NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

IMPACT REPORT 2022

Pippa is 5 and was diagnosed with intermediate Neuroblastoma in 2018. Pippa and her Mum raised over £1,000 for us by walking 10,000 steps every day in April 2021.

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

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COVER PHOTO

Evie diagnosed with stage L2 intermediate risk Neuroblastoma in Sept 2020 and her family have helped raise awareness by sharing their story with us.

CHAIRMAN OF THE BOARD OF TRUSTEES

TONY HEDDON

EXECUTIVE SUMMARY

- **Neuroblastoma UK's sole purpose is to improve treatments and outcomes for all children suffering with neuroblastoma**
- **To achieve this, we raise funds for vital medical research**
  - **To find a CURE for all children with neuroblastoma**
  - **To find less severe, but effective treatments with reduced short and long term side effects**

"As a charity we understand that we are accountable for our actions and, most importantly, how we spend money raised in our name.

Our Research impact report is designed to demonstrate the difference we are making. Our mission is to raise funds to facilitate research into funding more effective treatments and ultimately a cure for the terrible disease that is Neuroblastoma.

The distressing nature of the disease and the effect it has on children and their families means that there are opportunities to tap into the generosity of our supporters and the wider public. However, raising funds is only one aspect, the other important part is to ensure these funds are directed into the projects and researchers that will optimise the chances of success. We achieve this through a rigorous application and evaluation process involving multiple peer reviews, analysis from an international scientific advisory board of experts renowned in their field and finally ratified by the Trustee board. Once funded, each applicant has to submit reports highlighting results achieved and the potential benefits for the community, the children and their families.

The nature of research projects means that measuring the impact of funding can be a challenge but through continuous evaluation of performance, analysis of results, learning from each project and using this information to ensure continuous improvement in all that we do, our Research impact report provides valuable insight to determine future focus and objectives."

TONY HEDDON · CHAIRMAN OF THE BOARD OF TRUSTEES

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

"CHILDREN WITH CANCER DESERVE A LIFETIME"

WHO WE ARE

The Charity was started by the parents and friends of five year old Mathew Oldridge in 1982 under the Name – The Neuroblastoma Society. Nearly 40 years later, as Neuroblastoma UK, our mission is identical and remains - to improve treatment for this dreadful disease.

- This mission is only made possible by our supporters. We try to keep our expenses low, we have 3 paid members of Staff and 13 volunteer Trustees on the Board.
- 87p in every £1 raised goes on research.*
- Neuroblastoma UK's future and success is only made possible by the time and expertise given by our great core of volunteers.
- We are entirely powered by the donations we are given.

* Expenses to income averaged 2010-2019

WHY DOES NEUROBLASTOMA UK EXIST?

About 50% of children with high-risk neuroblastoma still die from their cancer

- Many of the survivors develop health problems from their treatment.
- There has only been one new drug licensed for the treatment of neuroblastoma in the last 40 years.

WE NEED TO CHANGE THIS AND GIVE THESE CHILDREN THE CHANCE OF A HAPPY CHILDHOOD AND A POSITIVE FUTURE.

"Our beautiful daughter Georgia was born in May 2004 - she should be celebrating her 18th birthday this month. But in October 2016, at the age of 12, our wonderful, happy child passed away after being diagnosed with neuroblastoma. We set up Georgia's Fund to help fund research into neuroblastoma, and have raised more than £200,000 so far."

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WHY CHOOSE OUR CHARITY?

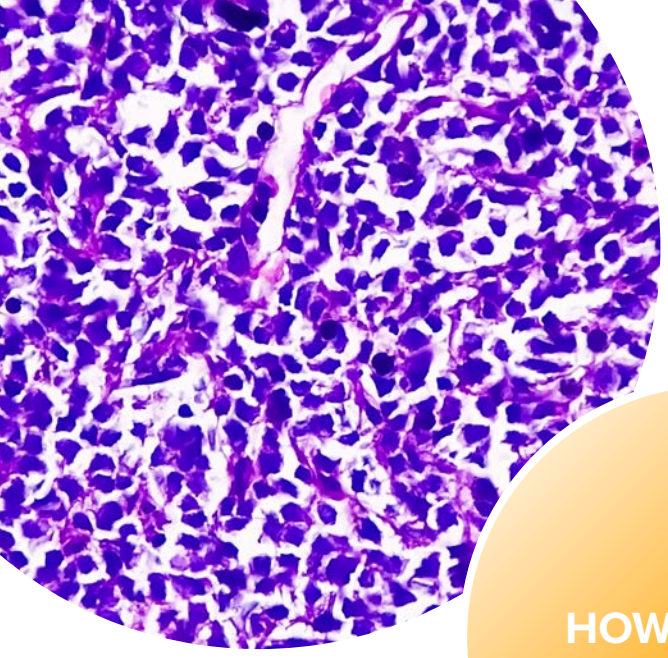
DOESN'T THE GOVERNMENT PAY FOR ALL RESEARCH?

