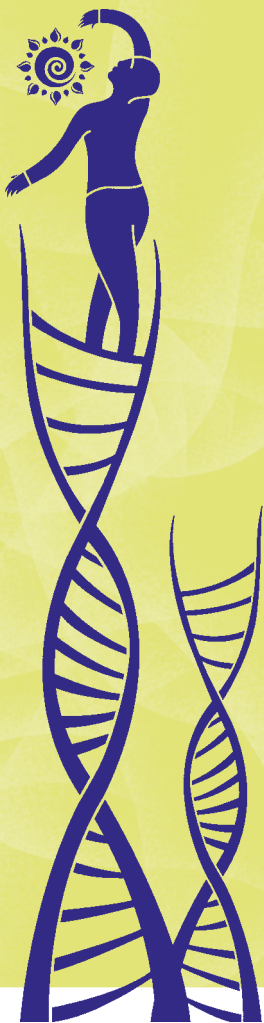


TAKING PART IN ALPHA-1 RESEARCH

Help Us Find a Cure
Join the Alpha-1 Research Registry

FORGING PARTNERSHIPS FOR A CURE



INTRODUCTION

Significant research on Alpha-1 Antitrypsin (AAT) Deficiency over the past four decades has advanced our knowledge about the condition, also known as Alpha-1. Advances include understanding the genetics, related emphysema and liver disease, and treatments.¹ Increased research is necessary to find a cure for AAT Deficiency, develop new therapies and to improve existing treatments. Research will also help find better means of detecting the disorder, give us a better understanding of what causes emphysema and/or liver disease in just some people with the condition, and help us fully understand and improve the social and legal implications of having Alpha-1.

OVERVIEW OF RESEARCH STUDIES

Great progress in disease prevention and treatment has been possible through medical research. One of the most crucial aspects of this research is the participation of human subjects, i.e. people like you. The National Institutes of Health (NIH) defines human subjects as those living people from whom a researcher collects data or private information. However, it is important to note that taking part in a research study is a personal choice. It is entirely up to you.^{2, 3}

Research refers to a step-by-step approach, often called a study, used to create or add to current knowledge. A clinical trial is a study on people that is designed to answer questions about what does and does not work in medicine and other fields of research. Trials may answer questions such as:

- Does a new drug or treatment work?
- Is there a better way of administering an existing drug or treatment?
- Is a new approach for changing people's health behavior beneficial?

WHAT CAN I EXPECT IF I ENROLL IN A STUDY?

The first thing you will need to do is provide your informed consent. During this process, staff will explain the details of the study, address your questions or concerns, and then have you read and sign a consent form. This is when you should ask the research team to define any medical or clinical terms that you do not understand.

The consent form should state the reason for the study, name the sponsor, list the rules that govern participation, explain current knowledge about new drugs or treatments, address the risks and benefits that may be involved, explain other treatment options that you may choose instead of participating, and list the expected study activities. It should also state who is responsible for any related costs.

The consent form should provide information about keeping your identity private, plainly state that the decision to participate is entirely up to you and explain your right to drop out at any time. The consent form should also list contact names and phone numbers that you may call to learn more about your rights.

Once you have read and signed the consent form, you are considered enrolled and you may proceed with the outlined study activities. These may include interviews or surveys, medical tests, educational sessions, or the administration of certain treatments, etc.

Be aware that your participation may end for a number of reasons. Typical reasons may include that you no longer want to take part in the study, completion of the specified treatment, or that the treatment does not appear to work for you. The study may also be stopped because the treatment was shown to work well or to be harmful, or due to breaches of the study protocol.

TRIALS MAY GO THROUGH FOUR PHASES:⁴

- ☐ **PHASE 1** trials are performed to find out the safety of a new drug or treatment, and are helpful in finding the safe dose and in uncovering any potential side effects. Phase 1 trials are performed on a small group (20 - 80).
- ☐ **PHASE 2** trials are performed on a larger group of people (hundreds), and are designed to investigate whether or not a given treatment works. In a Phase 2 trial, safety is studied further.
- ☐ **PHASE 3** trials are performed in still larger groups of people, typically hundreds to thousands. The purpose of Phase 3 trials is to gain a more thorough understanding of a treatment's effectiveness, benefits, and range of possible adverse reactions. Most trials are randomized and blinded. Following a successful Phase 3 trial, FDA approval for marketing a treatment to the general public can be requested.
- ☐ **PHASE 4** trials take place after the treatment has received approval by the FDA. The purpose of Phase 4 trials is to see how well the approved treatment works in the general population, compare the treatment with other approved treatments and make further observations about possible negative or adverse reactions.

