

**ACTION  
FOR A-T**



**Action for A-T**  
**RESEARCH STRATEGY**  
**2014-2016**

**‘There is considerable hope...it is just a matter of time and money’**

Professor Gatti, Professor at UCLA, California. Project starting 2014- developing a new model for testing drugs to treat A-T. The main aim of the project is to develop ‘read through’ compounds to treat individuals who have A-T caused by nonsense mutations (estimated to be around 30% of individuals affected by A-T). A research project funded by Action for A-T.

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**‘In the UK, and due to its National Clinic, Nottingham researchers are able to pull together more children with A-T to involve in the study than would be practically possible anywhere else, leading to the biggest study of its kind for A-T in the world.’**

Dr Dineen, Clinical Associate Professor at the School of Medicine at the University of Nottingham, UK. Project starting 2014 - the CATNAP study (the Children’s Ataxia Telangiectasia Neuroimaging Assessment Project). The main aim of the study is to develop biological markers which will measure the underlying disease process and help to assess whether future treatments work. A research project jointly funded by Action for A-T and the A-T Children’s Project.

## INTRODUCTION

### Why was Action for A-T established

Anyone who has a child diagnosed with Ataxia Telangiectasia (A-T) realises immediately and agonisingly that their lives will be changed forever, that the future holds a number of very difficult challenges for their child both physically and emotionally. Founded in January 2012 by parents of a child diagnosed with A-T, Action for A-T understand what that feeling is like and is committed to making a difference to those affected by funding high quality medical research.

In the UK, the amount of funding provided for research into A-T is very limited. Action for A-T was therefore established as a medical research charity to increase investment in A-T research and work to help push forward our mission.

### Mission

To fund medical research to speed up the process of identifying a cure for Ataxia Telangiectasia (A-T) or treatments that delay or prevent the disabling effects of this devastating childhood condition.

### Vision

A future where the effects of A-T are minimised.

We passionately believe that with increased funding and continued global and collaborative effort, effective treatments for A-T will be developed and the lives of those affected will be changed.

### Focus

We provide a dedicated funding stream for medical research. Our sole focus is to raise funds for this purpose and awareness of A-T. Over the last few years, we have become the leading charitable funders of A-T medical research in the UK.

## ABOUT A-T

**What is A-T?** A-T (Ataxia-Telangiectasia) is a rare, genetic and degenerative childhood disease that affects multiple systems of the body. Those affected with A-T lack the ATM gene, a gene that contains the instructions to make the A-T protein. The A-T protein controls the rate in which cells grow, divide and repair themselves. It also plays a vital role in regulating the immune and nervous systems.

**What are the signs and symptoms of A-T?** A diagnosis of A-T comes as a huge shock. There are no indicators at birth and most children with A-T appear 'seemingly healthy' in line with their peers in early childhood. The first signs of A-T are neurological: poor balance (ataxia) being the most prominent where children are often described as 'wobbly'. Other signs that develop are deterioration of motor skills, involuntary movements, abnormal eye movements, and difficulty with speech. Further features that may affect some children are diabetes, premature greying of the hair, difficulty swallowing, drooling and slowed growth. The severity and range of symptoms vary in individuals.

**How does the disease progress?** Research on 'why' and 'how' the disease progresses continues as does research into ATM and ATM-related processes. We know that as a child gets older, some types of brain cells start to die. They lose neurons called the 'Purkinje' neurons which are located in the cerebellum, a region of the brain that plays an important role in motor control. This degeneration in the cerebellum means A-T is a neurodegenerative condition.

**How does A-T affect those diagnosed?** Health progressively deteriorates causing an overall loss of coordination and muscle control. Children are usually confined to a wheelchair by the second decade of life (around the age of 10) and will need assistance with everyday living. Children often lose their ability to write, speech becomes slower or slurred and reading becomes problematic due to difficulty in eye movement control. A-T does not affect the mind, there are no learning difficulties linked to having A-T and children and adults affected are neither intellectually or socially impaired.

Those affected with A-T are also predisposed to developing cancer (in particular acute lymphocytic leukemia or lymphoma) and a weakened immune system, many are susceptible to recurring respiratory and lung problems. A-T is also characterised by telangiectasia's (red "spider" like veins), which often appear in the corners of the eyes and a sensitivity to ionising radiation (X rays, for example).

