SOHANA
RESEARCH FUND
second skin second chance

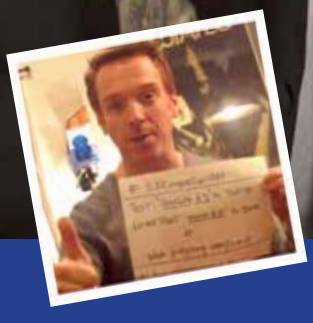
#CureEB

WINTER 2015

We congratulate Sohana on her 'Teenager of Courage' award at the Pride of Britain

LATEST RESEARCH

RECENT EVENTS



With renewed publicity around the #EBtonguetwister challenge we would love you to play along

LOOKING FORWARD

PATRONS DAMIAN LEWIS SEAN BEAN

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Sohana Research Fund is a charity registered in the England and Wales 1158672

THANK YOU FOR YOUR HELP

2015

It has been a busy year since receiving our charity number in September 2014.

Recessive Dystrophic Epidermolysis Bullosa "Hard to say. Hell to live with" is the strapline we used for the #EBtonguetwister challenge which was bravely and enthusiastically fronted by Sohana and was supported by a number of celebrities. It raised awareness of EB, profile for the new charity and of course important research funds. The text numbers are still operating and the social media reach has been fabulous. The EBSTEM trial was reported in the Journal of Investigative Dermatology and children on the trial have received two 'top up' infusions of Mesenchymal Stromal Cells (MSC). It is hoped that all paediatric patients may be given MSC's as part of their routine care but NHS funding is not guaranteed yet. As a follow on from this trial and to generate further evidence for this as an interim treatment, a similar trial in adults has started at Guy's Hospital (ADSTEM). Guy's Hospital and Great Ormond Street Teams are also progressing the case for Bone Marrow Transplants. A ground breaking gene therapy trial has started with the team from the Institute of Child Health and we are continuing to fund a world first Limbal Stem Cell project in Minnesota. A very successful dinner in May at RIBA and another wonderful donation from Goldman Sachs Gives has allowed us to make significant progress towards a trial involving patient gene modified cells in children. We are working hard at pushing forward gene editing work we hope to have exciting news about this in the new year.

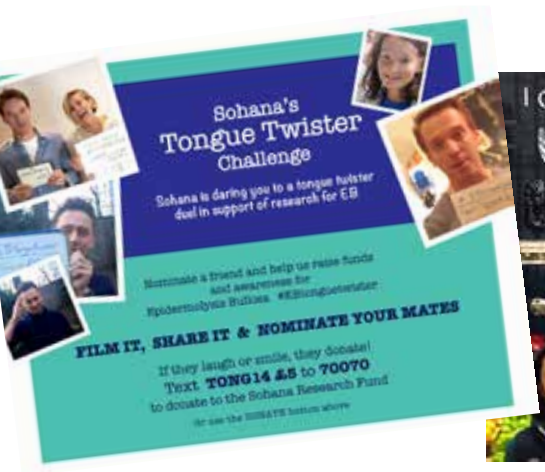
We have achieved so much in four years and it is all thanks to your kindness generosity and patience. The truth about RDEB, is that as a rare condition, sufferers are consigned to the incurables muck heap at birth and are left to suffer and die in silent pain. So it would continue to be, if it were not for the belief and support of people like you. Make no mistake - research and early phase clinical trials do not happen for rarer conditions unless patient groups/parents are able to make enough 'noise' and find enough funding to make them happen. You really are helping to change this condition, not only here in the UK but worldwide.

Very recent reports have made gene editing – considered by many to be the 'cure' – a tangible reality and not just the stuff of dreams. To be on this threshold is incredible but the anxiety is – how quickly can this hope be realised?

Try to imagine being in pain every minute of every day since birth, and you will understand that hope. Or imagine you are the parent of that suffering child – with HOPE sitting just there – out on the doorstep.

Thank you for your help,

Sharmila Nikapota



EBSTEM TRIAL

TESTIMONIALS FROM SOME OF THE CHILDREN ON THE TRIAL


With regard to the SRF work - The research is so important to us as it gives us hope and most of the time that's what keeps us going as a family - hope that in the future they will find a cure for this cruel disease and that can only happen or be possible through the research that the SRF supports.

Margaret Paczensky - Mother of Ciara, age 9

I have a son, Mason, who suffers with RDEB. The SRF charity have done amazing work so far and they are completely passionate about where and what the money they raise is used for.

