



RESEARCH BULLETIN



*An update on Epilepsy Ireland's activities
in supporting Irish epilepsy research*

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ABOUT EPILEPSY AND EPILEPSY IRELAND

Epilepsy is a neurological disorder characterised by a tendency to have recurring seizures.

Over 45,000 in Ireland have epilepsy including 10,000–15,000 people who are living with uncontrolled seizures. For this group in particular, the consequences of epilepsy can be long-lasting and significant.

It can affect the person's education, employment, social functioning, self-esteem, and independent living. People with epilepsy must also cope with the physical impact of seizures, the side-effects of medications and for many, the social stigma and economic impact that can be associated with it. The individualised impact on those who live with it means that it is often considered as a hidden disability.

There is also an increased risk of mortality associated with epilepsy with an estimated 130 epilepsy-related deaths in Ireland each year.

Epilepsy Ireland's vision is to achieve a society where no person's life is limited by epilepsy.

Since 1966, we have remained committed to working for, and meeting the needs of everyone with epilepsy in Ireland, their families, and carers.

As per our Strategic plan 2022 – 2026, our key aims are as follows:

- To empower people with epilepsy through support and education.
- To centre people with epilepsy and their families in the work of Epilepsy Ireland.
- To work collaboratively to improve the care of people with epilepsy and

knowledge of the condition.

- To transform perceptions of epilepsy and public policy relevant to the condition.
- To increase and diversify our income streams.
- To demonstrate the highest standards of governance and ensure structures are in place to meet objectives.

To learn more about all of Epilepsy Ireland's work or if you require information or support, visit our website www.epilepsy.ie for more information.

If you would like to make a vital donation to help continue this all this work, scan the QR code below.



FOREWORD



A Chara,

It is a great pleasure to be providing the foreword to our latest research bulletin to supporters of Epilepsy Ireland's research activities.

2023 was a significant year as we surpassed the €1.5 million mark in total investment in epilepsy-related research projects since we launched our Research Funding Scheme in 2009. This is a considerable investment for an organisation of our size; and an investment that would not be possible without your continued support.

This edition of our research bulletin will provide details of the new project which brought us above the €1.5 million mark;

share details of a project which aims to help improve the care and collaboration of people with epilepsy and their General Practitioners; and you will also find updates on some of our ongoing projects and hear directly from researchers on their progress to date.

I hope you will enjoy reading this latest update and take pleasure in the fact that you have helped to support everything you read about – projects which will ultimately take us closer to our overall vision of a society where no person's life is limited by epilepsy.

Should you wish to discuss any of our research activities further or have any questions or comments, please do not hesitate to contact me by emailing pmurphy@epilepsy.ie.

Thank you once again, and with your continued support, we look forward to hitting our next milestone of €2 million total investment in Irish epilepsy research in the not-too-distant future!

Peter Murphy
Chief Executive Officer,
Epilepsy Ireland

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RESEARCH TO ASSESS AND DEVELOP HEALTH INFORMATION AND EDUCATION RESOURCES FOR WOMEN WITH EPILEPSY FROM PRECONCEPTION TO POSTPARTUM



With an investment of €15,000 over two years, this vital new research project brought us above the €1.5mill total investment mark. The project began in 2023.

This project is being led by Dr. Aisling Walsh of the Department of Public Health and Epidemiology at the Royal College of Surgeons Ireland. Dr. Walsh will be supported by an extensive research team, all with expertise in supporting women with epilepsy – both in a research and clinical setting.

In Ireland, approximately 25% of all people with epilepsy are women of childbearing age. Although most women with epilepsy can expect normal pregnancy outcomes, reproductive choices are complex.

To date, no study has examined the health information needs of women with epilepsy and their families from preconception through to postpartum in Ireland. This new study will change that.

This study will identify and co-develop prioritised evidence-based resources to support women and health professionals during this period.

The researchers will firstly identify existing national and international evidence-informed resources. Secondly, they will explore the health information, education, and resource needs of women with epilepsy in Ireland, from the perspective of women,

families, and health professionals, through in-depth interviews.

Thirdly, they will undertake a consensus building real-time Delphi study to prioritise and plan health information and education resources. The Delphi technique is a well-established approach to answering a research question through the identification of a consensus view across subject experts. It allows for reflection among participants, who can nuance and reconsider their opinion based on the anonymised opinions of others.

Finally, researchers will co-design and co-produce health educational resources to support women with epilepsy and health professionals. Professionals will use these resources to complement their services from primary care to specialist epilepsy care and across maternity settings.