Life span is shortened, usually by respiratory failure or cancer. A-T is life-limiting with those affected generally living until their twenties. **There is currently no cure for A-T and no treatments to slow down or stop the progression of this devastating disease.**

## RESEARCH WE FUND

Scientific and medical research is vital for increasing our knowledge on A-T. Action for A-T's objective is to fund high quality research projects that have the potential to lead to treatments and cures for A-T. We will consider funding research which aims to:

- advance our understanding of the underlying mechanisms that lead to A-T
- identify interventions which will stop or slow down the progression of A-T
- find ways to repair the damage done by A-T
- develop treatments that relieve and ultimately cure symptoms caused by A-T

All research funded must demonstrate to be of actual or potential benefit to those affected. We are particularly interested in pursuing basic science or translational research projects in relation to two areas that have the potential to achieve the greatest outcomes for people living with A-T:

### 1. UNDERSTANDING THE DISEASE

#### 1. Understanding the disease

The most devastating effect of A-T is on the nervous system. The progressive neurological deterioration experienced by children with A-T contributes most to their decreased quality of life. Despite advances in research, we still do not completely understand what processes are taking place in those who have A-T and why A-T is progressive. Understanding exactly what happens to the structure, function and development of the brain and the immunology of the disease will provide clues that could lead to the development of new therapies and therapeutic strategies that may bring the greatest benefits to A-T patients.

#### 2. Improving symptom management

A-T is a complex condition with a range of symptoms; the symptoms that cause mortality in those affected are lung infections and also cancer predisposition. Determining the mechanisms that lead to lung failure and cancer in A-T patients, developing improved ways to prevent, manage and optimally treat lung symptoms and cancer would be of significant benefit to A-T patients.

### 2. IMPROVING SYMPTOM MANAGEMENT

## HOW WE FUND RESEARCH

When Action for A-T was first established, we did not have the resources or experience to evaluate research applications ourselves. We developed a partnership with Sparks, a leading UK children's medical research charity and research we funded was managed through them. We used their internal peer review process in addition to external feedback from scientists with A-T expertise to evaluate research applications. We also co-funded research with the expert team at the A-T Children's project (ATCP) in the USA. We are now in a position to evaluate research applications ourselves whilst continuing to maintain our partnerships and jointly fund projects with others.

### Grant applications

We will have two grant round applications per year. One in **April** (managed through our partner, Sparks) and one in **October** (managed by Action for A-T). Grant round funding and deadlines will be advertised on the Action for A-T website and other websites. Research calls will also be sent out electronically to researchers.

Applications are considered for high quality biological science or translational research projects that may lead to treatments and cures for A-T from applicants in the UK and worldwide. Grants are usually awarded for one to three year projects. For application details and terms and conditions, contact [taniawheeler@actionforA-T.org](mailto:taniawheeler@actionforA-T.org)

Collaborative applications between the UK and other International Centres of Excellence are particularly encouraged.

We also retain flexible funding so that we can jointly fund research with others during the year and are able to respond quickly to important emerging information and techniques.

### Our research selection process

All research grant applications received are subject to an initial screening internally to check the research is within Action for A-T's remit. Successful research grant applications are sent for external peer review. We will identify external scientific experts to give detailed written feedback on research applications. A minimum of two external reviewers with scientific expertise in A-T and/or with expertise in the area of research proposed in the application are sought. Applicants are given the chance to read and respond to the external scientific peer reviewers' comments and all of this information – application, external reviewers' reports and applicant's response is given to our Research Advisory Committee (RAC) for consideration and assessment. The RAC is Action for A-T's internal peer review committee, made up of independent experts with a wide variety of expertise who assess applications and make recommendations for funding to the board of Trustees. The Trustees will make the final decision, based on the RAC's advice and the funds available. The Research Advisory Committee members and their terms of reference can be found on our website.

Grants will be reviewed and awarded within 4 months.

### Research evaluation

Funded projects are appraised through the evaluation of our annual reports. When research is conducted in the UK, our Research Coordinator will visit the research site where possible. The impact of the research we fund will be measured in terms of achievement against original research goals; publication in highly-rated journal of key research findings and review by peers at the end of a grant funding period. We will also collect the outputs of our research projects via Research Fish, an online facility that enables research funders to track the impacts of their investments, and researchers to easily log the outcomes of their work. Evaluating our research will help us continually improve as a charity.



## Core principles

Research we fund relies on the generous support of all our fundraisers - the public and the family and friends of those affected by A-T who commit their time and efforts to raise vital funds for us to invest in research. We take the responsibility of spending those funds very seriously and work to three core principles:

**1. Peer review** - all our research applications are subject to peer review as outlined above. Peer review is an integral part of our decision making process enabling us to fund the best researchers and the projects with the most promise of making a breakthrough.

**2. Conflicts of interest** - Action for A-T make every effort to ensure that its decisions are fair, objective and transparent. We have a strict conflict of interest policy for external reviews, internal reviews and our board of Trustees.

**3. Working together** - Working with others is a key part of our strategy. We believe that collaboration and partnership is fundamental in the small A-T community. By sharing resources, knowledge and experience we can accelerate the pace of research, save time and money. None of which we can afford to waste.



## OUR FUTURE DIRECTION

This is our first research strategy which we will continue to develop over the next two years, in order to highlight initiatives and enhance our strategy, processes and the way in which we work. We will particularly focus on four areas to further enhance our strategy in 2016/2017. When we review, we will look at the direction of our future research funding, taking into consideration the experience we have gained, the results and impacts of previously funded studies and the wider context of global research into A-T.



For further information:

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