds through its sales, and help spread awareness through its distribution. The calendar achieved all those goals with over 700 now hanging on walls around the globe. Amazing!

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

the **pledge** Edition 23



01 Patient Support and Advocacy

Supporting everybody diagnosed with EHE, wherever they may live, 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 of the EHE foundations.

That support and advocacy is largely delivered through the Group's worldwide Facebook page which now connects with over 2,000 people in over 70 countries across the globe, and is provided through the tireless energy and contribution of so many of our members, many of them being EHE patients themselves.

We thank all our supporters who have contributed to this critical part of our activity, examples of which are provided in this section.

Not just a wall calendar

2020 was the year when finally, after lengthy periods of discussion, driven by the enthusiasm of Anna Wydro, the EHE Group finally launched its first ever annual Wall Calendar project. Anna's project team were not sure what the response would be, but need not have worried. Choosing landscape photographs, the call went out to the worldwide community, and over a couple of weeks, the team received hundreds of fantastic photographs from so many contributors. Choosing the final twelve was difficult.

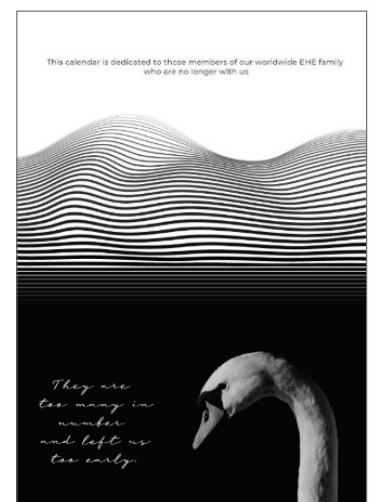
While the calendar was also a fundraising element, it also included sections to spread awareness of the disease, and provide information about the EHE research we are driving. The team also felt it was important that the calendar would recognise all those EHE patients who are no longer with us:

“We will never forget those of our EHE family who are no longer with us. Whatever we do, we do for them, and to defeat EHE.”

Equally important was the desire for the project to bring the EHE community together. As Anna said:

“I was hoping to bring people together with this calendar, and give some hope for a better upcoming year.”

Feedback has been hugely positive, with many asking for this to be an annual initiative. We can safely say that Anna's desire to help create group engagement was very definitely achieved.



Medha is raising awareness of EHE

In early October, Medha Deoras Sutliff, Executive Director of The EHE Foundation, was the subject of a long and informative article in Cancer Today about her professional journey that led from breast cancer, through broader cancer advocacy, to The EHE Foundation. That exposure for The EHE Foundation and for EHE more generally is a wonderful example of how our foundations, and people like Medha, are raising awareness of EHE. We want to congratulate Medha for such a great article, and for all she does in her role to raise awareness. You can read the article here: <https://fightthee.org/ehe-highlighted-in-recent-cancer-today-article/>



EHE in a different type of drama

Tina Biehl Nielander from Denmark shared a photo with subtitles which amazed her.

“WHAT ?! I sat and watched the series ‘Why Women Kill’ (created by Marc Cherry for CBS All Access) and one of the main characters (played by Ginnifer Goodwin) lied and said she had a rare cancer, and as you can see it is one we know well (even though they are Danish subtitles) ... strange!”



Many of our members spotted this and were stunned, but also pleased, to see EHE get such an unusual plug in a mainstream drama. Thank you Marc Cherry, CBS and Ginnifer Goodwin for a little bit more exposure for EHE.



01 Patient Support and Advocacy

Decals and masks

Spreading awareness comes in many shapes and sizes. Summer Keller launched her decal and sticker initiative in October, with EHE bumper stickers and window decals. Summer is helping to raise awareness for her husband, Ryan, and others who are fighting EHE. She said:

“The bigger black and white ones are mostly used for window decal in your car. The smaller stickers are more for a coffee mug, water bottle, school binder, snowboard, skateboard, anything you may want to put a sticker on.”

Summer soon branched out to selling EHE facemasks, which raises awareness while also helping to keep people safe. And Summer also used her campaign to raise funds for EHE research. We love these, Summer! Contact Summer at Rskeller7@hotmail.com if you'd like to place an order.



Wonderful 'Zoom Get Togethers'

Jane Gutkovich has always been passionate about sharing EHE information with the patient community, to help them understand EHE better, be aware of treatment options, and ultimately be as informed as possible. To assist in this, Jane hosts a 'Zoom Get Together' where she shares information in an online meeting about a chosen topic with members, often supported by an expert in the field.



Jane noted:

“Getting the format right has taken time, but a presentation by the specialist, followed by stories from our members, and then discussion within the group appears to be a good structure.”

This quarter Jane coordinated her next 'Zoom Get Together' around IRE ablation, with Dr Govindarajan Narayanan providing the expert's presentation. The group was so grateful for the hour that Dr Narayanan gave to them, and the chance to discuss IRE as a treatment modality for EHE.



Dr Narayanan

Later in the quarter Jane held a further meeting, this time joined by Dr Evan Rosenbaum from the Memorial Sloan Kettering Cancer Centre in New York. Dr Rosenbaum presented and discussed the results of the study that he and his colleagues from MSK conducted on more than 100 EHE patients. The study is so far the largest study analyzing various subsets of EHE and the factors influencing EHE behavior.

Those who attended agreed that the meetings were very informative.

Jane will be communicating with the group in due course regarding her next 'Zoom Get Together'



The meeting organized and hosted
Jane Gutkovich



Guest
Dr. Evan Rosenbaum
Memorial Sloan Kettering
Cancer Center in New York

Reaching out to UK sarcoma centres

One of the key objectives of the UK charity is to promote the work that it and the wider EHE group are doing; to make sure as large a group as possible know the EHERCC exists and is here to support EHE patients. Hugh Leonard, Chair of Trustees, explained:

“A key group who we want to make sure know about us are the clinicians who will almost certainly be the very first people to tell somebody that they have been diagnosed with EHE. In an ideal world, at that very first conversation with a new patient, they would be able to say “but you are not alone. Here is an organisation that is ready to provide information and support if you want to reach out to them.”

To try and maximise the chance of that happening, the EHERCC writes every year to every sarcoma unit in the U.K., to explain what the charity does, and sends them copies of the charity's annual report.

“This year we also sent each of them one of our new 2021 Wall Calendars as a gift, with the suggestion that they hang it in their sarcoma offices to just help bring a little more awareness of this ultra-rare sarcoma. And of course enjoy the brilliant photos!”

Hugh posted a photo of the packages ready to go out to help spread awareness. We love the idea that our calendars may now be hanging in sarcoma units across the UK.



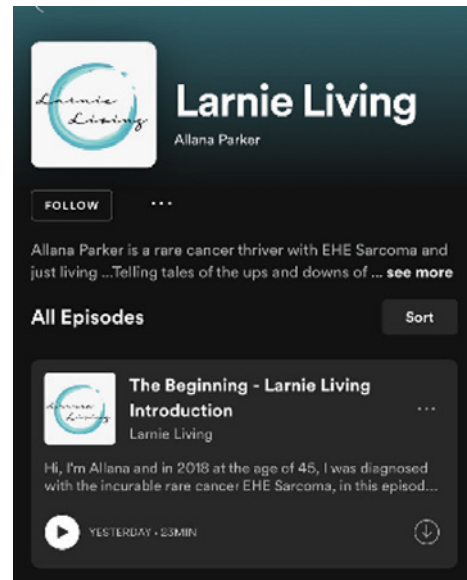
01 Patient Support and Advocacy

New podcast launched

Allana Parker was delighted to share with the group the news of the launch of her new podcast.

“Hi guys, just wanted to share my “happy” with you, I finally got my podcast out and published! The first intro episode is available on Spotify, Podbean and my website and in the next few days on iTunes and audibles.”