- According to current figures 66% of funding for cancer research in the UK comes from charitable sources (ARMC)
- With our present economy, charities are vital to support medical advances in the UK

THERE ARE SO MANY CHARITIES – WHY CHOOSE US?

- The large general cancer charities have so many different cancers to cover. Levels of investment are commensurate with the population it affects and Childhood cancer makes up less than 1% of all cancer deaths in the UK
- Of all the childhood cancers, high-risk neuroblastoma currently has one of the worst outcomes and is a major cause of death in children

THIS MUST BE CHANGED.



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HOW ARE THE GRANTS AWARDED?

Independent referees review the grant applications (2/3 reviewers per application). The independent referees are clinicians or researchers from around the world with appropriate scientific experience for the respective applications.

- **The applications along with all reviews** are then presented to the **Neuroblastoma UK Scientific Advisory Board** made up of eminent, international researchers and clinicians in neuroblastoma research.
- **The Scientific Advisory Board** then give recommendations to the **Board of Trustees** and the Board award the grants based on this advice.

THE 2021 GRANT ROUND INVOLVED 30 WORLDWIDE EXPERTS TO ADVISE ON THE BEST RESEARCH TO SPEND THE MONEY OUR SUPPORTERS RAISED.

We ensure that our peer review process meets or exceeds the principles set out by the Association of Medical Research Charities (a prerequisite of AMRC membership).

- **Accountability** Open and transparent about peer review procedures; all details of which can be found on our website with the names of our Scientific Advisory Board.
- **Balance** The Scientific Advisory Board must reflect a balance of experience and scientific disciplines.
- **Independent decision making** The Scientific Advisory Board must be independent of the charity's staff and trustees.
- **Rotation of scientific advisors;** they have a fixed term of office and do not have tenure.
- **Impartiality** The Scientific Advisory Board is created after the grant applications have been received so any conflict of interest should have been dealt with before they meet. We also have a conflict of interest policy which outlines that should a conflict occur, the implicated advisor must remove themselves from that discussion.

- **Projects** range from basic research to translational research.
- **A typical grant** would fund a postdoctoral or postgraduate researcher for 1-3 years at a UK or ROI University or Research Institution.
- **Since the inception** of the Charity 1982 – 2021 we have supported research with nearly £9m from donations.
- **Over the last 10 years** Neuroblastoma UK has invested >£4m of charitable donations Into research into the disease.

THE NEXT FEW PAGES DESCRIBE THE IMPACT THE GRANTS AWARDED SINCE 2010 HAVE MADE IN THE FIELD OF NEUROBLASTOMA.

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

SINCE 2010
CLINICAL IMPACT OF FUNDING

Laboratory research funded by Neuroblastoma UK has led to:

- **The development of five open early phase clinical trials of new drugs** or new drug combinations crizotinib and temosirolimus, lorlatinab, fadraciclib, PARC, idasanutlin and venetoclax and one in planning - PARP inhibitor and MIBG.
- **The first trial of a new immunotherapy (CAR T-cells)** for high-risk neuroblastoma in Europe.
- **A trial combining targeted radiotherapy** (MIBG with chemotherapy) - VERITAS.
- **The opening and running of the current trial** for high-risk neuroblastoma in the UK the SIOPEN HR2 trial joint funding Neuroblastoma UK and SKC.