So far we have been part of the stem cell trial and since then also had more stem cells after being signed off as a treatment and no longer a trial. Without SRF I know that this wouldn't have happened so soon, as every penny they raise goes towards what all us EB families want and that's research into hopefully one day a cure, to stop our children living a life of pain and suffering.

SRF have become a huge part of our lives and hopefully our children will be free of this horrific condition and will live a life they, at the moment, dream of. I believe SRF can make their dreams become a reality. The difference with SRF compared to other charities are that the family live and breathe EB which to me makes me think they are even more determined. We are thankful as a family that SRF exists and we will always support them as much as we can!

Kerry White - Mum of Mason, age 6


Gabrielius had loads of raw skin areas, itchy areas, some parts would not heal up since his birth. We had to change his dressings very often, about 6 to 8 times a day. We had to feed him loads of painkillers and anti-itch medicines, just to keep him calm and sleepy during night, because most of the nights one of us had to stay up just to prevent more damage to himself.

After the first infusion, the difference was un-believable. All raw areas were healing mega quickly, he begun to sleep normally and itchiness disappeared. It was a big relief for him and for us. Three months later all raw areas had skin, we completely stop painkillers and anti-itch medicines. Amounts of dressings and other prescriptions monthly order dropped probably by 30%. It was a massif relief for Gabrielius and for us. We actually could get him to start doing more physical and mental activities for his development.

I believe none of this would happen without SRF funding. It is absolutely amazing that you went so far, with raising so much money, involving famous people to participate and spread awareness about RDEB, funding research programmes in UK and USA. Everyone in our family is so grateful for SRF commitment and are proud to be part of it.

Linus Misurenkovas - Father of Gabrielius, age 2 years 9 months

The first attached photo of Isla was taken on Monday 13th April, 5 days after she received her stem cells at GOSH. What a difference they are making already. She's got so much more energy, is in less pain and wounds are finally healing after nearly a year! We can't believe how quickly we are seeing improvements. But more importantly, we can't thank SRF enough for funding this research and making the seemingly impossible more achievable. Even a treatment is more than we could hope for - a research-led cure would be all our dreams come true.

The work that the SRF does to raise money for funding research is a lifeline to our family and Isla in particular. It gives us hope and a more positive future. Living and dealing with EB is devastating and without research the future would be very bleak. We are so grateful for everything that the SRF does and all the fantastic results that funding the research brings.

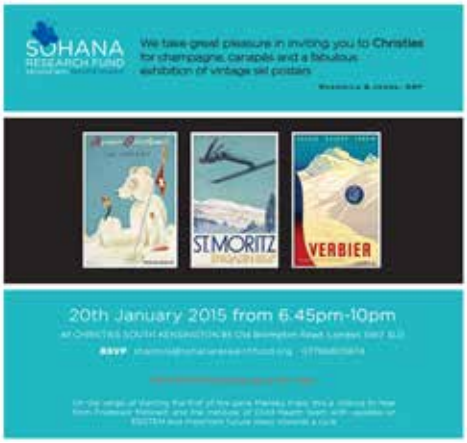
The second attached photo was taken today on the beach at Gairloch on the west coast of Scotland. A wonderful family day out where all cares, pain and EB worries were cast aside for a few hours! To be able to lead a 'normal' family life everyday, like most other families, would be heaven!

Rachel Grist - Mum of Isla, age 6

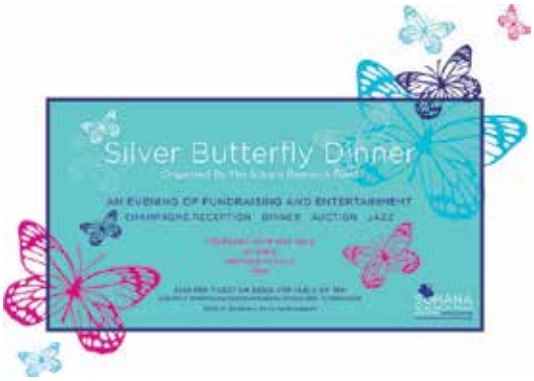

EVENTS

2015

Christie's South Kensington January 2015



Silver Butterfly Dinner at RIBA May 2015



EB Awareness Week at the Glass House Camden October 2015

THANK YOU

2015

Tom Davies Cycled around the world www.tomdaviesrtw.com

A MASSIVE thanks to Tom Davies who cycled around the world for three charities. We were very lucky to be one of them. I hope you will take time to look up Tom's website and have a look at some of the wonderful photo's he took along the way and the very funny blog that he had the energy to write too! A fabulous achievement being the youngest to cycle around the world. Tom raised in total for all three charities £80800.99

Rosie Megaw
and the Manor Prep School raised £1600.00

Commando Challenge
Nathalie Zoethout raised £509.69

Half Marathons
Rachel Beagles raised £5182.01
Bahar Leventoglu raised $5845.76

The Royal Masonic School for girls for making us charity of the year (ongoing fabulous fundraising!)