Allana is telling her listeners about EHE, and how it has affected her. She will also be talking about the EHE Rare Cancer Charity, the wider EHE community, and many other subjects. We want to congratulate Allana on her new project and look forward to listening to many more episodes.

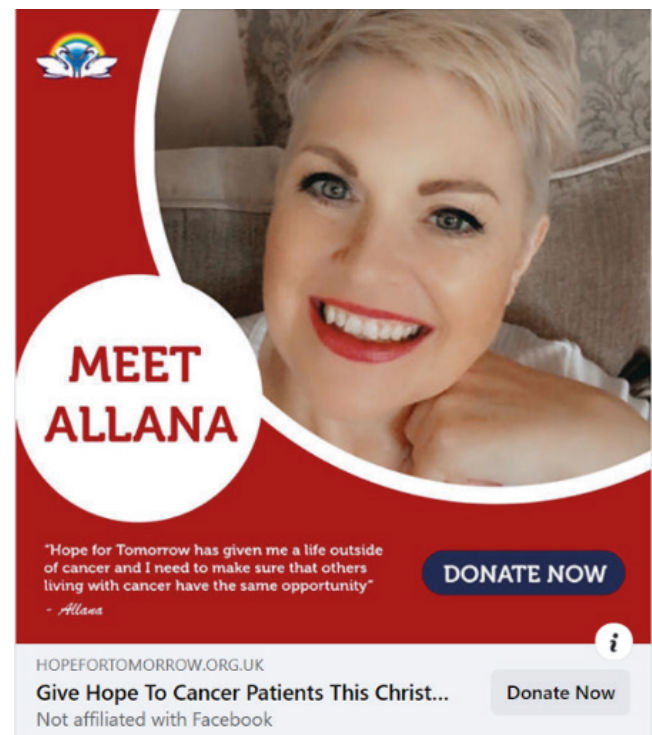


A Christmas campaign

Allana Parker shared a link in December for the Christmas Campaign of the charity Hope for Tomorrow.

“Just wanted to share with you a Christmas campaign I was asked to front this year for ‘Hope for Tomorrow’ who supply mobile cancer treatment units all over the UK. This has also meant the story of EHE has been told to so many more, nationally and possibly internationally. It may not be our own fantastic charity, but Hope for Tomorrow do great work, and I know that awareness of EHE will be greater after the campaign than before, which is great.”

We want to amplify Allana's message. Cancer care and treatment is not just about EHE. So whenever a chance arises where EHERCC and/or our members can help some of these other great charities, we will grab it. And if that also spreads awareness of EHE then that is a fantastic result too. Well done Allana for being such a great poster-girl for cancer care and treatment.



International EHE Conference is on the horizon

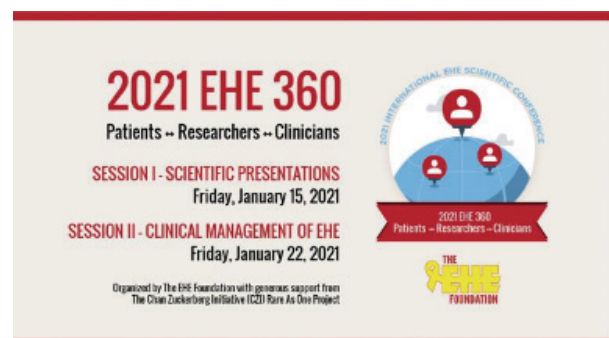
The EHE Foundation continued to publish news through the quarter about January's exciting international EHE scientific conference called "EHE 360". The goal is to create a global, patient-led research network strategically focused on shared research priorities ultimately leading to treatments and cure for EHE! Presentations are mostly targeted to the researchers and clinicians interested in EHE research and patient management, but the global EHE community is welcome to participate and gain a "front row seat" at this ground-breaking event!

Conference recordings will be available to those who are not able to attend this event. To view the recording simply register at <https://fightehe.org/2021-ehe-360>. Registration for both sessions is free and open to the global EHE community. We are grateful for the Chan Zuckerberg Initiative for funding this event.

We look forward to hearing from these amazing speakers, who are taking their time to share their knowledge on EHE.



Denise Adams, MD, Children's Hospital of Philadelphia
 Cristina Antonescu, MD, Memorial Sloan Kettering Cancer Center
 David Casimir, The EHE Foundation
 James Chen, MD, The James, OSU Comprehensive Cancer Center
 Patty Cogswell, Consultant
 Lisa De Young, The EHE Foundation
 Jordan Driskill, UTSW Medical Center
 Professor Robin Jones, The Royal Marsden, UK
 Jenni Kovach, President, The EHE Foundation
 Professor Valerie Kouskoff, The University of Manchester, UK
 Govindarajan Narayanan, MD, Miami Cancer Institute
 John Lamar, PhD, Albany Medical College
 Hugh Leonard, EHE Rare Cancer Charity, UK
 Scott Okuno, MD, Mayo Clinic
 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



02 EHE Research

COVID19 has continued to slow research through the fourth quarter of 2020, but several of our researchers have restarted work in their labs, with projects now once again moving forward. Reports where available are included in this section. But as in the previous two editions, we have again taken the chance to provide an overview of some of the areas of EHE research that the EHE group is helping to deliver.

The previous two quarters focused on the USA and the UK respectively. This quarter, in the last of our regional overviews, we are focusing on EHE projects in Australia.

Progress through the quarter

ESMO (European Society of Medical Oncology) holds major EHE event

At the start of December, Dr Silvia Stacchiotti chaired a virtual ESMO meeting on the *“Development of the Consensus and Guidelines for EHE treatment”*. This is a standard ESMO procedure where disease experts are brought together to discuss all aspects of the disease with a view to agreeing the *“Consensus and Guidelines for EHE Treatment”*. Hugh Leonard from The EHE Rare Cancer Charity in the UK and Medha Deoras Sutliff and Jane Gutkovich from THE EHE Foundation were all invited to attend the meeting as patient representatives.



The 6-hour meeting involved 90 oncologists, surgeons, radiation oncologists, and palliative care specialists, mostly from Europe, but also included guest specialists from the USA, Japan, Canada, and India. The meeting started with a presentation of 4 difficult EHE cases for



multidisciplinary discussion. This was very interesting as different specialists proposed different possible procedures, demonstrating the range of approaches that can be considered.

The EHE Rare Cancer Charity was invited to address the group on behalf of all the EHE foundations, prior to the main Consensus discussion starting. Hugh Leonard initiated the presentation, but due to technical issues had to hand over to Medha Deoras Sutliff to complete the **‘Introduction to the EHE Group’**.

The main body of the meeting, lasting over four hours, followed and consisted of an extraordinarily thorough discussion of all aspects of EHE management including proper diagnosis, prognosis, treatment of EHE in different organs, the role of systemic therapy etc. Doctors developed a preliminary consensus on the proposed clinical approaches. The edited draft will be circulated when ready for final comments, and the final draft will be submitted to the journal “*Annals of Oncology*” for publication.



The last 30 minutes of the meeting were dedicated to an analysis and discussion of the most urgent research projects. People willing to lead and/or collaborate on these projects also made themselves known. The importance of PRO “*patient-reported outcome*” information was recognized as being the most useful in EHE, with doctors pledging to incorporate PRO in their studies.

The EHE Group will be taking this matter forward into the forthcoming **EHE 360 Conference** to be held on 15 and 22 January, where a major goal is to start the development of an global integrated and collaborative research strategy for EHE. As the main EHE-patient-representative organisation, the EHE Group will be looking to play a major role in developing, funding and delivering this global research programme.