" I would also like to take this opportunity to thank Neuroblastoma UK for their support. For my whole career, I have been a developmental biologist but support from Neuroblastoma UK has allowed me to take that developmental biology expertise and purpose it towards developing an understanding of neuroblastoma, working towards rational new therapies exploiting latent differentiation potential of neuroblastoma cells. I am now continuing this work with 4 post-docs funded by a 5-year CRUK programme grant for neuroblastoma research, something that would have been quite impossible without Neuroblastoma UK previously taking a chance on someone from outside the field, and for this I am very grateful. "

ANNA PHILPOTT
PROFESSOR OF CANCER & DEVELOPMENTAL BIOLOGY,
UNIVERSITY OF CAMBRIDGE, UK

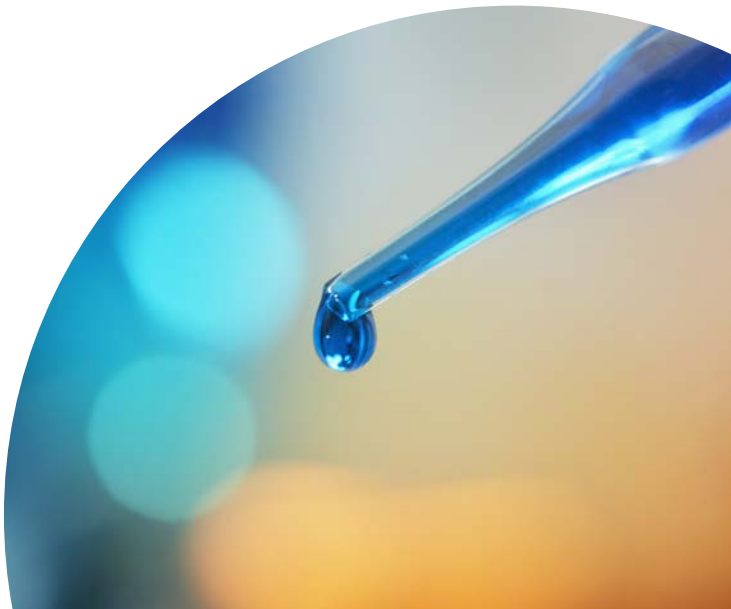
NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

SINCE 2010
NEW DRUGS DISCOVERED FROM INITIAL RESEARCH
Funded by Neuroblastoma UK

- **Mutations in the anaplastic lymphoma kinase (ALK)** gene occur in about 10% of neuroblastomas and confer a worse outcome. Prof Louis Chesler through laboratory research, funded by two Neuroblastoma UK grants in 2010 and 2012, has developed a drug combination (crizotinib and temosirolimus) to test in ALK driven neuroblastoma and determined that the third generation ALK inhibitor, lorlatinab is the most active drug currently available.
- **From Neuroblastoma UK funded research in 2014** Prof Louis Chesler discovered that fadraciclib was an effective agent in blocking the MYCN gene, which drives many cases of high risk neuroblastoma.
- **Professor Tweddle demonstrated in the laboratory from a Neuroblastoma UK grant** awarded in 2014 that idasanutlin was active in neuroblastoma especially in combination with venetoclax.
- **Dr Mussai using Neuroblastoma UK funding in 2016** found that depleting arginine with PARC was a potential therapy for neuroblastoma.

Novel Compounds obtained or developed due to Neuroblastoma UK funded grants between 2010-2018
(ie it is a new discovery which possesses special or enhanced properties in the field of neuroblastoma)

5
NOVEL COMPOUNDS FOUND



Data based on Survey info collated 2021 – 87% respondents of all research grants awarded during this time period

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

CLINICAL TRIALS AND THEIR IMPACT

designed from laboratory research funded by Neuroblastoma UK

- **Crizotinib and temosirolimus** are currently being tested in the Innovative Therapies for Children with Cancer (ITTC) European wide trial – CRISP funded by Cancer Research UK.
- **Fadraciclib is currently being evaluated** in the European ITCC-eSMART trial funded by Cancer Research UK.
- **The combination of a PARP inhibitor and MIBG** is being planned to be funded by Solving Kids Cancer UK.
- **Lorlatinab has just been included in the North American Children's Oncology group** front-line high-risk neuroblastoma trial and will soon be incorporated in the European SIOPEN trial funded by Solving Kids Cancer UK.
- **PARC is investigated in an early phase trial** funded by Cancer Research UK.
- **Idasanutlin with venetoclax** are being investigated in an industry study.
- **The first trial of a new immunotherapy (CAR T-cells)** for high-risk neuroblastoma in Europe.