The study is funded by the Health Research board under the Applied Partnership Awards 2022 and will see a €174,609 investment across 2 years, of which €15,000 is provided by Epilepsy Ireland. Co-funding of €15,000 is also provided by the HSE's National Women and Infants Health Programme.

We believe the study has the potential to make a huge impact on the future care of women with epilepsy in Ireland, who are planning pregnancies in the future. The potential long-lasting legacy of this work would not have been possible without your support.

EPILEPSY RESEARCH MATTERS – A SPECIAL EVENT WITH FUTURENEURO



Our Training and Quality Manager, Edal Curran, expertly MCing at our event in May.

While directly investing in epilepsy-related research is the priority of our research activities, an equally important part of our activities is communicating and increasing understanding of epilepsy research both amongst the wider epilepsy community and the public.

During National Epilepsy Week in May, the theme of which was *Epilepsy Matters*, we collaborated with our colleagues in FutureNeuro to host a special in-person event focused on epilepsy research entitled “*Epilepsy Research Matters – a showcase of Irish Epilepsy Research!*” FutureNeuro is the Science Foundation Ireland Research Centre for Chronic and Rare Neurological Diseases.

The event featured leading scientists, clinicians and researchers investigating epilepsy in Ireland and highlighted some of the incredible research that is underway to drive new discoveries in epilepsy. This included Dr. Peter Widdess Walsh, Consultant Neurologist, discussing breakthroughs and developments in the treatment of epilepsy; Professors David Henshall and Gianpiero Cavalleri, Director and Deputy Director at FutureNeuro, speaking on FutureNeuro’s breakthroughs on epilepsy genomic diagnostics and e-health; as well as a panel discussion featuring a range of stakeholders from

within the epilepsy community (including those with lived experience) on what their personal priorities were for epilepsy research in the future.

As well as this, the event also featured talks from researchers working on projects that Epilepsy Ireland has invested in – the projects you have helped to make possible via your continued support of our research activities.

With a full theatre (on a very sunny Friday evening in May!), we were delighted with the response the event received, and to receive feedback from the entire epilepsy community on what they feel are the priorities for epilepsy research in the future.

While direct investment in research related projects is paramount, events like this mean that people impacted by epilepsy can stay informed about all the ongoing efforts in Ireland and around the world to lessen the burden of the condition. We’d also like to thank our colleagues in FutureNeuro for their support in organising this fantastic event, something we hope to replicate in the future!

If you’d like to watch the event back, you can do so by visiting our website.

▶▶ <https://bit.ly/ERMEI>

REDUCING RISK AND ENHANCING CARE BY DEVELOPING AN IRISH CONSULTATION GUIDE FOR PEOPLE WITH EPILEPSY AND FAMILY PHYSICIANS

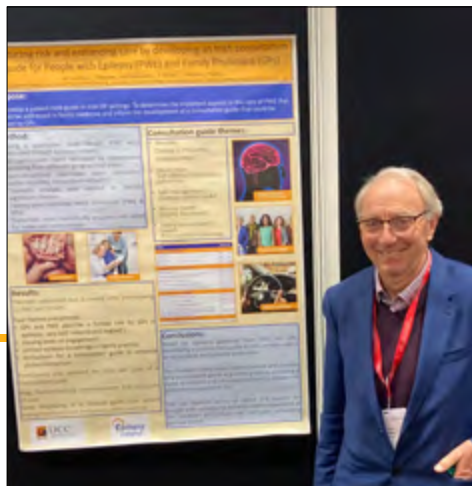
Since 2020, Epilepsy Ireland has been working with University College Cork as part of a continuing research project aiming to improve care and collaboration between people with epilepsy and their family General Practitioners. The project was funded under the Sláintecare Integration Fund.

For many people with epilepsy in Ireland, their GP will be their first port of call for all their medical needs. However, when a long-term condition such as epilepsy is involved, there can be a reliance on specialist care. One of Sláintecare's key goals is to bring care closer to the community wherever possible and this project was specifically focussed on this theme.

This project aimed to understand both the perspective of people with epilepsy on how they utilise their GP; and the perspective of GPs on how they treat people with epilepsy in order to gain a greater understanding of where care could potentially be improved and reduce pressure on specialist services.

As part of the research, 21 interviews were conducted with 11 people with epilepsy and 10 General Practitioners. Through these interviews, several themes emerged. These included:

- GPs and people with epilepsy described a limited role for GPs in epilepsy care.
- There were varying levels of engagement from people with epilepsy and their GP,



Prof. Henry Smithson presenting this research at the International Epilepsy Congress.

and vice versa.

