Research Strategy

The Society's aims are set out in its mission statement, which is:

> **To improve quality of life and quality of care for people living with A-T while actively promoting research to lengthen lives and ultimately bring about a cure.**
>
> One of the ways we do this is by:
>
> **Promoting and funding high quality A-T research**

This strategy sets out how we aim to achieve this.

The challenges of A-T research

There are a number of particular challenges to be overcome if A-T research is to move forward.

Clinical research lags behind lab-based research

While significant progress is being made in research at the molecular level into the ATM gene and protein, there are major gaps in our basic understanding of the aetiology and development of A-T as a condition. For example we don't properly understand the mechanisms underlying the progressive neurological deterioration or the development of lung disease, which is such a major cause of death.

Much of the progress which is being made is driven by interest in the role of the ATM protein in cell regulation and DNA repair and in particular how these relate to the development of cancer. This is of great interest both to academic institutions and bio-technology and pharmacological companies and funding is comparatively healthy. Research into A-T as a condition, by contrast, is fragmented and for the most part poorly funded.

Rarity

For most of those who are involved in researching the condition, whether full-time researchers or clinicians with a research interest, A-T is only a part, often a small part, of their work. This is largely due to the rarity of the condition. The most reliable estimates for the number of people with A-T, in the UK at least, is 3 per million.

As a result many clinicians see few patients and those that see more, tend to see them infrequently. This makes it difficult to build up a systematic body of data on the clinical progression of the condition. These clinicians, too, may have little time to devote to finding out about and keeping up with other A-T research and to the time-consuming formalities which go with planning, carrying out and documenting research. Funders, too, may be unwilling to support research which will help such a small number of people.

Complexity
Another problem is the complexity of the condition, which presents challenges to a number of different medical specialities: genetics, neurology, immunology, respiratory medicine, cancer-treatment, in particular, but also endocrinology, ophthalmology, orthopaedics and so on. This can lead to the situation where many experts have a 'partial' expertise but few are expert on all aspects of the condition and how they interact. As a result, while progress is made in some areas, others may lag behind or be missed.

Need for co-operation
The rarity and complexity of A-T bring other problems. A range of different studies may need to be carried out on the same small group of patients. There may also be problems in organising trials that produce statistically valid results. To do this may require that research is carried out across different countries, which is likely to increase the costs and complexity of the project as well as raising issues of research governance.

Funding
Funding is also an issue. The scarcity of patients means that there is little motivation for pharma companies to invest in A-T research. There are a handful of 'charitable' organisations around the world which raise money for A-T research, but these are mostly very small, run by volunteers and tend to provide funds reactively, often to support locally-based researchers. The main exception to this is the A-T Children's Project in the USA whose principle objective is to support A-T research and which regularly supports a variety of different projects.

The role of the A-T Society

Over the last 7 years, the Society has directed approximately one third of its expenditure to research, on average a little less than £50k per year. While this is a reasonable proportion of income compared to other similar organisations[1], we would like to see the proportion increase and, as we aim to raise our overall income, we hope this will significantly increase the funds we invest in research in years to come.

Nevertheless, this remains a 'drop in the ocean' in terms of the funding required. It is therefore important to us that we use our limited contribution strategically, in ways that will give it the biggest impact. For us this means prioritising efforts to overcome the challenges set out in the previous section.

Key to this will be working to achieve greater co-ordination and effectiveness of the current research effort. At the same time we will aim to draw in new researchers and new sources of funding. It also requires us to be more proactive than we have been in the past, having a clear vision of what we need to achieve and stimulating and supporting research to do this. At the same time, though we must maintain the ability to react to new opportunities.

To achieve all this will require building new and stronger partnerships. We hope that this strategy, in its initial form at least, will be instrumental in helping us to do this. It is our aspiration

[1] The following figures give the percentage of all spending assigned to research in the latest published accounts: Muscular Dystrophy Campaign, 10%, MS Society 12%, Parkinson's, 22%, Prostate Cancer Charity 30%, Cystic Fibrosis Trust 38%, Ataxia UK 48%

that the Society's research work will eventually be part of a wider international 'strategic co-operation' to understand, treat and ultimately 'cure' A-T.

Our research objectives

There are two overriding strategic aims for our research programme:

- **to develop new and improved treatments which will help people with A-T live longer, with better quality of life**
- **to bring about a cure**

However, in order to achieve these two aims, we recognise that we need to add a third:

- **to gain a better understanding of the mechanisms of A-T**

We will only fund research which contributes directly to achieving these aims and while we will give consideration to supporting any research which does so, we will focus our support on clinical and translational research and in particular the collection of clinical data to develop new treatments and drugs.

To ensure that we make the most effective use of our resources, we have established three priority areas set out below. However, we do not intend to limit ourselves completely, and will be willing to consider promising proposals which do not fall into one of these categories, but help to deliver our aims.