Goldman Sachs Gives	IGY Foundation	Arle Capital
Maria Marina Foundation	Garfield Weston Foundation	REN Skincare
Sir James & Deirdre Dyson Trust	The Tudor Foundation	Independent Talent

HELP! Would your school, club or business like a GREAT charity to support? Look no further! At this crucial time, volunteers to help with events, day to day running, offers of corperate sponsorship, expertise taking the research into treatments – would all be incredibly valuable and very much appreciated.

SOHANA RESEARCH FUND
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RESEARCH UPDATE

PROJECTS FUNDED BY SOHANA RESEARCH FUND

Making a difference to people living with RDEB means new treatments have to be developed and tested in clinical trials. These new treatments are likely to involve a combination of cell, gene, protein and drug therapies, all of which (individually or together) strive to correct the genetic weakness in the skin that causes the life-long blistering. Since we started fundraising in 2011 our focus has been funding Stem Cell Research and Clinical Trials associated with this in the UK and US and towards:

EBSTEM Phase 1/11 Clinical Trial of Mesenchymal Stromal Cells in RDEB

Professor John McGrath, Kings College London with Great Ormond Street Hospital for Children NHS Trust (London) and collaborating with Utrecht, Netherlands.

Funding from Goldman Sachs Gives through Sohana Research Fund £450,000.

Project overview: This was the first UK trial aiming to lead to a treatment for children with RDEB. It seeks to establish if MSCs from unrelated donors who do not have EB can benefit children with RDEB in a safe efficacious way. It led to reduced skin inflammation, blistering and better wound healing. This trial may be extended to use matched cells either cord or matched donor cells to see if there are further benefits of introducing cells that have a compatible tissue match. GOSH transplant surgeon Dr Paul Veys is overseeing BM transplant possibilities.

The EBSTEM Trial was the subject of a BBC Health news report in Nov 2013.

STARTED JULY 2013. 2 YEAR DURATION *(reduced to 1 year)*

COMPLETED

The EBSTEM results have now been published in the Journal of Investigative Dermatology 23 April 2015 under the title "Potential of Systemic Allogeneic Mesenchymal Stromal Therapy for Children with Recessive Dystrophic Epidermolysis Bullosa". JInvest Dermatol dol:10.1038/jid.2015.158; accepted article preview online April 23, 2015.

Equipment award 2014

£40,000 to University College London (UCL) Hospital Funding towards the purchase of high speed and ultracentrifuge equipment required for the translational research in the pre-clinical development of gene therapies for EB.

TALEN based approach to developing safer, more effective treatments for people with EB

Dr Jakub Tolar, University of Minnesota, USA.

Funding from Sohana Research Fund $250,000.

Project overview: The goal of this project is to develop safer, more effective, individualised treatment options for children with EB. The aim of the project is to develop a treatment based on a patient's own cells, corrected in the laboratory for the gene defect, and returned to the EB individual: the advantages of this approach would be absence of the severe potential side effects associated with the Bone Marrow Transplant procedure and the problems of rejection of cells from unrelated donors. To date, such approaches have been hindered by difficulties in tailoring gene correction strategies for a unique patient mutation as well as in producing patient-derived cells that are suitable for transplant. This project will combine two technologies, iPSC (induced pluripotent stem cells) and TALEN (transcription activator-like effector nuclease), aiming to develop a safer, more effective treatment.

Original Article, Subject Category: Vector Engineering and Delivery
Molecular Therapy (2013); 21 6, 1151–1159. doi:10.1038/mt.2013.56

STARTED JULY 2013. 1 YEAR DURATION

COMPLETED

ADSTEM

Professor John McGrath, Kings College London. Guy's and St Thomas's NHS Trust.

£432,000 Funding from Sohana Research Fund.