- Limited epilepsy knowledge was cited as being a challenge for GPs working in family practices.

Alongside the themes above, there was enthusiasm expressed by people and GPs alike to develop a patient-held consultation guide for people with epilepsy, to help them with discussions about their condition with their GP; and to increase GPs awareness of other aspects of a person's condition in relation to their epilepsy.

As a result of this research, a guide was developed – as well as a video resource to aid GPs increase their knowledge of epilepsy. The research was presented (poster and digital presentations) at the 35th International Epilepsy Congress in Dublin this year.

If you would like to view the guide, you can do so by visiting our website below:

▶▶ <https://bit.ly/EIGPGuide>

Researchers and collaborators on this project are continuing their work, with the aim of enhancing the care of people with epilepsy alongside their GP.

INTERNATIONAL EPILEPSY CONGRESS

In September, we were delighted to have Ireland as the focus of the international epilepsy community with the International Epilepsy Congress taking place in Dublin.

Over 3,000 healthcare, scientific and research professionals from across the world were in attendance to share expertise, knowledge, and research developments with their colleagues.

Epilepsy Ireland were delighted to play a leading role in the Congress, by working with our colleagues in the International Bureau for Epilepsy (IBE) and the International League Against Epilepsy (ILAE) to organise the first-ever public sessions at the Congress.

Historically, the Congress was for scientific and medical professionals exclusively, but our events brought the event directly to people with epilepsy and their families. With close to 400 people attending across our two-night event, and approximately 300 tuning in online each night, it is fair to say that the event was welcomed by the entire epilepsy community.

The public events featured the latest international research developments throughout the two nights, and featured some of the leading minds from across the globe who are researching epilepsy. Topics included Climate Change and Epilepsy; the Genetics of Epilepsy; and what we have learned about the use of medical cannabis to treat epilepsy; amongst much more.

We are proud to have hosted these innovative public events and we hope that they will become a fixture of the congress as it moves around the world in the years ahead.



Dr. Stephen Klaus speaking to international delegates about the research you helped make possible!

We would like to thank all our speakers who took the time to take part in these events; all those who attended; and our colleagues in the IBE & ILAE for making these events possible. We wanted to highlight this historic event to supporters of our research activities as you may be interested in watching the recordings of the events and learning more about global developments in epilepsy care and research. You can do just that by visiting our website below:

▶▶ <https://bit.ly/IEC23Dub>

As part of the main congress, we were also delighted to have EI-supported projects featured in digital and in-person poster presentations. Prof. Henry Smithson presented the current findings on our project featured on page 6, Dr. Stephen Klaus presented some of his findings from his project on the impact of driving restrictions, and Dr. Yvonne Langan also presented some of her findings on her study surrounding epilepsy mortality in Ireland to international delegates – bringing research you have supported to an international audience!

UPDATES ON CONTINUING PROJECTS

While we have featured one new research investment in this edition, it is important to remember that your support is helping to continue a number of ongoing projects. On these pages, we have featured ****some**** of those with updates from the researchers working on them.

Remember, all the projects we have invested in with your support are featured within the 'Research' section of www.epilepsy.ie so please visit the site if you'd like to remind yourself about all the projects you are helping to support!

Circadian biomarkers in pre-clinical and clinical Dravet Syndrome

2022 – 2024; investment of €32,509 over 2 years

Dravet syndrome is a very difficult to treat epilepsy syndrome characterized by seizures that start in the first years of life. People with this condition commonly present nocturnal seizures, sleep problems and high risk of sudden unexpected death in epilepsy (SUDEP) that most commonly happens at night.

This may be associated with circadian rhythms. The circadian system acts as an internal clock synchronizing many functions in our bodies, setting their rhythms. Despite the evidence, the precise mechanisms of the disruption of the circadian system in Dravet Syndrome are poorly understood. Moreover, we still do not have any biomarkers to predict the risk of developing severe sleep disturbances, nocturnal seizures or SUDEP.

Dr Radharani Benvenuti and her supervisor Dr Cristina Reschke, from the RCSI University of Medicine and Health Sciences and the FutureNeuro Research Centre, are focusing

on understanding the molecular clock in Dravet Syndrome. They believe that this is the first step to develop new biomarkers that could, in the future, be used to predict who could be high risk of developing severe circadian-related traits.

Pre-clinical findings from this research have shown that indeed the internal clock is disrupted in different stages of Dravet Syndrome. Currently, Dr Benvenuti and Dr Reschke are working to deeply characterise and understand the circadian patterns in people with Dravet syndrome using multiple clinical assessment tools.