Clinical Trials resulting from NBUK funded research grants from 2010-2018

OVER A THIRD OF RESEARCH FUNDED IN THIS TIME HAS GONE ONTO ESTABLISH A CLINICAL TRIAL

Total grant spend during this period £2.85m
Data at 2021

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

SINCE 2010
MIBG CLINICAL TRIALS AND THEIR IMPACT
designed from laboratory research funded by Neuroblastoma UK grants

“ It was nice for me to participate in a review that was truly focused on patient impact vs pure scientific elegance and rigor. While the science is clearly important, the impact is often not appreciated for years and there are many, many funding mechanisms for “good science.” The translational piece often makes for less “impactful” or “sexy” publications, but is definitely closer to changing practice and/ or creating new treatment options for patients. It is not clear to me why this type of research has been historically hard to fund, but I am delighted that Neuroblastoma UK has opted to prioritise these types of projects.”

JULIA GLADE BENDER
SCIENTIFIC ADVISORY BOARD FOR NEUROBLASTOMA UK
• VICE CHAIR, DEPARTMENT OF PEDIATRICS AT MEMORIAL SLOAN KETTERING, NEW YORK

- **Two research projects** to improve the activity of **MIBG** – targeted/molecular radiotherapy for neuroblastoma.
- **The laboratory research has been undertaken** by Prof Robert Mairs in Glasgow.
- **The researchers have investigated** if different drugs could enhance the effect of MIBG.
- **A Neuroblastoma UK funded project** demonstrated synergy between **topotecan and MIBG**.
- **This research led to the VERITAS Study;** an international European SIOPEN randomised study funded by Cancer Research UK in patients with poorly responding neuroblastoma, opened in October 2018.

Edwin, diagnosed with 4s Neuroblastoma at just three days old and is an inspiration to all that meet him. His family and friends have taken on a number of fundrasing initiatives on our behalf; including his Mum & Dad shaving their heads!

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

SINCE 2010
CLINICAL TRIALS AND THEIR IMPACT

Immunotherapy (CAR T-cells) research funded by Neuroblastoma UK in partnership with Action Medical Research

- **A research project** Optimising cellular immunotherapy for neuroblastoma.
- **The laboratory research** has been undertaken by Prof John Anderson at University College, London.
- **The research led to the first trial** of a new immunotherapy (CAR T-cells directed at GD2) for high-risk neuroblastoma in Europe, funded and sponsored by Cancer Research UK.
- **The laboratory research continues** aiming to improve CAR T-cells directed at GD2 and develop CAR T-cells directed at B7H3.

CLINICAL TRIALS CURRENTLY FUNDED BY NEUROBLASTOMA UK

Multi country multi centre study of children with Opsoclonus-myoclonus syndrome OM

Opsoclonus-myoclonus is a rare but devastating neurological condition associated with neuroblastoma. Treatment is not effective in many patients. This European study aims to develop new treatments and understand the science behind this neurological complication.

SIOPEN High Risk 2 trial

Neuroblastoma UK has funded with Solving Kids Cancer, the very important current trial for all children in the UK with high-risk neuroblastoma. All children with high-risk neuroblastoma will be enrolled on this trial. It aims to improve outcomes.

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FIGHTING CHILDHOOD CANCER

SINCE 2010 RESEARCH, INITIALLY FUNDED BY NEUROBLASTOMA UK

catalyzing subsequent funding

- **Professor Chesler's work on ALK and MYCN** continues to be further developed through a Cancer Research UK Programme Award for five years 2022-2027. This would not have been possible without the work undertaken with the seed grant funding from Neuroblastoma UK.
- **A Cancer Research UK Senior Clinician Scientist Fellowship** was awarded based on Neuroblastoma UKs initial funding to Professor Chesler.
- **Professor Philpott received three funding grants** from Neuroblastoma UK in 2012, 2014 and 2016 to investigate differentiation therapies for neuroblastoma focusing on Ascl1. This has resulted in her research receiving a 5 year programme grant from Cancer Research in 2017.

NBUK research grants between 2010 - 2018 which have already led to further funding

YES	NO
95%	5%

The discoveries generated from these predominately pre clinical Neuroblastoma UK grants have resulted in excess of £7.7m in further funding

2010 – 2018 → **41 Subsequent publications** → **Leading to >£7.7m in additional funding post initial Neuroblastoma UK grants**

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

MEETINGS

NEUROBLASTOMA UK HAS FUNDED SEVERAL MEETINGS SOME OF WHICH HAVE BEEN INSTRUMENTAL IN HIGHLIGHTING CLINICAL DIRECTION

- **Neuroblastoma UK biannual international two day scientific symposiums** have encouraged presentations from young scientists and collaborative discussions between clinicians and researchers – these have been landmark in neuroblastoma research.
- **"Accelerating drug development for neuroblastoma"** held in 2018, brought together European and North American researchers and identified the important drugs for development.

