

# 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, facilitating and funding high quality A-T research**

This strategy sets out how we aim to achieve this.

## 1. The role of the A-T Society

The A-T Society is unique in the world in both providing a professional information and support service to people with A-T and their families and also funding and promoting bio-medical research. While this means we have to divide our available funds between these two areas, it also gives us great opportunities to bring together researchers with families and clinicians.

Over the last 7 years, the Society has directed nearly one quarter of its expenditure to research, on average £81k per year. While this is a reasonable proportion of income compared to other similar organisations, we would like to see the proportion increase and we aim to significantly increase the funds we invest in research in years to come.

However, we have also done and continue to do much to promote A-T research in other ways and to bring families and research together. We work actively with clinicians and researchers to encourage and nurture new projects, we play a key role in publicising and recruiting participants to studies and trials, we have organised and hosted workshops to involve families and get their input into research and we have done a lot to communicate to them what is going on in the world of research through a wide range of media and meetings.

## 2. Principles underpinning our research work

Given the relatively limited funds that we, and indeed all A-T research charities collectively, have available, coupled with the high cost of funding research, it is important that we use our contribution in a considered and strategic manner, in ways that will give it the biggest impact. To help us do this, the Society's Scientific Advisory Board has agreed a number of basic principles which will underlie our research work and the decisions that we make about this

### 2.1 *Working in partnership*

Working in coordination with other organisations will both enable us to maximise the impact of our work by drawing in other resources and also help improve the efficiency of the overall research effort. More resources can be directed at areas of particular interest or importance and

duplication of effort can be avoided, both very important when the field and the available funding are so limited.

We already have strong partnerships with some sister organisations and the international research community but we will look to strengthen these and to build relationships with other organisations beyond the immediate A-T field. The international A-T clinical research conference series and clinical research network that we run will continue to be key elements of this work.

## **2.2 Strategic focus**

Given the relatively limited funds available for A-T research, we feel it is vital that those funds are focused on stimulating and supporting research in those areas likely to have the biggest impact in developing treatments for A-T and its symptoms. The relatively low number of people with A-T means that these areas are those not well funded by the major research-funding organisations. These priority areas for research will be determined by our Scientific Advisory Board in consultation with people living with the condition. This means that we will usually be looking to fund projects in particular areas rather than having open calls for research projects.

Nevertheless, we also recognise that advances in research can come from surprising directions and we will remain open to using our resources to exploit new or unexpected opportunities.

Likewise, while our primary focus is on research aimed at improving treatments for the symptoms of A-T, we recognise that our current limited understanding of the mechanisms underlying these symptoms means that we may on occasions need to fund some more basic research.

## **2.3 Developing the A-T research field and infrastructure**

It is vital for A-T research that new researchers are encouraged to get involved with research into the condition and that those already working in the field are helped to feel that it is a rich and productive one. This serves both to expand the scale of A-T focused work as well as to bring in new ideas, energy and skills. Encouraging new younger researchers to take an interest in A-T is a particular priority given that a number of the biggest names in the field have reached or are about to reach retirement age.

The clinical research conferences and network are amongst the means that the A-T Society uses to support and encourage researchers, as are our annual Family Weekends, where we bring them together with people living with the condition and organise talks and consultation workshops. Other types of practical support and engagement that we offer, include:

- Organising/ funding meetings and conference calls
- Small grants for equipment or other resources
- Help with communications, patient-literature etc.
- Information about the condition or other research initiatives
- Engaging with people living with A-T for consultation or participation in research

### **3. Strengths of the A-T Society's research programme**

#### **3.1 *Engagement with large cohort of people with A-T***

In the UK, there are around 170 people living with a diagnosis of A-T and the A-T Society is in contact with almost all of them. We are also in regular contact with another 15 or so in the Republic of Ireland. This is the second largest contactable cohort of people with the condition, after the United States. For the majority of these people, our support team has a good knowledge of the individual, their family situation and how they are affected by the condition. This can be very helpful in identifying the areas where research is needed to improve the quality of life and in identifying individuals or groups for particular studies or trials.