This research may shine a light on possible signatures and biomarkers related to sleep disturbances, circadian seizure occurrence and SUDEP risk, which would be of great value for people with Dravet Syndrome, their carers and for the broader scientific community.

miR-CDD: Molecular mechanisms, therapeutic targets and biomarkers for CDKL5

2022 – 2026; investment of €36,000 over 4 years

CDKL5 deficiency disorder (CDD) is a rare developmental and epileptic encephalopathy with infantile-onset epilepsy (before 3 months of age). Most individuals with CDD develop refractory epilepsy with multiple seizure types, severe neurodevelopmental impairment and profound lifelong disability.

Despite some benefit from existing interventions such as the ketogenic diet and vagal nerve stimulation, there is no disease-modifying treatment available for CDD.

This research aims to uncover the underlying cause of CDD, the associated molecular biomarkers and therapeutic targets and then

test whether we can target these molecules to identify new therapeutic strategies to treat CDD.

To date, the study has found that there is a significant dysregulation of microRNA and protein expression in the CDKL5 mouse model which may be causing the extreme characteristics of the disorder.

Researcher Erva Ghani explains:

"With no treatment available, this is a novel approach to target the dysfunctional gene expression in cells in order to correct the damage already done by the lack of a functional CDKL5 protein. Since beginning our research, we have identified the characteristics and molecular signatures

in a CDKL5 mouse model by conducting behaviour tests for memory, hyperactivity, anxiety, and motor activity. We have also found potential targets and pathways which will be investigated in the next year in the hope that these may prevent seizures and positively affect the behaviour of our model. This research will advance our understanding of CDD and potentially enable the development and testing of treatments capable of substantially changing the disease course in young children with CDD. This would not have been possible without the support of everyone who contributes to Epilepsy Ireland's fundraising. Thank you for your support."

Predicting and monitoring outcomes in Autoimmune Encephalitis (POTA)

2022 – 2025; total investment of €149,924 over three years via HRB-HRCI joint funding scheme

Autoimmune encephalitis (AE) is an inflammatory disease of the brain. This means that the body's own immune system attacks the brain, just like it would if it were attacking a virus or a bacteria, by producing an army of proteins called 'antibodies' which 'attack' healthy tissues, often leading to seizures.

Treatment involves medications which suppress the immune system, rather than traditional anti-seizure medications. However, even after treatment, some people with AE continue to experience effects from their disease such as fatigue, memory problems and even long-term epilepsy. It is difficult at present to accurately predict who this will happen to.

Dr Mark Kelly, who is part of the research team, explains the goals of the study:

"We want to identify what drives these long-term effects and identify the people at greatest risk of them so we can design better treatments. We are particularly focusing on the symptoms that people with encephalitis and their friends or family have told us are most troublesome to them.

"With collaborators at the University of Oxford, we have collected clinical information and samples of blood and spinal fluid from dozens of people with autoimmune encephalitis. From these samples, we can isolate the antibodies which cause this condition, and at the FutureNeuro Research Centre in RCSI, we are studying the seizure-producing effects of these antibodies and investigating how they contribute to the long-term symptoms of the illness".

IN CONVERSATION WITH PROF. GARY BRENNAN

For this edition of our Research Bulletin, we sat down with Prof. Gary Brennan to discuss EI-funded research on the role of long non-coding RNAs in epilepsy. This research began in 2022 and is set to complete in 2025. In this conversation, Prof Brennan provides an update on his work so far. . .

First of all, what are RNAs, and how does RNA differ from DNA?

The DNA in each of our brain cells provides instructions on how to produce RNA and this RNA is used to produce proteins. Proteins are thought to be the main controllers of how our cells behave. However much of the RNA produced by our DNA does not contain information for proteins and we call this RNA non-coding RNA. There are different types of non-coding RNAs, some are short and some are long. While we understand the function of many of the short non-coding RNAs, the function of the long non-coding RNAs are less clear.

So, could these long non-coding RNAs be involved in epilepsy?

There are thought to be over 80,000 different long non-coding RNAs which suggests that at least some of them may be important for brain function.

Recent studies have identified that long non-coding RNAs may regulate important steps of RNA production and are involved in many brain diseases and cancers. Whether long non-coding RNAs are important in epilepsy is unknown, and that's what we're trying to understand in this study.

What does the study hope to achieve?

Firstly, we want to profile the amounts and changes in long non-coding RNAs in epilepsy. Secondly, we want to test whether targeting the long non-coding RNAs which are altered in epilepsy using specialised



drugs can restore their normal function and influence seizure development and progression. This is the first study of its kind in epilepsy and could potentially reveal new therapeutic strategies for the prevention or treatment of epilepsy.

