Research Strategy

Reverse Rett is a UK medical research charity working to speed treatments and a cure for Rett Syndrome. Rett Syndrome has already been reversed in the lab. We work to drive these promising lab developments into tangible treatments and a cure for people living with Rett Syndrome today.

Our Vision

Our vision is a world where girls with Rett Syndrome are diagnosed much quicker and earlier than they are at the moment. A world where we know much more about the progression of the condition and the factors that affect that progression. A world where at every stage of development, treatments are available to mitigate against the distressing symptoms which can occur, and ultimately a world where treatments are available which cure the condition and allow the girls to live normal lives.

Our Mission

Our mission is to speed treatments and cures for Rett Syndrome and related *MECP2* disorders by funding research that will have a practical and positive effect on our children's lives.

We fund research from basic science to clinical trials, and work to facilitate the translation of this work to clinical applications for people with Rett Syndrome and related *MECP2* disorders

Our Purpose

Reverse Rett exists to accelerate treatments and a cure for Rett Syndrome.

We fund international Rett Syndrome research through our longstanding partnership with the US based, Rett Syndrome Research Trust (RSRT) who are responsible for peer review and monitoring of those projects.

Our UK work has a translational impact with clear patient benefits. We work to ensure that as treatments and a cure for Rett Syndrome become viable, they are accessible to patients in the UK.

What is Rett Syndrome?

Rett Syndrome is the most physically disabling of the autism spectrum disorders. It strikes at random in early childhood, affecting little girls almost exclusively. Many girls live into adulthood, requiring total, 24-hour-a-day care.

There is no treatment beyond supportive, and often ineffective, measures such as feeding tubes, bracing, orthopaedic and GI surgeries, and medications for anxiety and seizures.

First recognized only 25 years ago, the prevalence of Rett Syndrome equals that of Cystic Fibrosis, Huntington's and ALS but is vastly underfunded in comparison to those disorders.

What causes Rett Syndrome?

Rett Syndrome is most often caused by mutations in a gene called *MECP2*, on the X chromosome.

This gene makes a protein, also called MeCP2 (but written differently), which is necessary for normal brain function. We know from the reversal experiments of 2007, that when this protein is replaced at adequate levels in mice, the symptoms of Rett Syndrome go away.

It wasn't until 2013, that researchers found a tangible way to translate those original reversal experiments into something that could potentially work in a human with Rett Syndrome; gene therapy.

Our Work:

Reverse Rett has one clear goal; to accelerate treatments and a cure for Rett Syndrome and related *MECP2* disorders.

- We fund lab research from basic science to clinical trials with a particular emphasis on projects seeking to replace the missing protein and transform lives.
- We work to facilitate the delivery of emerging treatments for patients with Rett Syndrome and *MECP2* disorders in the UK so that the distressing symptoms of these disorders can be addressed as quickly as possible.
- We run the only current national Rett Syndrome Patient Registry in the UK.

International Research funding

Reverse Rett works in collaboration with the US based Rett Syndrome Research Trust (RSRT) and other organisations internationally, to compound a global effort to accelerate treatments and a cure for Rett Syndrome and related MECP2 disorders.

Since 2010, Reverse Rett has made quarterly contributions to existing RSRT projects, which have undergone RSRT's rigorous peer review process and review by the RSRT Scientific Advisory Board.

UK Funding

Within the UK, we aim to use funds deployed nationally in ways that will have the maximum practical and positive effect on the lives of patients with Rett Syndrome in the UK, with particular regards to their ability to access emerging treatments.

New projects will be assessed against our project selection criteria to ensure we focus on activities that make the best use of our funds.

All new projects must fall within the scope of our purpose and must pass a stage 1 assessment before progressing to stage 2.

Project selection criteria

Stage 1 Assessment (Gateway questions)

1. What is the specific unmet clinical need being targeted?
2. How does the project fulfil this need?
3. Is the research underpinned by scientific excellence?

Stage 2 Assessment

1. How will the research help patients?
2. Has the right team been identified?
3. Why is this research needed now?

Our Research Review Committee

Our Research Review Committee comprises of a mix of industrial, academic and clinical experts.

The RRC is responsible for assessing applications and making recommendations to the trustees, ensuring that UK research funds are spent wisely.

The RRC is also asked to provide feedback and recommendations to the Trustees of the charity regarding:

- Development of the charity's research strategy
- External referees for applications
- Assessment of and final recommendations on applications
- Reporting and dissemination of research results.

Reverse Rett is committed to impartiality. The RRC comprises of a significant number of experts who are not in receipt of charity research

funding. The RRC has a Conflict of Interest Policy and those with a conflict are not in a position to influence funding decisions.

Criteria for funding UK research

Reverse Rett will fund research which supports the basic principles enumerated in this document.

Reverse Rett does not invite applications on a rotational basis.

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