Jane Gutkovich shares a new study

Jane Gutkovich was delighted to share a new study with our members in October:

“A relatively new study of EHE (35 patients) confirms again and again that EHE is not one cancer but a spectrum, and that it is very important for pathologists not only to diagnose EHE correctly but to look for certain signs that the disease may be aggressive. Such signs (this study looked at Ki-67) can help doctors to determine the best line of treatment at the time of the diagnosis, enabling early initiation of treatment if required. Ki-67 is a proliferation marker that tells us how many cells (a percentage) are actually dividing in the sample. Very few pathologists perform this test on EHE because they are not aware that it can make a difference.”

We want to thank Jane for her continued vigilance for new EHE studies, and for bringing these to our attention. Here is the link to this study: <https://www.researchsquare.com/article/rs-91622/v1>.

RESEARCH

Clinical Characteristic and Prognosis of Epithelioid Hemangioendothelioma: 35 Cases from Single Center in Recent Decade

> Qiaoqi Li, Ledu Lin, Jielang Li, Xiaojuan Zhou, Yong Xu



02 EHE Research

First European research contract signed

The EHE Rare Cancer Charity and The EHE Foundation were delighted to be able to report that they had completed the signing of their first joint EHE project in Europe. Hugh Leonard explained:

“This is an exciting project as it is the first time we have signed a funding agreement with a European research facility. It is also the first collaborative research project we have supported that involves a collaboration with three different organisations.”

The European entity is The Istituto Nazionale dei Tumori (INT) in Milan, Italy, who will be collaborating with The Institute of Cancer Research (ICR) in London, UK. The third entity is Memorial Sloan Kettering (MSK) in New York, USA. The EHE funding is for INT and the ICR only, as the MSK work is being funded by a private donation in the USA.

The project has PIs in all three locations. In Milan there are joint PIs: Dr Silvia Stacchiotti and Dr Nadia Zaffaroni. Dr Paul Huang is the PI for the project at the ICR, while Dr William Tap will be the PI at MSK.

The project, ‘**The evaluation of cytokines and hormones as biomarkers for EHE**’ has two key objectives:

1. To assess i) the profiles of circulating cytokines, hormones (and miRNAs), and ii) the ER α , Er β and GPER expression and the YAP/TAZ activation in tumour tissues, as a function of the clinical course of the disease. To this end the analysis will be conducted on the whole study patient population compared to healthy controls, and by stratifying EHE patients who will enter the study in 3 subgroups according to disease behaviour (non-growing disease, slow- growing disease, highly aggressive disease with evidence of pleural effusion and systemic symptoms); and
2. To identify and validate novel biomarkers to inform patient management (prognosticators and predictors of response to medical agents) as well as potential therapeutic targets.

The EHE Group is thrilled to have three such prestigious institutions engaged in this important research. We look forward to providing further updates in future editions of The Pledge.



FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI



The Institute of
Cancer Research



Memorial Sloan Kettering
Cancer Center

Manchester PhD making good progress

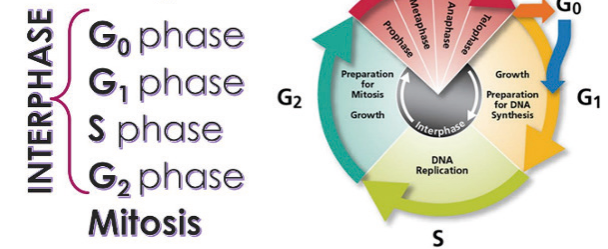
2020 was a tough year for our researchers, with university laboratories completely shut down early in the year and then reopened but with restricted access through a large part of the rest of the year. Despite this, Emily Neil who is undertaking the EHE research PhD at the University of Manchester in Dr Valerie Kouskoff's laboratory, has been able to make good progress through the last quarter of the year.

Emily's PhD is seeking to show how EHE affects endothelial cells, and in particular to determine how TAZ-CAMTA1 activity and expression is regulated in endothelial cells.

During the fourth quarter Emily was focused on three different approaches:

1. The first approach is to evaluate the transcriptomics of different endothelial cells. Transcriptomics is the identification of genes, using RNA sequencing, which are produced during the transcription process in cells. This analysis was undertaken by inducing TAZ-CAMTA1 in endothelial cells. The cells were then separated into four different groups of cells with different levels of TAZ-CAMTA1 expression. These are: (i) uninduced cells; (ii) cells with no TAZ-CAMTA1 expression; (iii) cells with low TAZ-CAMTA1 expression, and (iv) cells with high TAZ-CAMTA1. RNA sequencing will be used to identify the genes produced, and the resultant differences for the four different groups of cells will be used to begin to understand what biological processes within the cell are altered as a result of TAZ-CAMTA1 expression. This final RNA sequencing is planned for the start of 2021.
2. The second approach is to use cell cycle analysis, as naturally-occurring TAZ is known to be involved in the cell cycle. The cell cycle is the name for the process by which our cells grow and proliferate, with different phases of the cycle given different names. The S phase is the part of the cycle where the genetic material in the nucleus replicates in preparation for cell division which occurs in the M phase, while the G1/G2 phases relate to cell growth periods. The G0 phase is a sort of 'holding pen' where cells are held until they are ready to move on to the S phase. M phase is where the cells divide to produce two identical cells.
3. The third approach involves seeing, in cells that are exposed to external mechanical stimuli, whether TAZ-CAMTA1 localisation and/or expression is affected. This is of interest as it is known that normally occurring (wild-type) TAZ is affected by such stimuli. This is also an interesting point because the mechanics within tumour tissue are quite different to surrounding non-tumour tissues.

Cell Cycle



The objective of this part of the research was to see if TAZ-CAMTA1 affects the cell cycle. By analysing endothelial cells where TAZ-CAMTA1 was induced, and then stained and analysed using flow cytometry, the number of cells in the different phases could be seen for different levels of TAZ-CAMTA1 expression. Early results have shown that cells with TAZ-CAMTA1 have a higher proportion in the S phase than cells with no TAZ-CAMTA1, but a corresponding lower proportion in the G0/G1 phase. There was however no obvious differences in the proportions in the G2/M phases between all cell types. This suggests that TAZ-CAMTA1 expression increases the ability of cells to enter the S phase of the cell cycle. The question remains as to whether this leads to greater cell proliferation, or whether the cells remain arrested in the S phase, something that may be indicated by the lack of difference in cell proportions in the G2/M phases. Emily will be undertaking further research to try and answer these questions.



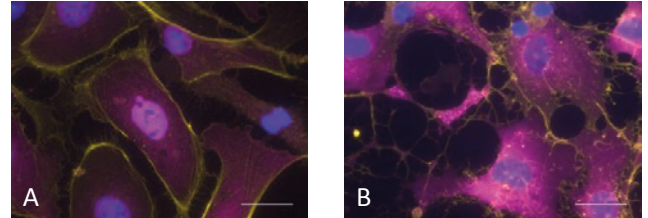
02 EHE Research

The experiment took endothelial cells, induced TAZ-CAMTA1, and then introduced three different inhibitors of three proteins that are known to communicate mechanical stimuli to wild-type TAZ. The inhibitors used in these experiments are altering the internal cell cytoskeleton, so the current approach isn't actually altering the mechanics of the environment directly, but is blocking the effect that such mechanical stimuli might have on the target cells. The effect of these three inhibitors was then investigated by analysing where TAZ-CAMTA1 appeared in the endothelial cells.

Early results showed that these inhibitors did have an effect on TAZ-CAMTA1 expression. In one case the inhibitor appears to have reduced the overall number of cells expressing TAZ-CAMTA1, while the other two inhibitors did not reduce the overall number of cells expressing TAZ-CAMTA1, but did appear to reduce the level of TAZ-CAMTA1 expression in those cells.