Prof Andy Pearson (Neuroblastoma UK Research Trustee)

"In the past the evaluation of new anti-cancer drugs and the introduction into front-line treatment in neuroblastoma has been very slow e.g. 26 years elapsed between the first time a child received the anti-GD2 antibody, Unituxin, to its incorporation into standard treatment. For the sake of children with neuroblastoma **THIS PROCESS MUST BE ACCELERATED**"


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Available online at www.sciencedirect.com

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journal homepage: www.ejcancer.com

EJC

Review

Accelerating drug development for neuroblastoma: Summary of the Second Neuroblastoma Drug Development Strategy forum from Innovative Therapies for Children with Cancer and International Society of Paediatric Oncology Europe Neuroblastoma

Lucas Moreno [a,*,1], Giuseppe Barone [b,1], Steven G. DuBois [c,1], Jan Molenaar [d], Matthias Fischer [e,f], Johannes Schulte [g], Angelika Eggert [g,h,i], Gudrun Schleiermacher [j], Frank Speleman [k], Louis Chesler [l,m], Birgit Geoerger [n], Michael D. Hogarty [o,y], Meredith S. Irwin [p], Nick Bird [q], Guy B. Blanchard [r], Sean Buckland [s], Hubert Caron [t], Susan Davis [u], Bram De Wilde [k], Hedwig E. Deubzer [f], Emmy Dolman [v], Martin Eilers [w], Rani E. George [c], Sally George [l,m], Štěrba Jaroslav [x], John M. Maris [o,y], Lynley Marshall [l,m], Melinda Merchant [z], Peter Mortimer [z], Cormac Owens [aa], Anna Philpott [ab], Evon Poon [m], Jerry W. Shay [ac], Roberto Tonelli [ad], Dominique Valteau-Couanet [n], Gilles Vassal [ae], Julie R. Park [af,2], Andrew D.J. Pearson [l,m,3,2]

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

NEUROBLASTOMA UK FUNDED RESEARCH

IMPACT

HOW DOES THIS TRANSLATE... FROM BENCH TO BEDSIDE

Discoveries emanating from the NBUK grants awarded between 2010 – 2018 have led to:

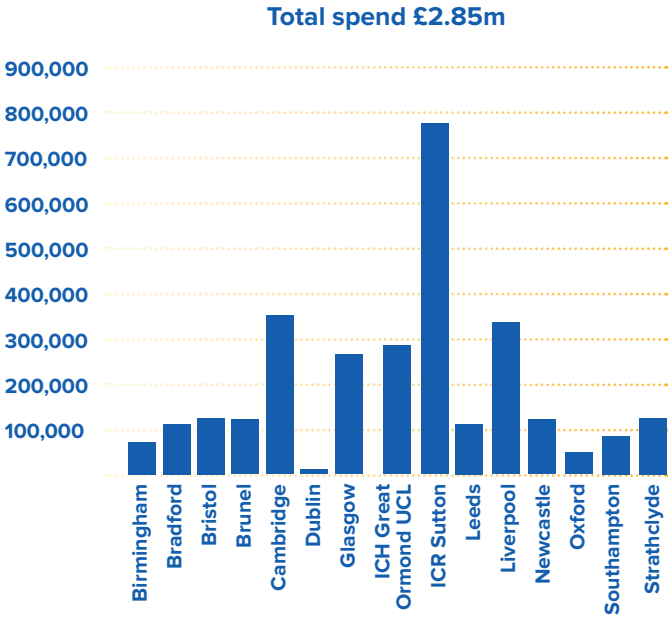
- **Five open early phase clinical trials** of new drugs or drug combinations and one in planning.
- **The first trial of a new immunotherapy (CAR T-cells)** for high-risk neuroblastoma in Europe.
- **A trial combining targeted radiotherapy** (MIBG with chemotherapy) - VERITAS.
- **Opening and running** of the **current European trial** for high-risk neuroblastoma in the UK - SIOPEN HR2.
- **Forty one publications**
- **Sponsorship of Accelerating** drug development for neuroblastoma 2018.
- **Neuroblastoma UK biannual** international two day scientific symposiums.
- **Leveraging funding from Cancer Research UK** and other charities enabling novel, innovative research funded by Neuroblastoma UK to be developed further.