A follow up study in adults understanding how allogeneic Mesenchymal Stromal Cells given intravenously can modify disease severity in Recessive Dystrophic Epidermolysis Bullosa. There will be ten patients on this trial and the first patient injections have been given. The main objectives of this study is:

1 to assess the clinical responses in adults with RDEB receiving intravenous MSCs.

2 to identify the best cohort of individuals to target for future trials and therapies.

3 to improve understanding responsiveness to MSCs.

4 to identify candidate molecules necessary to activating MSCs and make them clinically more potent.

5 to assess its impact on reducing disease.

This is a prospective, non-randomised, open label study. All study participants will receive two intravenous MSC infusions at baseline Day 0 and Day 14 and will be followed up for a 12 month period following the first infusion. Each subject will undergo an initial screening including physical examination, assessment of vital signs and disease severity assessment.

START DATE 07/2015. 2 YEAR DURATION

RESEARCH UPDATE

PROJECTS FUNDED BY SOHANA RESEARCH FUND

Prof Waseem Qasim, Prof Jakub Tolar & Prof John McGrath

Gene Therapy

Lentiviral-mediated COL7A1 gene-modified cell therapy for RDEB

Dr Waseem Qasim, Prof Adrian Thrasher and Prof John McGrath. Institute of Child Health, Guildford Street London.

The costs of this trial is £499,319.87 from the Sohana Research Fund.
(Preclinical work was funded by debra Austria €500,000).

The group have developed a Lentiviral vector which encodes a collagen VII gene, modified to reduce the likelihood of instability of the gene and have now produced gene-corrected fibroblasts under clinical good manufacturing process (GMP) conditions. Ethics and MHRA have given regulatory approvals and the clinical trial, LENTICOL-F (A prospective phase I study of lentiviral-mediated COL7A1 gene-corrected autologous fibroblast therapy in adults with recessive dystrophic epidermolysis bullosa) has started this year.

This study proposes to take skin samples from 6-10 adults with RDEB to produce "person-specific" gene-corrected fibroblasts. When sufficient cells have been grown, they will be injected back into the donor's skin. Three injections will be given 1-2 millimetres under the skin surface, covering an area about the size of a once pence piece. Blood analyses and skin biopsies will be performed at various time points as per the monitoring schedule over 12 months. The primary objective is to evaluate safety, but also to allow analyses of type VII Collagen expression and anchoring fibrils in the injected skin and assess immune response to newly expressed collagen VII. The first patient has been injected with the fibroblasts on 30/11/2015 and we await results of this ground breaking work, which is a world first in this condition.

RESEARCH STARTED 2012

CLINICAL TRIAL START DATE 10/2015. 2 YEAR DURATION

ONGOING

Limbal Stem Cells for treatment of corneal wounds in Epidermolysis Bullosa

Dr Jakub Tolar Professor of Paediatrics, University of Minnesota.

Project commissioned by the Sohana Research Fund. $250,000 towards the first year of the project from Sohana Research Fund.

Most people with RDEB experience corneal erosion, an exquisitely painful condition that causes loss of corneal clarity and compromises clear vision. The aim is to combine cutting-edge gene correction and Limbal stem cell technologies to fill this therapeutic gap and realize the potential of individualized, targeted, genomic-medicine based cellular therapy for RDEB. This is the first project in the world trying to address the problems associated with RDEB eyes.

STARTED 2014

ONGOING

The one year report has been very satisfactory and we have recently agreed a further 2 years of funding for this work ($250,000 per year for two years).

Gene Therapy Lenticol-M Workpackage 1

Mesenchymal Stromal Cells engineered to express collagen VII for the treatment of Recessive Dystrophic Epidermolysis Bullosa. The expectation is that patient derived gene modified cells will have a longer lasting effect than donor MSCs. Pre Clinical proof of concept. This project follows on from Lenticol F and aims to provide an intravenous treatment for RDEB.

Cost of project £467,185-00 from the Sohana Research Fund.

Work package 2 and 3 to follow.

RDEB SCC Exome Sequencing

Lay summary extract from the full application submitted to SRF.

Dr Andrew South, Thomas Jefferson University USA.

Dr Raymond Cho University of California USA.