Finally, fluorescence microscopy techniques were used to visualise where TAZ-CAMTA1 is situated within the endothelial cells. This revealed that TAZ-CAMTA1 was predominantly located in the nucleus of uninhibited endothelial cells. The addition of each of the inhibitors however increased TAZ-CAMTA1 presence within the cell cytoplasm, but did not completely remove it from the nuclei (see Fig 1). Taken together, this provides preliminary evidence that mechanical stimuli may have a role in TAZ-CAMTA1 regulation, resulting in its degradation and relocation into the cytoplasm.

Fig 1



Slide A shows endothelial control cells expressing TAZ-CAMTA1 but with no inhibitor treatment. The pink/purple areas show the location of TAZ-CAMTA1, almost exclusively in cell nuclei.

Slide B shows endothelial cells treated with inhibitor (blebbistatin). Again the pink/purple areas show the location of TAZ-CAMTA1 which is now predominantly present in the cell cytoplasm, but with some presence remaining in the nuclei.

All three of the approaches taken are delivering very interesting results about TAZ-CAMTA1 and its effects on the biology of endothelial cells. These of course are preliminary results, with further experiments required and planned to understand exactly what the implications are to endothelial cells, and therefore EHE disease and ways we may treat the disease.

We want to congratulate Emily Neal for the excellent progress made, in very difficult circumstances, and look forward to seeing further exciting results in due course.

Exciting times ahead with Dr Lamar's project

Dr Lamar's laboratory have established two cell lines that stably express TAZ-CAMTA1, one using NIH3T3 cells and a second using HEK-293 cells. The team then confirmed that their reporter assay used in the lab can accurately measure changes in TAZ-CAMTA1-dependent transcriptional activity in these cells, demonstrating that this assay can be used as a means to identify and study regulators of TAZ-CAMTA1. Dr Lamar's team have also developed two assays for TAZ-CAMTA1-dependent tumorigenesis. In combination, these models can be used to identify and test potential regulators of TAZ-CAMTA1.

Using these models, Dr Lamar was able to test several candidate genes that they hypothesized would repress TAZ-CAMTA1 activity and function, and identified six genes (AMPK α 1, AMPK α 2, GSK3 β , PTPN14, GSN, and CFL1) that did indeed impair the transcriptional activity of TAZ-CAMTA1. Subsequent studies have focused on AMPK α 1, AMPK α 2, and GSK3 β where ongoing experiments, using the assays described above, are testing if expression of these proteins can impair the expression of TAZ-CAMTA1 regulated genes and tumorigenic function using cell lines that stably express AMPK α 1, AMPK α 2 or GSK3 β .

The team have already shown that treating cells with a small molecule compound known to activate AMPK can repress TAZ-CAMTA1 activity in NIH3T3 cells, but this effect is not as dramatic as overexpression of AMPK; a fact that they are now trying to understand.

Related experiments have shown that in NIH3T3 cells if AMPK is inhibited with a different small molecule inhibitor, this dramatically increases TAZ-CAMTA1 activity,

demonstrating that in these cells the existing AMPK pathway is functioning to repress TAZ-CAMTA1 activity, and suggests that if they could find a way to increase the activity of AMPK further, it may repress TAZ-CAMTA1 even more. Dr Lamar is also testing if activation of proteins upstream of AMPK can also repress TAZ-CAMTA1. By understanding the critical component(s) of this pathway, the team hopes to identify potential proteins that can be exploited therapeutically.

Very recently, through their collaboration with Dr Brian Rubin, the team have also acquired ascites fluid from Dr Rubin's EHE mouse model. This fluid contains EHE cells on which they are beginning to test different approaches to purify and isolate these cells with the hope of generating an EHE cell line. The team will also be seeing if AMPK can repress TAZ-CAMTA1 function in these cells.

Dr Lamar was also excited to report that they have now generated all the tools they need to begin testing some of their candidate proteins in their tumor models in mice. These are the exciting experiments which have just begun, and where preliminary results are expected within 6-10 weeks.

This is another extraordinarily exciting research project where the team are delivering exciting results well ahead of the schedule we had anticipated. We want to congratulate Dr Lamar's team, including Ryan Kanai who has been instrumental in delivering all aspects of the research, and look forward to those exciting results in the near future.



02 EHE Research

Jane Gutkovich takes on new role

The EHE Foundation were thrilled to announce the news that one of the group's fearless founding leaders, Jane Gutkovich, would be stepping away as Research Director but moving to a position as The Foundation's first Board Member Emeritus! In this prestigious role, Jane will work strategically with The Foundation to continue to do what she does best – supporting patients worldwide and recruiting researchers to EHE. Jane was not only one of the founding members of The EHE Foundation, but has also given the last six years of her life to moving research forward. Without Jane's determination and commitment, EHE research would not be where it is today. Thank you, Jane, for your unwavering commitment to the EHE global community! Please keep going!

You can still engage with Jane on the EHE Facebook page, and through Jane's ongoing programme of Zoom Get Togethers detailed in our Patient Support and Advocacy section of this edition of The Pledge.



Overview of projects that the EHE Group has contributed to

The EHE Group continues to support and engage with EHE research in the USA, Canada, the UK and Australia. Here we have provided a summary of the main projects in Australia that the group has been supporting. We hope you find these project summaries informative and inspiring as our engagement and participation has only been possible due to the wonderful support we have received from many of you.

International Sarcoma Kindred Study (ISKS)



The ISKS enables rare sarcoma communities, like EHE, to study genomic risks relevant to their cancer type. Importantly, this one-of-a-kind resource is available for researchers across the globe. But it can only deliver meaningful data and results if patients participate.

To help encourage everybody in the EHE family, Prof David Thomas (Director of the Kinghorn Cancer Centre, Head of Genomic Cancer Medicine at the Garvan Institute of Medical Research, and advisor to the EHE Rare Cancer Foundation Australia) provided us with an EHE-dedicated message for all EHE patients.

“My name is David Thomas... I’m writing to make you aware of the International Sarcoma Kindred Study (ISKS), which aims to create a genetic database for all sarcomas, including EHE. All patients with sarcomas are welcome to participate in ISKS, and participation is free.

I encourage you to sign up to the ISKS, so we can create a unique EHE genetic database for answering questions about why EHE happens to some people and not others, and to open up new ways to better manage EHE. Research of this kind is essential to improving the lives of those affected by EHE.

Contributing to the study is easy. The EHE Foundations worldwide are committed to signing up as many EHE patients to the ISKS as possible, and your participation and support is key. Please join the study if you can, and be part of the search for answers to EHE.”

We are delighted to report that 47 EHE patients from across the globe have already enrolled and provided samples (blood or hair follicles) to support this invaluable study. With the first 20 EHE patient samples having already undergone Whole Genome Sequencing (WGS), the balance is to soon follow during Q1 2021 thanks to funding support from the EHE Rare Cancer Foundation Australia.



David Thomas

The EHE Group wants to endorse Prof Thomas’s message that the participation of EHE patients is key to enabling and progressing important research, and again showing that the EHE community is worth engaging with. So please register your interest in ISKS now by contacting isks@garvan.org.au.



02 EHE Research

Overview of projects that the EHE Group has contributed to (continued)

Australian IRE ablation study moving forward

This study is being led by Dr Helen Kavnoudias, Research Director of the Radiology Department at The Alfred in Melbourne, Australia. IRE (NanoKnife) has been successfully used to treat EHE liver tumours, but only in a small number of cases. It is not widely accepted as a treatment modality for EHE because it has been used in so few cases, a classic challenge for ultra-rare diseases like EHE.

The intent of the study is to bring together interventional radiologists from across the globe to collate retrospective and prospective cases, analyse and present facts about IRE ablation and how it works for EHE. The study team hope that the findings will scientifically validate the benefits in EHE patients and lead to its acceptance as a key treatment option. The study group already has support from some of the most experienced radiologists who have been actively using IRE with EHE, including Dr Govindarajan Narayanan (Dr Raj), Professor of Radiology and Chief of Interventional Oncology at the Miami Cancer Institute.