Percentage of grant holders (during the period surveyed 2010- 2018) that believe that their research will/might still have clinical impact in the future

YES **90%**

NO **10%**

RESEARCH SPEND £ BY INSTITUTION 2010 – 2018



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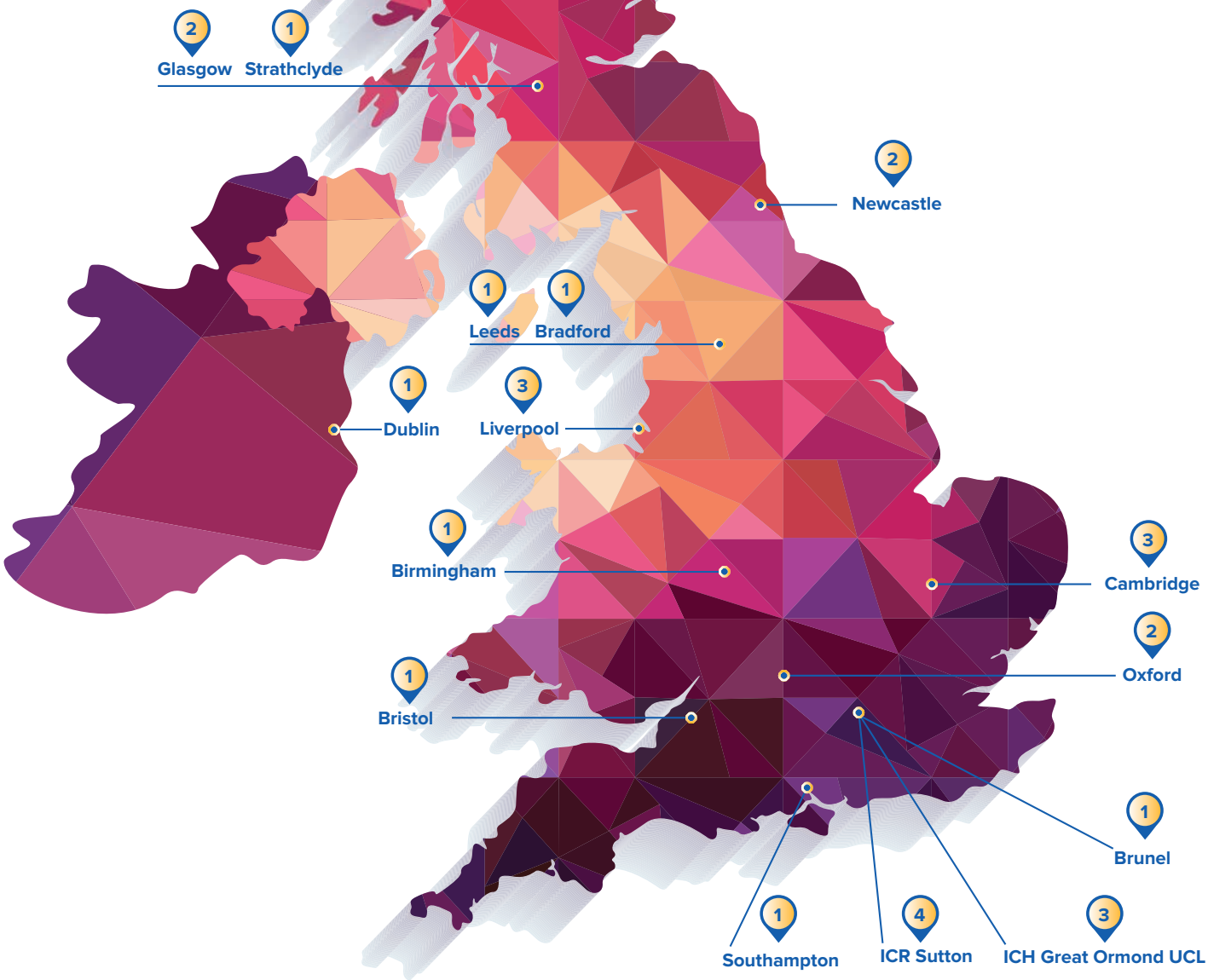
PROJECTS AWARDED

2010 – 2018



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CURRENT GRANTS

Ongoing or recently completed and preparing for publication:

Prof Suzanne Turner	**Cambridge**	Development of personalised therapeutics to prevent and treat ALK-positive neuroblastoma resistant to ALK inhibition
Prof Louis Chesler	**ICR, Sutton**	Understanding and targeting of B7-H3 in neuroblastoma development and microenvironment via stem cell models.
Dr Juliet Gray	**Southampton**	Understanding and improving the mechanism of anti -GD2 monoclonal antibody therapy in neuroblastoma
Dr Olga Piskareva	**Dublin**	Modelling neuroblastoma – immune cell interactions in a tissue-engineered 3D platform
Dr Andrew Stoker	**ICH Great Ormond UCL**	Characterising the Tumour-Supporting Roles of HMMR in Neuroblastoma
Prof Heike Laman	**Cambridge**	Nanobody based strategies to investigate and targer the oncogenic transcriptopn factor, N-Myc
Dr Anestis Tsakiridis	**Sheffield**	Establishment of an in vitro model of neuroblastoma initiation using pluripotent stem cell differentiation
Dr Karin Straathof	**ICH Great Ormond UCL**	Next Generation GD2 – directed T-cell therapy for neuroblastoma
Dr Zoe Walters	**Southampton**	Evaluating the efficacy of combination epigenetic and differentiation therapies for the treatment of high-risk neuroblastoma
Prof Falconer/Dr Guo	**Bradford**	Exploring the potential for a ketogenic diet to enhance minimum residual disease therapy
Prof John Anderson	**ICH Great Ormond UCL**	GN2400: Optimising Cellular Immunotherapy for Neuroblastoma
Dr Hurst/Dr Jahangiri	**Birmingham**	Investigating the contribution of transposable elements and endogenous retroviruses to gene deregulation and pathogenesis of neuroblastoma

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GOING FORWARD

GRANT ROUND 2021

- An objective this time was to foster **international collaboration**
- Priority was given to applications which would have the **greatest clinical impact**
- Focusing on areas of **translational research**

2 GRANTS AWARDED WHICH WILL START IN 2022

PROF CHESLER, INSTITUTE OF CANCER RESEARCH

£469,093

Institut Curie Paris • Princess Maxima Utrecht • Institute of Child Health/ Great Ormond Street, London

Blood-based Biomarker Testing to Guide the Diagnosis and Treatment of Neuroblastoma Patients

DR GAZE, UNIVERSITY COLLEGE LONDON

£214,385

Four Research Institutions across London in collaboration with: Erasmus Medical Center Rotterdam • Princess Maxima Center, University Medical Center Utrecht.

Dinutuximab-Beta as the theragnostic vector for non-invasive molecular imaging and radiotherapy of high risk neuroblastoma

SMALL GRANTS

- **We continue to offer our small grants programme.**
  These are small grants of £5,000 or under to help researchers establish innovative projects that aim to improve our understanding of how neuroblastomas develop.

WE HAVE AWARDED TWO TO DATE IN 2022:

DR EWING, SOUTHAMPTON

How does the Zika virus kill Neuroblastoma cells? A potential new oncolytic virotherapy for Neuroblastoma

DR JINHUI GAO, SOUTHAMPTON

Investigating the role of Enhancer of Zeste homolog 2 and natural killer cells in neuroblastoma

NEUROBLASTOMA UK
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ACKNOWLEDGEMENTS

THIS RESEARCH

has all been made possible with kind contributions from our Co-funders.

Neuroblastoma UK sets high standards

amrc PEER REVIEW AUDIT 2020

Hallmark of quality research funding
AMRC membership also means that our grant holders are eligible for CRSF and NIHR additional funding too

International make up of Scientific Advisory Board

Eminent clinicians and researchers in the neuroblastoma field

As a small charity we can make a greater contribution to research by working with others. This enables us to broaden our capabilities and hopefully generate more impact. THANKS to:

Smile with Siddy

BradleyLoweryFoundation
Supporting Fundraising Campaigns

GEORGIA'S FUND
NEUROBLASTOMA RESEARCH

action medical research for children

Solving Kids' Cancer

Children's Cancer and Leukaemia Group

Friends of Rosie

NNS
FIGHTING CHILDHOOD CANCER

And thank you to our Researchers, Scientific Advisors, Volunteers and Supporters.

We will all continue to work together to improve the treatment for children with neuroblastoma as there is still so much to be done.

June 2022

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