

Sohana at WE DAY  
youth social action movement



RECENT EVENTS

LATEST RESEARCH

LOOKING FORWARD



PATRONS DAMIAN LEWIS SEAN BEAN DANIELLE DE NIESE SIR JAMES & LADY DYSON

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

# THANK YOU FOR YOUR HELP

2016

“Stick your tongue out at EB – because Sohana and other EB kids can’t”

## Another year and a different social media campaign though still with tongues!

One of our most important tasks is raising awareness of the condition, which was the focus of this campaign. We had great engagement and more people taking part themselves than with the tonguetwister and yes, it raised funds too. We got to try out ‘Boomerang’ videos as well, with some hilarious consequences.

I would describe this as a waiting year. We have been waiting eagerly for both the ADSTEM and LENTICOL F Trials to enrol and complete. ADSTEM has now reached its conclusion and analysis of samples begins. LENTICOL F was delayed starting and is therefore still on-going. We are pursuing gene editing work with as much ‘gusto’ as we can. Whilst it is very likely that other gene editing reagents may be discovered, the CRISPR/Cas9 system seems to have caused sufficient ‘buzz’ around it and with Professor Jakub Tolar’s recent publication, holds great hope of gene editing treatments in the near future. To that end, funding is critical. ‘Nothing

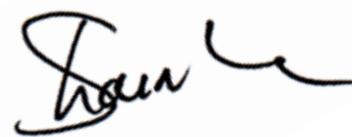
is too small’ is one of our mantras. With all donations going to the research projects, your efforts do speak volumes and will move mountains in research. I have learnt over the years that everything really does add up. We have had a musical theme to the year with two wonderful public concerts and a private opera evening. Runners have completed 10K’s, half marathons, marathons, and ‘anything goes’ at Parallel London. We had cyclists and cake bakers, teddy bear sales and weddings, walks and birthdays. Our SRF family day was great fun and was a lovely informal way of listening to Professor McGrath updating us on world-wide research and progress towards treatment, whilst the children had fun with games, arts and crafts. We have been charity of the year and have taken part in a Charity day. Some grants we won and others we didn’t, but when one door closes we look for another to open. We have been very lucky with corporate donations and we hope to widen horizons next year. Sohana became an #iwill ambassador and her youth social action is to continue to raise awareness of EB for SRF and we are enormously proud of her. She will appear in a little

video clip for Professor McGrath when he talks to 12-18 year olds at The Royal College of Physicians’ at which he is giving a lecture titled “Santa brought me a new skin” – if only that were true on the 25th of December.

We are, as ever, hugely in debt to your generosity, interest and patience. For Sohana and all with EB, we are so grateful for your help. There is no underestimating its value and we will get to treatments sooner, with it. Thank you very much and please stay with us. Here I want to quote Professor Tolar, University of Minnesota “This is a great opportunity, to be part of a legacy, to support research and bring clinical advancements into EB sufferers lives. To change the lives of people who - without us - would not have futures.”

Thank you and have a very happy Christmas and exciting New Year.

Thank you for your help,



Sharmila Collins FOUNDER SRF





# WHAT RESEARCH MEANS FOR US

TESTIMONIALS FROM EB PARENTS WITH KIDS WHO WERE ON THE EBSTEM TRIAL

It is really hard to describe in a few sentences how important research is.

The daily routine of dressing changes, pain and challenges a child has to go through is heart-breaking. I don't have enough words to describe it; you need to see it to appreciate this horrible condition. I'm not even mentioning what tremendous work parents do to keep your child healthy and happy. As a parent, all you want for your child is to be happy, to be able to do normal activities, run, swim, kick the ball, be able to develop normally, with EB you don't have that. And the most frightening thing is that tomorrow will be no different.

That's why the research is one of the most important things to us and Gabrielius, it gives us a chance, even if it is one in a million, but it is still a chance, a hope, that one day we will defeat EB and we are very very thankful to SRF for that chance.

*Linus & Jolita Misurenkovas - Parents of Gabrielius, age 4*



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 7*



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 10*

SRF has given us hope for the future that there could possibly be a cure for this terrible condition. We can only imagine how happy we could be as parents if our one and only dream came true and Poppy could live a life without pain.