The study team will be reaching out in the near future to all EHE patients who have undergone or will soon be undergoing IRE to tell them how they can get involved. We hope that you will all consider taking part as the group is small and so every person's data will be important to the study's success. The first step is for participants to express their interest and leave contact details - <https://redcap.link/Oadxq45k>.

International Collaboration Gaining a Better Understanding of EHE

In a powerhouse of collaborative effort, Prof Kieran Harvey's lab (at Australia's Peter MacCallum Cancer Centre) together with the Anne-Claude Gingras lab (at Canada's Mt Sinai Hospital) and Munir Tanas' lab (at USA's University of Iowa) have been studying EHE's TAZ-CAMTA1 and YAP-TFE3 fusion proteins and how they lead to and influence cancer progression in EHE.

Using transduced cell lines and xenografts (mouse models), data from their study indicates that the

cancer causing properties of the EHE fusion proteins can be explained by their nuclear enrichment, dysregulation of the upstream Hippo pathway, and interaction with key transcriptional regulatory proteins.

In further studies, they identified YEATS2 and ZZZ3, components of the Ada2a-containing histone acetyltransferase (ATAC) complex, as key interactors, indicating the histone acetyltransferase complex is an oncogenic driver in EHE and representing a unifying therapeutic target for EHE.

We look forward to other exciting developments to come out of this group over the coming years.

WEHI Stafford Fox Rare Cancer Research Program's EHE Study (WEHI-EHE)

EHE research under the leadership of rare cancer expert Prof Clare Scott, Prof Tony Papenfuss and Senior Research Fellow Dr Holly Barker is starting to take shape. The study is open to EHE patients throughout Australia and involves:

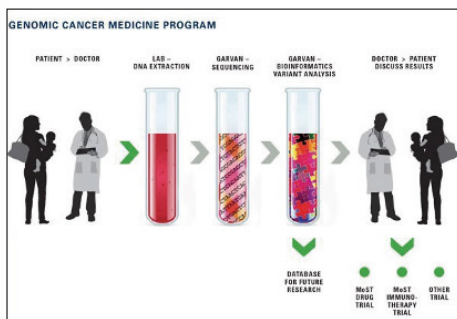
- Collection of patient data;
- Biobanking (archival blocks, fresh tissue, blood, etc);
- Development of pre-clinical research models (cell lines, organoids, patient-derived xenografts); and
- Identification of novel EHE treatment options.

In 2018, WEHI saw the first of its EHE patient enrolments, data collection and specimen collection from a patient's surgical procedure.

Please contact the EHE Rare Cancer Foundation Australia (EHE-RCFA) (info@ehfoundation.com.au) if you have any queries regarding this study, wish to participate, or to notify us of a recent/upcoming surgical procedure. For upcoming surgical procedures, please provide as much notice as possible.

Australia's Innovative Molecular Screening and Therapeutics (MoST) Program

Precision Oncology and Sarcoma expert Prof David Thomas and his team have developed MoST, an innovative program that uses the power of genomic technology to characterise molecular changes in a patient's cancer to help to identify a targeted therapy and evaluate the effectiveness of new treatments in patients with high-mortality cancers like EHE.



In the MoST program, tumour samples from patients undergo comprehensive genomic/molecular screening.

Patients may then be assigned to clinical sub-studies of targeted therapies based on their specific genetic variations. The MoST program looks to understand how targeted therapies work and find new biomarkers that can predict which patients will benefit from these treatments.

The MoST program is also conducting clinical studies to test novel immunotherapy drugs in patients with high-mortality cancers like EHE. Several biomarkers have been suggested to predict response to treatment with immunotherapies, including the presence and change of certain immune cells in the tumour and blood, patterns of immune-related gene expression, proteins released by immune cells, inhibitory proteins displayed on tumour cells, genetic changes in tumour cells and inherited genetic changes in immune genes.



So far 21 Australian EHE patients have been enrolled in the MoST program (which is projected to have 40-50 EHE patients by 2023). There have been 4 EHE patients enrolled to date on MoST sub-studies including (2) double immunotherapy and (2) eribulin. The EHE Rare Cancer Foundation Australia enjoys maintaining contact with these patients and wishes them well with their treatment.

For all Australian EHE patients interested in learning more or enrolling, please contact most@garvan.org.au or phone (02) 9355 5874.

Treatments and Outcomes Case Series (TOCS) Questionnaire

The Treatments and Outcomes Cases Series (TOCS) Questionnaire is an EHE Rare Cancer Foundation Australia (EHE-RCFA) joint-venture study under the leadership of sarcoma expert Prof David Thomas and developed with former Oncology Fellow Dr Rajiv Shinde. It involves a 15-minute online questionnaire for patients from across the globe to complete. The study aims to:

- Provide insights into patient demographics, disease presentation, progression, treatments and outcomes;
- Identify hospitals / institutions / professionals with expertise in various aspects of care;
- Contribute to a growing international body of knowledge to support patients, clinicians and researchers now and into the future; and
- Identify priority areas for new research.

EHE-RCFA directors Jane Biddlecombe and Jonathan Granek with input from the UK and USA based foundations and Prof David Thomas, developed the list of key questions for the TOCS study. We look forward to reporting on further development and launch of this study in the near future.



03 EHE Fundraising

We are continuing to work with all our wonderful supporters to get EHE fundraising activities back up and running after the COVID shock through the middle of the year. The support has once again been inspiring, with stories from the fourth quarter included below.

In addition, and because this year is the 5th anniversary Year for The Rare Cancer Foundation Australia, we wanted to celebrate The EHE RCFA's birthday by reminding ourselves of some of their fundraising events over those five years. We hope you enjoy this brief trip down our fundraising memory lane!

Donna and Amy raise over £500

October saw two of Allana Parkers fantastic support network, Donna Watson and Amy Mills, complete their fundraising event for the EHE Rare Cancer Charity. Donna explained:

“ Last year was alcohol free for 1 month, and I raised £235! We would love to beat this. This year we are exercising before or after work for 31 consecutive days, biking, walking or running for 2 miles a day, a pretty big challenge for us as we haven't exercised for months.”

So in early November, Allana was thrilled to be able to report how well her friends had done:

“ I'm so so happy, my friends have finished their October challenge and have managed to raise £502 for EHERCC, topping the £235 they raised last October. I'm a very lucky person to have wonderful friends like these 🥰💖.”

We want to thank Donna and Amy too for such a brilliant effort. Well done indeed, ladies. You are both awesome.



5th Annual EHE Fun Run and Walk continues

The EHE Foundation's 5th Annual EHE Fun Run and Walk was extended over the whole year of 2020, due to the pandemic. Many EHE supporters in the US continued completing their virtual events during the fourth quarter. As The EHE Foundation plans for the 2021 Fun Run and Walk, there are still many sizes available in the 2020 version. They are great shirts to wear for EHE awareness! Register here: <https://fightthee.org/product/5th-annual-ehe-fun-run-and-walk/>

Kelly Kley shared news of their walk and said:

“ Today we walk. We walk for EHE research. We walk for EHE exposure. We walk for a cure. We walk to take out this horrible disease. We walk for hope. We walk for one we love and one we lost”

Taryn Nicole posted a photo of friends who had joined them to support the campaign and said:

“ We are so happy we can spread the word of EHE awareness!! Thanks to our family for taking this walk/run with us!”



03 EHE Fundraising

2021 Wall Calendar is a great success

Our 2021 Wall Calendar initiative was started by Anna Wydro, to bring the EHE community together, but to also raise funds for EHE research. Using 12 photographs submitted by members of our worldwide EHE community, the final calendar looked spectacular. Perhaps that is why so many people wanted copies. We were able to produce 4 versions: the EHRCC and EHE Group versions both in English, plus an Italian version and a German version.