Patients with Recessive Dystrophic Epidermolysis Bullosa (RDEB) frequently develop aggressive, life-threatening skin cancer, the reasons for which are incompletely understood. We hypothesize that RDEB cancers share common genetic mutations that enable aggressive clinical behavior so early in life, an extremely unusual occurrence outside of this disease. Therefore, identifying the mutational landscape of RDEB cancers should provide critical insight on how a cancer can develop so quickly in the absence of risk factors in the general population such as lifelong sun exposure and DNA damage. Understanding such mechanisms should elucidate modes of prevention and early detection unique to RDEB. Furthermore, an increasing number of anti-cancer drugs that target specific genetic mutations are currently in clinical use or development, thus identifying genetic mutation associated with cancer in RDEB may match a known treatment to patients. We aim to find tractable therapy options or targets for future development, both clinically and experimentally.

Gene Editing

We are continuing to support Gene Editing projects with a view to Clinical Trials within a 3-5 year framework.

We are pushing forward research here in the UK and at leading centres in the US. The aim is to get to a proof of concept clinical trial within five years, on both sides of the Atlantic and as fast as the regulatory authorities will allow. This area of research is moving so fast it is difficult to accurately define timelines. It is clear that if funding limitations are lifted progress would be accelerated.

This work will not just benefit EB but will in theory be applicable to the people who suffer one of the 5,400 Genetic Disorders in the world, which accounts for 10% of people, 30 million in Europe alone.

BBC Health Report 1 Dec 2015 http://www.bbc.co.uk/news/health-34972920

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LOOKING FORWARD

FUTURE FUNDING

Gene Therapy Lenticol M

Following on from Lenticol F, providing proof of concept for intravenous gene modified cells and an associated clinical trial.

Estimated £2million

Costs associated with the work:
Batch of vector £450K
Generate patient MSCs £300K
Run a trial to test Lenticol M £750K
Appoint a project manager, post doc and trial coordinator £450K

The UK team at Great Ormond Street and the Institute of Child Health has a world first in using TALENS to cure a baby with Leukaemia (reported on BBC health http://www.bbc.co.uk/news/health-34731498). We hope this work will have a positive impact on the pursuit of gene editing cures for the 5400 genetic conditions in the world today.

Bioreactor

at Guy's Hospital (Kings College London)

Estimate Costs £700K for two reactors with a years running costs

Bringing Cell Therapy to Clinic - Intravenous infusions of MSCs seem to reduce inflammation and lead to better wound healing. Though changes are not permanent and not a cure, they appear to be therapeutic. The aim is to establish a facility to buy equipment and employ the right scientists to make MSC's available for more routine treatments and for clinical trials.

Gene Editing

Pushing forward research here in the UK and at leading centres in the US, working towards a collaborative framework to accelerate progress. The aim being to get to a proof of concept Clinical Trial within five years. We are continuing to fund gene editing projects that aim to harness the potential of using edited cells for systemic treatments as well as to treat localised areas that need special consideration like in the eyes.

Estimation of costs associated with getting gene editing to trial within Limbal Stem Cells:

YEAR 1

Characterization of limbal stem cells $450k
Identification of tests that distinguish RDEB and wild type cells $650k
Establishment of cell lines for experimentation $350k

YEAR 2

Expanding the platform of gene editing nucleases so that many different type VII mutations can be corrected $750k

YEAR 3

Transfecting the nucleases and donor DNA templates into the cells prepared in Year 1 $400k
Validating their characteristics (cell surface markers not changed from before). Main-taining their "stemness" $700k

YEAR 4

Optimizing the rate of gene correction at a specific type VII mutation $600k
Assessing corresponding expression of type VII collagen protein $300k
Deep-sequencing genome for any off-target effects $550k

YEAR 5

Prepare fully validated standard operation procedure dossier for both genomic and cellular engineering portions of the protocol to be submitted to the EMA and/or FDA $250k

There are many other projects that we would love to support. Novel approaches to treatment which feeds into the concept of combination therapies; reducing the likelihood of the terrible scarring that leads to severe deformities; more study into the particularly aggressive malignant skin cancer that leads to death among RDEB young adults and how to prevent and treat such cancers.

Additional items that would help:

Upgrade of the Dermatology Labs and EB care facilities

at Guy's Hospital, London

Up to £3m

Provides a naming opportunity

Senior Lectureship

in Dermatology at King College London

£500k For a 5 year post

Provides a naming opportunity

FORTHCOMING EVENTS

Recorder Concert on 12 May 2016

VLM April 2016

Cadogan Hall Concert on 7 December 2016

SRF update meetings to be finalised *watch this space!*

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