What progress have you made over the past year or so?

We have analysed the abundance of all long non-coding RNAs which are disrupted during epilepsy development. We have used computer-based analyses to identify the disrupted long non-coding RNAs which are most relevant in human brain and which are most likely linked with epilepsy. We have identified several hundred epilepsy-related long non-coding RNAs and selected the top targets. We then designed drugs which can be used to block the activity of these long non-coding RNA targets.

What happens next?

We are now testing whether using these new drugs we have designed can alter seizure development or progression in pre-clinical models of the disease. We will also identify how these long-non-coding RNAs of interest may contribute to the formation of epilepsy by using molecular and cellular approaches.

Thank you Prof Brennan for taking the time to speak to us for this edition of our bulletin. You can learn more about Gary's research which is funded via the HRB-HRCI joint funding scheme, by visiting the 'Research' section of www.epilepsy.ie.

TIME FOR A BREAK



A huge thank you to everyone for your continued support for our Time for A Break draw!

The draw sees all entrants entered into a monthly draw for a €300 Select Hotel voucher. We have outlined details of our lucky winners below. We hope you have all got a chance to enjoy one or more of

the fabulous range of Select Hotels across Ireland!

For those who have not been lucky yet, we hope you will take solace from reading this edition of our research bulletin and learning more about the projects you have helped to support through your participation in the draw! Maybe next year will be your year!

2022 Winners

Jan: K. Keoghnan	July: T. Walsh
Feb: M. Nugent	Aug: B. Burke
Mar: D. Ahern	Sept: H. Cooke
Apr: J. Budds	Oct: B. Hanley
May: D. Brady	Nov: K. Magee
Jun: F. Lynch	Dec: A. Norris

2023 Winners

Jan: N. Bolger	Jul: M & B Kennedy
Feb: M. Smith	Aug: W. Fitzgerald
Mar: E. O'Connor	Sep: F. Galvin
Apr: I. Agar	Oct: C. Carolan
May: A O'Sullivan	Nov: To be drawn
Jun: M Brady	Dec: To be drawn



THANK YOU!

For the final time in this latest edition of our Research Bulletin, we would like to thank you for your interest in and support for Epilepsy Ireland's Research activities. The projects you have helped to support will truly bring us closer to a society where no person's life is limited by epilepsy.

Thank you.

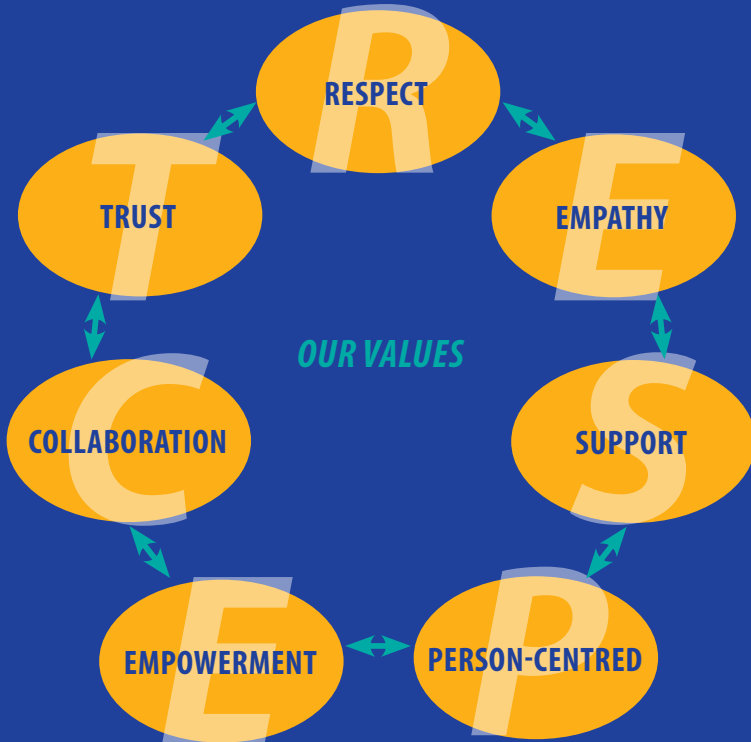


OUR VISION:

To achieve a society where no person's life is limited by epilepsy.

OUR MISSION:

To empower all those affected by epilepsy to achieve their full potential by providing high-quality community-based support and education, raising public awareness, conducting effective advocacy and supporting research.



The Scheme to Support National Organisations is funded by the Government of Ireland through the Department of Rural and Community Development