A total of 730 calendars were produced and distributed worldwide, including the UK, USA, Canada, Australia, Italy, Germany, Portugal, Finland, Poland, Greece, Ireland, Holland, Estonia, Hungary, and Belgium. Funds raised for EHE research totalled over £6,300 or US\$8,500. Everybody agreed it was a great success. We thank and congratulate Anna on a great campaign, and Artur Rozwalak who, with Anna, provided the photographic and artistic input that made the calendars so special.

February



Mary-Ann Farrington lives in Tavistock in Devon. She has three children; Jamie, Emily and Natasha. She is supporting EHE research as one of her oldest friends was diagnosed with the disease.

This photo was taken at the Four Winds in Merrivale in the Dartmoor National Park.

"This is a popular meeting spot on Dartmoor, with lots of ponies and foals sheltering under trees. Walking on Dartmoor makes me happy and alive and helps me forget all the challenges that life can throw at us. I spend hours exploring Dartmoor, just me, my dog and my camera."

August



Artur Rozwalak has always had a passion for photography and travel. However, having developed aggressive EHE in his knee in the early stages of his illness, Artur underwent an above-the-knee amputation because so little is known about this disease and how to treat it.

Diagnosed in 2016, Artur and his partner Anna, continue to advocate for research, and to increase awareness of this rare disease. This photo was taken at Loch Lomond in Scotland.

October



Benjamin Palmer lives in Paignton, in Devon. He learnt about EHE when Nicola, a friend he has known from age 6, was diagnosed with the disease in 2014.

"My image is from Man Sands Beach, Brixham South Devon, and was taken in August. In the morning, especially at sunrise, when this image was taken, the beach is tranquil with only the sounds of the waves and birds, for company, a place I am drawn too for its peace."

@benjaminpalmerphotography

September



João Silva lives in Semide, a small village near Coimbra, in Portugal. His best friend, Mariana, from 7th grade, was diagnosed with EHE in 2016 which was a huge shock. João, who suffers from depression, and Mariana became even closer providing each other with love and support.

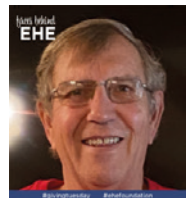
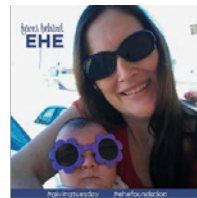
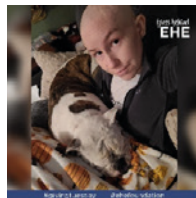
"The photo was taken in Odeixe, Algarve. Like many photos about nature, it gives me joy to know that our planet is a precious gem and that it's quite a gift to live in it."

Giving Tuesday raises substantial research funding in the USA

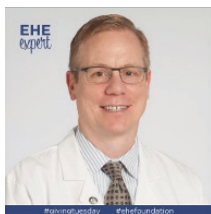
Over the last few years, Giving Tuesday has become The EHE Foundation's biggest annual fundraising event. Giving Tuesday is a global movement to celebrate and encourage giving after Thanksgiving, Black Friday, and Cyber Monday. The EHE Foundation once again secured fantastic matching promises and raised a tremendous amount of awareness for EHE. Doubling of funds of \$35K were guaranteed, while in some cases funds could be as much as quadrupled (by Facebook and possible employee matches).



As always, The EHE Foundation created imaginative and exciting graphics to support their campaign.



These included their wonderful 'Faces Behind EHE' and 'EHE Experts' posters. Thanks to Amanda Roach, Amit Tandon, Sandy Meaders, and the families of Kari Kewish and Rosemary Kalair above for sharing their touching stories.



Many thanks to our EHE Experts, (left to right: Dr Brian Rubin from the Cleveland Clinic; Dr Scott Okuno from the Mayo Clinic; and Dr Denise Adams from Boston Children's Hospital).

We want to congratulate everybody at The EHE Foundation and all the Faces and Experts, for yet another extraordinary Giving Tuesday campaign that raised over \$87,000 for EHE research, a truly staggering result in the current difficult environment created by the COVID19 pandemic. This amount does not include any Facebook matching, which will be announced in 2021.

But most of all we want to thank every single person who raised funds, by whatever means, to deliver these stunning results. **THANK YOU!!**



03 EHE Fundraising

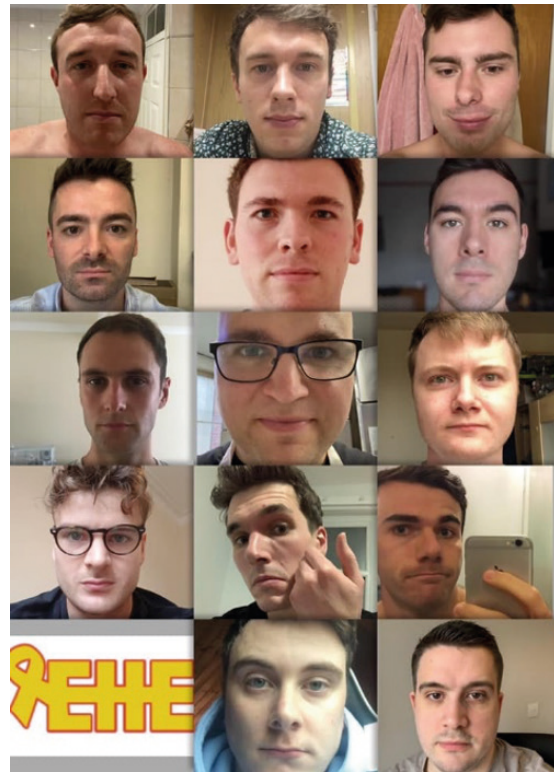
A surprise for a mother

Tracey Betts shared news at the start of November of a huge surprise, when without telling her, her son Conor and thirteen of his friends launched their campaign to grow moustaches through November in support of Tracey and EHE research. Conor explained:

“2020 has been a difficult year and has recently become more difficult when my mum, Tracey, was diagnosed with Epithelioid Haemangioendothelioma (EHE). Because of this, my friends and I will be participating in Movember this year. However, instead of the donations going to a Prostate or Testicular cancer charity organisations, we have collectively agreed to donate all proceedings to EHERCC.

So please help my friends and I as we participate in Movember a little differently this year, by raising money and awareness for EHE. And a special thank you to all that are taking part with me: @Sam Wills; Adam Seddon; Matt Willis; @Matthew Rumble, @Adam Griffin, @Alex Griffiths, @Josh Bolton, Matthew Thorpe, Ryan Woodward, Jordan Naylor, Tyler Lewis, Lloyd Price, and Michael O’connor”

Conor and his friends, with donations and gift aid, raised a staggering £3,031. That was doubled to over £6,000 with our Giving Tuesday matched funding that included their campaign. Thank you so much guys! And for everybody, here are the before and after photos, demonstrating how good a moustache is as part of a disguise!



Don't forget Amazon Smile

Many of us use online shopping sites like Amazon Smile. These sites simply provide a portal through which you can shop online. They do not change the price of the good you buy, but a small percentage of the total price is then donated to the charity of your choice. It is probably the closest we will ever get to free money, so please use these sites as often as you can. Other sites are also available. Instructions to enroll with these sites can be obtained from any of the EHE foundations.



Funding for a new mouse

Two mutually exclusive gene fusions define EHE. The TAZ-CAMTA1 fusion affects 85-90% of all EHE patients, while the YAP1-TFE3 affects approximately 10-15% patients.