Priority 1

Understanding the mechanisms underlying the development of AT

There are many significant gaps in our knowledge of how A-T develops and the mechanisms underlying the symptoms and pathologies of the condition. Understanding these is essential if we are to be able to develop effective treatments. We will support research which contributes to this, including but not limited to:

- The collection of systematic data about A-T patients, their symptoms and outcomes
- Establishment of a register of people with A-T in the UK
- Studying the links between genotype and phenotype
- Longitudinal studies, e.g. of the nature and course of lung disease or neurological deterioration
- The use of new imaging and other techniques to study the processes of disease development
- Studies of less-well understood characteristics or symptoms of A-T such as scoliosis or endocrine disorders
- Analysis of the links between A-T and other conditions such as diabetes, premature aging and osteoporosis.
- Identifying disease markers to predict or measure progress of the condition.

Priority 2

Understanding, treating and preventing lung disease
Almost all people with A-T that do not die of cancer, die of lung disease. However there is no single form of lung-disease associated with the condition and much is still unknown about its aetiology and development. Progress in preventing or treating lung disease would potentially have a significant impact in improving the quality and length of life of people with A-T. A multidisciplinary workshop on pulmonary disease in A-T, held in Baltimore in 2009 and written up by McGrath-Morrow et al, set out a wide-ranging agenda for research into lung disease. It is a priority for us to ensure that as much as possible of this research gets carried out, including but not limited to:

- Characterising more accurately the origin and pathology of the different forms of lung disease found in A-T
- Identification of the pathogens particular to A-T infections
- Examination of the effectiveness of different drug and treatment regimes, including different forms of antibiotic, immunoglobulin, steroids, vaccines
- Improving the testing of lung-function and identification of markers to improve the early identification of lung disease,
- Evaluation of the most effective forms of non-radiographic or low-dose imaging studies
- Evaluating the impact of physical therapies and training or exercise regimes on lung-health
- Research to determine the optimal modes for providing ventilation in peri-operative and critical care

Priority 3

Improving the infrastructure in A-T clinical research
Research into A-T and clinical research in particular is fragmented and poorly funded, depending as much of it does on clinicians for whom A-T is only part of their work. We aim to make it as easy as possible for those interested in A-T research to keep abreast of work elsewhere, reducing duplication and maximising opportunities for cooperation. We aim to encourage new researchers and new resources to support A-T research. We will also seek to provide support in overcoming the administrative and practical barriers to research. We will achieve this through:

- Establishment of and support to international A-T Clinical Research Network
- Establishment of and support to series of international A-T Clinical Research Workshops
- The development of an international register of people with A-T, both as tool for increasing our knowledge or A-T and as a way of identifying people for research projects
- The development of methods of measuring the progress of the condition and thus the impact of treatments

- Ensuring that clinical researchers in the UK have access to the resources they need to carry out their research, including administrative support
- Encouraging new researchers to focus on A-T and fostering new partnerships with and among researchers interested in related fields or conditions which will take forward our understanding of or ability to treat A-T
- Enabling international co-operation in trials and clinical research projects where this is necessary to enable progress to be made

How will research be funded?

The Society is prepared to consider a range of different types of funding. These are:

Project funding: full or partial funding for particular research projects, usually for up to two years but potentially for up to 3 years, contingent on satisfactory progress being made.

Studentships or **Fellowships:** the Society will consider funding or contributing to PhD studentships or research fellowships. As these require a significant ongoing commitment of funds, they will need to demonstrate that they are likely to make a significant contribution to one of our research priorities.

Equipment grants: to enable the purchase of otherwise unavailable equipment necessary for A-T-related research

Research support grants: the Society will consider making small grants to cover support or administrative costs, to enable research to be carried out, written up or disseminated where these are necessary and cannot be covered in any other way

Travel grants: a limited number of travel grants may be given to enable the attendance at important international research events of professionals engaged in A-T research, where this would otherwise not be possible

Whatever the form of funding requested, applicants will have to demonstrate how their proposal, if agreed, will contribute to taking forward this strategy.

As set out elsewhere in this strategy, we give great importance to the building of partnerships in promoting and supporting A-T research. Where possible, and where it will not unduly hold a project up, we will look to involve other organisations in joint funding.

All Project funding grants and Studentships or Fellowships will be subject to Peer Review as will Equipment grants of over £5,000. A condition of all grants will be that the grant-holder subsequently provides a report in lay-language, setting out the impact that the grant has had.

While the Society has a particular responsibility to support and promote A-T research in the UK, our over-riding aim is to achieve the objectives outlined above for the benefit of all people with A-T. We are therefore happy to consider applications for support from anywhere, as long as they demonstrably take forward this strategy.

Timescale for the strategy

This is the Society's first proactive strategy and we recognise that it will evolve over time. Initially, it will be reviewed once a year by the Society's Scientific Advisory Board and appropriate changes made. In time it may be possible to extend the period before review.