*Kate Asher - Mother of Poppy*



The enthusiasm, dedication and tireless commitment from the Sohana Research Fund to raise awareness, to find a treatment, and ultimately a cure, for EB keeps us all going. They shine a light in the dark places and give hope to families like ours affected by this cruel skin disorder. It's difficult to imagine the challenges posed by EB without the support of the SRF.

It is thanks to SRF funded research that there have been so many substantial advances in understanding EB and its causes. We are incredibly grateful to them for giving us this hope and the opportunity for a positive future.

*Rachel Grist - Mum of Isla, age 7*



# EVENTS

2016

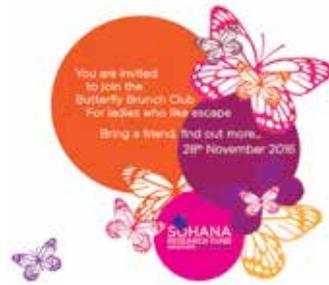
SRF Family Day  
4th Sept, Timber Lodge



LIO 30th Gala Concert  
7th December, Cadogan Hall



Butterfly Brunch  
28th November



Baroque Concerti raised £7,000  
12th May, St. George's Hanover Square



PARALLEL LONDON  
4th Sept, Olympic Park





# THANK YOU

2016

Vitality 10K London Run  
RAISED £12,000

Exotix Charity Day  
RAISED £20,000



Royal Masonic School  
RAISED £10,000

"Give a bear a home"  
RAISED £649

Nick Sleep & la Weirup Marathon  
RAISED £10,000



Crowcombe Court  
Flanders & Swan evening  
RAISED £3,000

Pauline & Tim  
Walk for Sohana  
RAISED £4,900

Clare & Will Wedding  
Donations  
RAISED £1,500



Grant Paczensky Ride London  
RAISED £1,000

North Kessock Bowling Club  
RAISED £1,000

Leonie Perera Half Marathon  
RAISED £3,000



## PROJECTS FUNDED BY SOHANA RESEARCH FUND

Great strides are being made in RDEB research, with early phase clinical trials for stem cell and gene therapies underway in centres around the world. There is every possibility of interim treatments being developed in the quest for a cure. 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 main focus has been funding stem cell research and clinical trials associated with this. We are keen to progress gene therapy research and specifically gene editing work.

### ADSTEM Clinical Trial

*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 JULY 2015. 2YR DURATION**

**UPDATE: The trial has ended and sample analyses and monitoring has begun.**

### LENTICOL-F Clinical Trial

*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 COST OF THIS TRIAL IS £499,320 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) started last 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 one 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 was 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 OCT 2015. 2 YEAR DURATION ONGOING**

### Limbal Stem Cells for treatment of corneal wounds in Epidermolysis Bullosa

*Professor 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**

**The one year report was very satisfactory and a further 2 years of funding for this work (\$250,000 per year for two years) has begun – see above.**

### Gene Therapy Lenticol-M Work package 1

COST OF PROJECT £467,185 FROM THE SOHANA RESEARCH FUND

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.

**UPDATE: This project is ongoing, we expect a detailed update in Jan 2017, where evaluations will be made regarding progress to clinical trials.**

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.*

PROJECT COMMISSIONED BY THE SOHANA RESEARCH FUND. \$250,000 TOWARDS THE FIRST YEAR OF THE PROJECT FROM SOHANA RESEARCH FUND

**UPDATE:** Our sequencing study of mutations that arise in RDEB cancer has provided us with tremendous insight into how these terrible cancers develop. Our work shows that RDEB cancers are more similar, in many ways, to cancers in the general public which arise in the mouth, rather than those cancers that arise in the skin and which are caused by UV light. This observation may open new horizons to explain why RDEB cancers are very aggressive, because mortality rates in the general public are higher for cancers of the mouth compared with similar skin cancers. We've also discovered that mutation processes associated with microbial infection are enhanced in RDEB cancer which may lead to new ideas for cancer prevention. Finally, our data show that a number of pathways which can be targeted with new therapies are activated in RDEB cancer, and this study now provides rationale for pursuing these targets for therapy development. We are very grateful to the Sohana Research Fund for supporting this important study of RDEB cancer, which we believe has been extremely successful. We are now in the process of submitting the results of this study for scientific publication.