Following Dr Rubin's success in creating his genetically-engineered mouse model for TAZ-CAMTA1 driven EHE, interest has grown in creating a second mouse for the alternative YAP1-TFE3 driven variant of EHE. Lael Bellamy, whose son Foster has the YAP1-TFE3 variant, was happy to be able to update the group with news of their progress. She said:

“While we're sharing successes, Lynne Heckman and I have been fundraising for Dr. Rubin and the Cleveland Clinic to create a genetically engineered mouse for the YAP-TFE3 variation of EHE. Many of these are small donations, and we appreciate the support of the EHE Foundations around the world as well.”

If you wish to support this great cause, and help fund the “YAP1-TFE3” genetically-engineered mouse model, go to: <https://give.ccf.org/Mouse>

We want to congratulate Lael and Lynne for their great progress on this important subject. Let's give TAZ-CAMTA1 mouse a cousin!!

give.ccf.org

Cleveland Clinic
The Power of Every One

Thank you for making an impact with your gift to Cleveland Clinic.

Fundraiser
Lael Bellamy & Lynne Heckman Rabinowitz

\$82,060 Raised \$200,000

Foster's Mouse
Thank you for supporting ultra rare cancer research. Developing a mouse model is critical to curing EHE (YAP-TFE3), which is caused by one gene. YAP is essential to tumor growth in other cancers, and this mouse could be the key.

DONATE



03 EHE Fundraising

More great support in Canada

Fiona Ross again wants to stress the benefit of our EHE members sharing their stories, and the potential help that could come from unexpected sources. She is excited to share five examples from this quarter alone:

“A reminder that where possible share your story. Most people really want to help. I have been doing local bottle drives with great results. This expanded to the staff at several local schools and then to a person who had a barn full of empties. One run today with a friend was over \$200.

Another local family, the Boltons, recycle bottles and old electronics and donate to charity. The last few months they have picked EHE/ Sarcoma as the chosen charity. I met them this Saturday to pick up an amazing cheque for \$1500. I have to admit that I was a little teary eyed behind my mask.

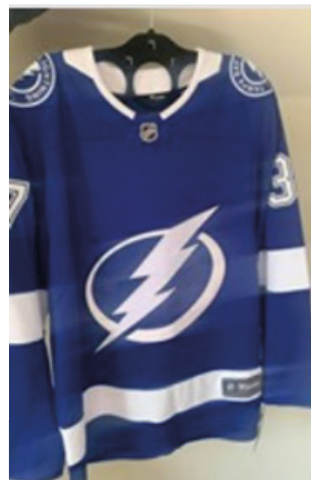
Thanks to a generous Canadian donor we were able to auction a “personalized, signed, authorized NHL Jersey for #37 Yanni Gourde of the Tampa Bay Lightning. That shirt helped us raise another \$450.

Another friend made two pairs of gorgeous thrummed mittens and sold them for \$200 which she donated to me.

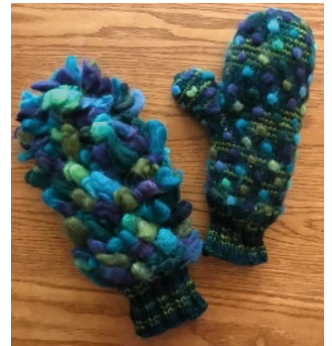
Authors have also donated signed versions of their books to sell as I worked in a school library. So even before I add the calendars all these things have added up to over \$1000. Canadian calendar sales will add another \$2000 plus.

So share your story, you never know who will step up to help.”

We think Fiona Ross's examples are ample proof of how generous people will be, and how much they want to help. We just need to make sure they know about our stories.

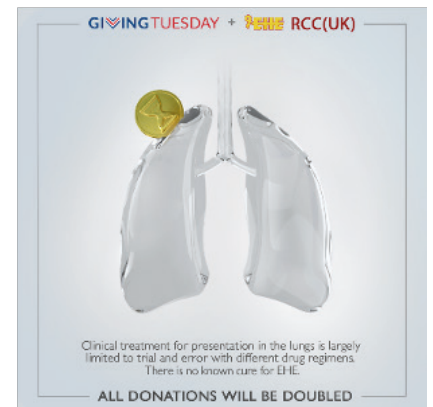
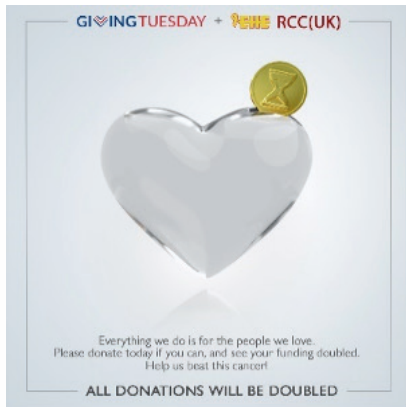


32AUCTIONS.COM
Hockey Jersey for EHE Sarcoma
Silent auction 'Hockey Jersey for EHE Sarcoma'
hosted online at 32auctions.



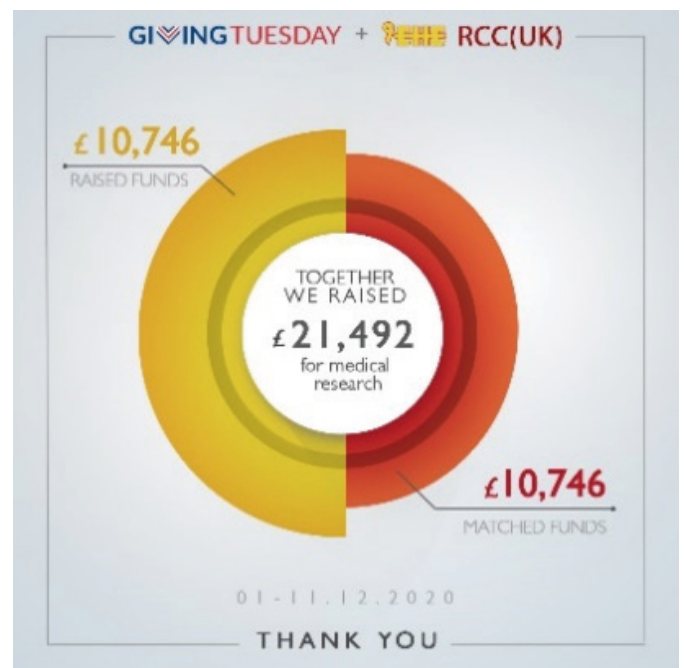
UK Matched Funding campaign raises over £20,000

2020 was a tough year for charitable organisations across the globe, and the UK was no different. So the EHERCC were delighted when, at the end of November, a kind benefactor offered to match all donations made to the EHERCC in the UK around Giving Tuesday. The offer was capped at £10,000. The EHERCC immediately brought this wonderful offer to the attention of the whole EHE group, asking for all donations that people could spare.



With the back drop of the pandemic, the charity was still unsure of what support it would receive. Recognising the difficulties faced, the donor generously agreed that other fundraising efforts ongoing at the time could be aggregated into the total. That generous offer, coupled with the usual brilliant support from so many of their regular supporters, meant that the target of £10,000 was exceeded, with a total of £10,746 raised. With the matched donations, the total sum raised for EHE research was £21,492.

We congratulate the EHERCC for this great result, but we also want to express our sincere thanks to the matching donor, and to all our members and their supporters who helped reach this amazing total.



03 EHE Fundraising

EHE Circle of Friends Monthly Giving Program Kicks Off!

The life blood of any foundation or charity is the donations that it receives. These come in many types, but a common message is that the most important are the regular repeat-giving donations. These can provide a foundation with regular and reliable funding, making planning and support for its activities much more manageable. The EHE Foundation launched its **Circle of Friends Monthly Giving** initiative in October with information for possible donors.



“ We invite you to join our Circle of Friends! With so much uncertainty around us, your consistent support means more than ever. Why a monthly giving campaign?

🕒 **It's Sustained Support:** Monthly gifts allow us to predict our donations and plan ahead by expanding research and strengthen The EHE Foundation.