Furthermore, round 1/3 of these people attend our annual family meetings each year, giving opportunities for direct consultation or engagement.

#### **3.2 *Engagement with specialist centres***

A particular strength of the UK is that nearly all people with the condition are seen by the single national A-T service, in which the A-T Society plays an active role. There are two dedicated National Specialist A-T clinics for children (Nottingham) and adults (Cambridge) that the A-T Society supports and administers. These offer internationally-important centres of expertise and cohorts for research studies. Natural history studies are already ongoing at the Children's clinic with funding support from the A-T Society.

Thanks to the work of Malcolm Taylor's laboratory at the University of Birmingham, also part of the national A-T service, mutations have been identified and lymphoblastoid cell lines established for almost the entire UK cohort.

#### **3.3 *Engagement with the international A-T research and clinical community***

The A-T Society has strong links with researchers and clinicians across the world. In partnership with our US sister organisation the A-T Children's Project, the Society leads the organisation of the biennial A-T Clinical Research Conference series which brings together leading figures in both fields to share information and ideas and plan improvements in treatment and new research initiatives. Between conferences, the community is kept in contact via the A-T Clinical Research Network and its e-bulletins.

The Society also has a strong track-record of assisting in trials and clinical research projects. For instance it is currently working closely with teams involved in two international A-T clinical trials the Erydex trial and the Intrabio trial. Both these trials have sites in the UK and we are working closely to assist at various levels, with study design, contact with regulators and in recruitment of participants to the trials.

### **3.4 Registry**

The Society has established an international registry to collect a wide range of clinical data on people with A-T and related conditions. The data is provided by clinicians rather than patients themselves and covers all the principal areas affected by the condition. While in its early stages, we are keen to develop this as an effective tool to support research and facilitate the organisation of clinical trials.

## **4. Research objectives and priorities of the A-T Society**

### **4.1 Long term aims**

There are two long-term 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**

We will only fund research which contributes to achieving these long-term aims and while we will give consideration to supporting any research which does so, recognising that there is much still to understand about how the genetic abnormality gives rise to the different aspects of the condition, we will give precedence to clinical and translational research and the collection of clinical data to push forward the development of new treatments and drugs.

To ensure that we make the most effective use of our resources, we have established a number of research priorities, which are 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.

### **4.2 Research priorities**

The main priority area for research identified by the A-T Society's Scientific Advisory Board is:

**To better understand and develop treatments for the neurological symptoms of AT.**

This decision was based both on the fact that this is the aspect of A-T that most strongly affects quality of life and on the desire to focus our research effort in order to maximise our impact. In making the decision, the Board reviewed the current research landscape and where resources are already being directed.

#### **Key areas of focus for research:**

Within this overall aim, there are a number of more specific objectives that we are particularly interested in:

- the development of good well characterised cell model systems for pre-clinical studies and to assess neurodegeneration

- to understand the molecular defects causing neurodegeneration in AT and gain an understanding of how ATM-deficient neurones die in order to accelerate the development of targeted drugs
- the development of new biomarkers to be used to improve the success of trials and to assess AT neurodegeneration
- new or improved strategies for the treatment of neurodegeneration in A-T

In achieving the above, we have a particular interest in whether or how an understanding of neurodegeneration in closely-related disorders may contribute to an understanding of the mechanisms of in A-T.

A second priority area is:

**To better understand the occurrence of cancer in both A-T individuals and also heterozygous carriers of the ATM gene in order to improve surveillance and diagnosis and to improve treatments and outcomes.**

## 5. 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, and will be supportive of applications involving co-funding.

All Project funding grants and Studentships or Fellowships and equipment grants over £5000 will be subject to Peer Review and assessed according to good practice set out by the Association of Medical Research Charities (AMRC), of which the A-T Society is a member. The AMRC regularly audits its members and the A-T Society successfully passed the latest audit. 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.

The A-T Society has a role in disseminating information about research and clinical trials to people with A-T, giving them the opportunity to take part in studies and trials where relevant. The Society will also facilitate and promote the collection of samples from people with A-T as these are a very useful resource for research. These include tissue samples from individuals and brain samples for Brain Banks.

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