# RESEARCH

PROJECTS FUNDED BY SOHANA RESEARCH FUND

## NEW PROJECTS

### Stem Cell Regeneration of the Ocular Surface in Recessive Dystrophic Epidermolysis Bullosa

Aiming to establish a high-quality preclinical platform for therapy of corneal disease in people with RDEB. Goal is to develop a three-dimensional (3D) cornea with ABCB5-expressing limbal stem cells derived from induced pluripotent stem cells in which the RDEB-causing mutations in the type VII collagen gene have been gene edited using the CRISPR/Cas9 system.

**START DATE 1 JULY 2016. 2YEAR DURATION**

**\$250,000 per year**

### Gene Editing

Project agreements are in progress regarding a next generation genome sequencing project 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. More details to follow. 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>.

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>.

*New article in nature.com 8 Dec 2016* CRISPR/Cas9-based genetic correction for Recessive Dystrophic Epidermolysis Bullosa. <http://www.nature.com/articles/npjregenmed201614>.

### To follow Lenticol F

### Gene Therapy Lenticol M Work packages 2 and 3

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

**ESTIMATED £1.5 MILLION.** We are holding funding towards this trial.

**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**



Dr Andrew South



Prof Jakub Tolar, Prof Waseem Qasim & Prof John McGrath

## COMPLETED

### 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 VIA 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". Invest Dermatol doi:10.1038/jid.2015.158; accepted article preview online April 23, 2015.*

**UPDATE:** The use of MSC cells for clinical care is being discussed.

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

*Professor Jakub Tolar, University of Minnesota, USA.*

FUNDING FROM SOHANA RESEARCH FUND \$250,000.

**PROJECT OVERVIEW:** The goal of the project was to develop safer, more effective, individualised treatment options for children with EB. Developing a treatment based on a patient's own cells, corrected in the laboratory for the gene defect, and returned to the EB individual would have the advantage of the absence of 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. The project combined 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**

**UPDATE:** Professor Tolar is currently testing other gene editing techniques.

### 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.

## FOR FUTURE FUNDING

### Intravenous gene modified stem cell trial

Trial using gene modified MSC intravenously. Viral vector gene modification techniques.

### Gene editing

Pushing forward research here in the UK and at leading centres in the US, working towards a collaborative framework to accelerate progress. 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. Aiming for proof of concept clinical trials in 3-5 years. Increased funding will cut time estimates.

This in combination with iPSC technology.  
Clinical trial funding associated with the above.

### Bioreactor at Guy's Hospital (Kings College London)

Accessing an interim treatment. Costs associated with 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.

### Testing gene modified stem cell delivery systems

#### GMP facilities

Gene modification and gene editing requires space in GMP facilities. Often these are shared with other conditions and there is waiting list for available space. Ideally dedicated spaces would be created.

**Novel approaches to treatment which feeds into the concept of combination therapies;** reducing the likelihood of the terrible scarring that leads to severe deformities.

**Studying the aggressive malignant skin cancer** that leads to death among RDEB young adults and how to prevent and treat such cancers.

#### Biological skin substitutes Protein Therapy

Shire pharmaceutical bought up a promising protein therapy, which appears to have been shelved. Work is under way to find another candidate. Protein therapy would be a good treatment though is not expected to be curative.

## ADDITIONALLY

### Senior Lectureship in Dermatology

£500k for a 5 year Senior Lectureship post.  
*Provides a naming opportunity.*

### EB treatment suite

Guy's and St Thomas', King College London.



**“The Sohana Research Fund is our way forward as a family for helping to find a cure for RDEB. We cannot express enough how much we need this charity in our lives so we can take this horrific condition away from our children and give them a life free from pain which they so deserve.”** *Kerry White, Mum of Mason, age 7*

## FORTHCOMING EVENTS 2017

**28 FEBRUARY** Research Update meeting

**23 APRIL** Virgin London Marathon    **18 MAY** Silver Butterfly Dinner RIBA

**11 JUNE** On the Heath    **JULY** Vitality 10K London Run

**3 SEPTEMBER** SRF Family Day    **OCTOBER** Butterfly Brunch Club Speaks

**100% OF DONATIONS GO TO FUND RESEARCH FIGHT FOR A LIFE FREE OF PAIN. TO END EB. RESEARCH THE CURE**

**TRUSTEES** SHARMILA NIKAPOTA JAMES COLLINS MICHAEL DELATHAUWER TAZIM HALL PROFESSOR DAVID KELSELL

**PATRONS** DAMIAN LEWIS SEAN BEAN DANIELLE DE NIESE SIR JAMES & LADY DYSON

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