👥 **It's a Community:** Becoming an EHE Circle of Friends member allows you to join a dedicated group of supporters who understand the importance of making a sustaining commitment for EHE research.

☕ **It's Affordable:** By giving monthly, you invest in our mission based on what makes sense for you and make an incredible impact over the course of your membership.

💪 **It's Powerful:** You'll be recognized on our virtual “EHE Circle of Friends” donor wall coming soon on our website. This demonstrates to researchers, potential grantees, and outside agencies that we have a strong community of supporters standing behind The EHE Foundation's mission.”

As always with our wonderful members, support arrived quickly. AnnMarie McConnell (pictured with her husband, Brian, and sister, Marcey) are just one example:

“ I support The EHE Foundation because we want to see a cure of this rare cancer. Even today, many people (even doctors) do not know about EHE. My sister, Marcey Flood, passed away from EHE in June 2020. Marcey was my husband’s sister, but she was also my sister because we never considered each other sisters-in-law. Marcey loved her family and her faith more than anything. She always put everyone else ahead of herself, and she loved teaching her pre-school kids. We turned to the EHE Foundation when my sister told us about it. It has helped our family in dealing with everything. We will continue to fight EHE in memory of Marcey and for the entire EHE community from around the world who have supported us along the way.”



Bryan Hansen is another to see the benefits and join the Circle of Friends:

“ I give to the EHE Foundation for a few reasons. Firstly, because a very special person in my life became afflicted and made me aware of EHE. Secondly, rare cancers do not get the publicity and thus the funding that many other cancers do and I want to contribute to increased awareness. And lastly, because God has blessed me with some discretionary income that I wish to share.

Everyone to whom much was given, of him much will be required...”



Thanks to those who signed up as monthly, quarterly, or annual donors. All donors’ names will be on the “EHE Circle of Friends” wall of giving on the foundation’s website. Join the EHE Circle of Friends today at <https://fightehe.org/donate-now/>.



03 EHE Fundraising

And now for those fundraising memories!

2015

Australia got its fundraising up and running almost immediately, starting with simple concepts such as **static collection boxes** to be placed in public venues



2016

Australia launched its first fundraising cocktail reception in Darwin, organised by **Jane Biddlecombe, EHE patient and Director of the EHE Rare Cancer Foundation Australia**. Jane took the chance to talk about EHE to all the guests, and explain how difficult living and battling with such a rare cancer is. There was a fantastic turn out, great support, dancing and laughter, and of course some serious fund raising.



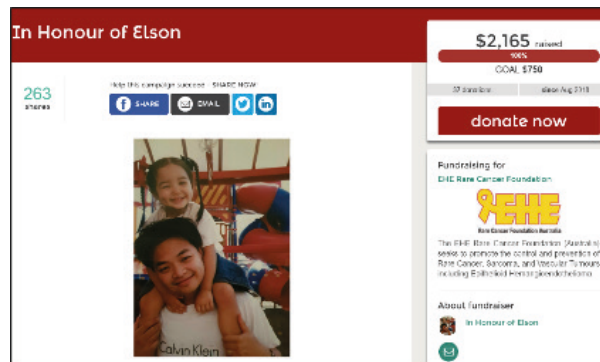
2017

The EHE Rare Cancer Charity Australia launched its **10,000 steps campaign** in October. By registering, participants were sent a pedometer funded through a generous grant from the **Darwin City Council**. The challenge? To walk 10,000 steps a day for a month, get fit, and raise funds for EHE research in the process.



2018

Eden Woolard posted news in August that she would be running the 2018 City to Bay Fun Run on 16th September in honour and memory of her father **Elson** who lost his battle to EHE in the previous April. Eden wanted to do this to raise awareness of EHE, **raise funds for the EHE-RCFA**, but most of all for her Dad.



2019

Australia were delighted to be able to run their **'tin-rattle' collection**, held over a two-hour period as the crowd arrived for an evening **Aussie-rules football match** at the **Melbourne Cricket Ground stadium**.



04 And in other news...

Just Live personified

Our EHE Group motto and motif, **Just Live**, which you can see at the bottom of every page of The Pledge, is dear to our hearts. So we love it when members post photos of how they are ensuring that they do indeed **Just Live!**

This quarter we loved a post from Veronica Flores in Miami, Florida, which most definitely complied with the Just Live spirit. As Veronica put it:

“Enjoying our private pool before I have my 2nd IRE mañana.”

Thanks for the great photo Veronica, and we hope the procedure went well.



A new arrival

Periodically, members of our group post news of a new arrival in their families. Such positive stories are always welcomed with joy and enthusiasm, congratulations and best wishes. This quarter we were delighted to see Bill Desjardins post the news, with this stunning photo, that they had received an early Christmas blessing with the arrival of their first grandchild, Connor William Desjardins. This is indeed a very special blessing. What a truly wonderful Christmas gift for the whole Desjardins family. We send all of you our congratulations, hugs and love at such a special time.



Photo therapy

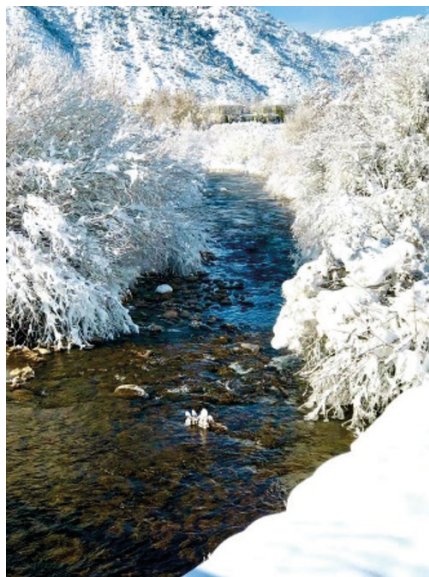
This quarter, as readers will have seen above, photographs have played a big role in bringing the EHE community together in our worldwide 2021 Wall Calendar initiative. But every quarter we publish some of the great photos sent in by our members to inspire us all. This quarter is no different, so here is the Q4 gallery:

We are always delighted when we get posts and photographs from countries that appear less frequently on our EHE Facebook page or in editions of The Pledge. We were thrilled therefore to get such a post from Anne Pitkänen from Finland, with a Christmas message for the EHE community worldwide. Anne's message simply said.

“Merry Christmas! This year has been totally full of sadness but at the same time full of life and hope ❤️.”



Carl Dixon posted this image.
“A little more of the beauty of snow”

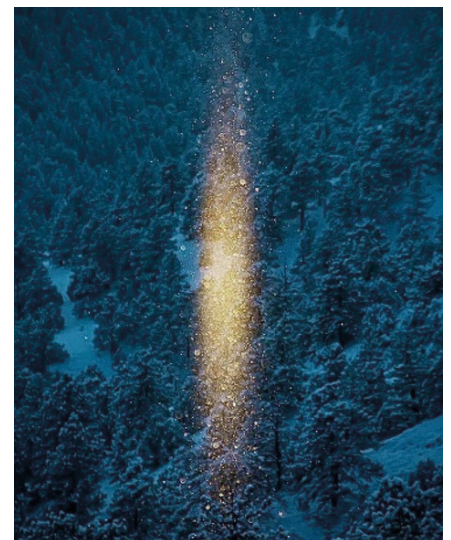


Carl also wanted to share some humour, so we could not resist including this photo of Carl in his Christmas present from Elizabeth...a giant pink fluffy rabbit suit. Just brilliant. ***Just Live!***



...and this photo of a sun pillar.
Carl explained:

“A light pillar is an atmospheric optical phenomenon in which a vertical beam of light appears to extend above and/or below a light source. The effect is created by the reflection of light from tiny ice crystals that are suspended in the atmosphere or that comprise high-altitude clouds, isn't nature entertaining? There is so much to watch for and live for in this world. *Just Live!*”





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