HOW IS MY PRIVACY GUARDED?

There is a federal law, the Health Insurance Portability and Accountability Act of 1996 (HIPAA), which provides safeguards to keep your health information private.

The informed consent that you sign should say how your privacy will be guarded and the information stored. Often, the information is kept in a password-protected computer or locked file cabinet with limited access. The informed consent should state:

- ☐ Who has access to your private information. Usually, access is limited to the study staff and sponsors.
- ☐ How long the information is kept;
- ☐ If and when it will be destroyed, and
- ☐ Whether any identifying information will be used in scientific papers or presentations.

WHO SPONSORS RESEARCH?

- ☐ The U.S. Department of Health and Human Services, which includes the National Institutes of Health
- ☐ Drug companies
- ☐ Biotechnology companies
- ☐ Not-for-profit organizations

WHO CAN PARTICIPATE?

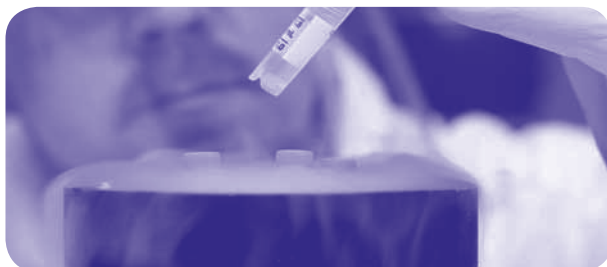
Each study has certain eligibility guidelines that govern enrollment. The guidelines help to ensure that the research addresses questions that can, in fact, be answered. Enrollment may be determined by the:

- ☐ Age and gender of the patient
- ☐ Family history of a given disease or condition
- ☐ Stage of disease or condition
- ☐ Treatments that a person must have had prior to enrollment or that may exclude their participation, or any combination of these
- ☐ Length of time since the last treatment
- ☐ Results of certain lab tests
- ☐ Participation in specific health-related behaviors (like exercising three times a week) or lifestyle choices (such as smoking)
- ☐ Use of certain drugs or treatments

Any person who meets the study criteria and is able to provide informed consent is eligible to participate. Informed consent is the process through which a person receives appropriate information, understands that information and agrees to participate. The ability to provide informed consent means that you:

- ☐ Understand the purpose of the research
- ☐ Know what your participation would entail
- ☐ Understand the risks and benefits
- ☐ Can weigh the risks and benefits against each other.

Remember, it is your choice whether to participate in a study.



GETTING INVOLVED IN RESEARCH

Research into Alpha-1 is conducted throughout the United States and the world. In addition to funding research grants, the Alpha-1 Foundation supports research by providing funding for four programs that serve both scientists and patients: The Alpha-1 Research Registry, the Alpha-1 Coded Testing (ACT) Study, the DNA and Tissue Bank, and the Genetic Modifier Study.

The Alpha-1 Research Registry is an information and data resource for both patients and scientists. Joining the Registry means that you will be notified of the opportunity to take part in clinical trials. To join, call 877-886-2383, email alphaone@usc.edu or visit the Registry website at www.alphaoneregistry.org.

The Alpha-1 Coded Testing (ACT) Study provides a free and confidential Alpha-1 test to people who participate in a research study. The Study investigates people's thoughts and feelings about the risks and benefits associated with learning genetic information. For more information, call 877-886-2383 or send an email to alphaone@usc.edu.

The DNA and Tissue Bank is a central storage facility for scientists who need biological material necessary for their research. For more information about donating to the DNA and Tissue Bank, call 866-284-2708 and use option 3 or email alpha1lab@medicine.ufl.edu.

The Genetic Modifier Study is searching for siblings who share the ZZ phenotype in order to understand the other genes involved in the presentation of Alpha-1. If you choose to participate, a researcher will visit your home to administer a breathing test, complete a questionnaire and collect blood. Call 617-525-2290 or email rejm@channing.harvard.edu for more information.

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IS IT SAFE?

There are many safeguards in place to ensure the welfare of people taking part in research. *The Belmont Report - Ethical Principles and Guidelines for the Protection of Human Subjects* provides the basis for the current laws governing human subject research. This report formed and outlined three ethical principles that apply to all research on people:⁵

1. **RESPECT:** This rule acknowledges dignity and independence. It calls for special safeguards for people who may be vulnerable or who have little independence, such as children. It also demands informed consent from all participants before they join the study.
2. **BENEFICENCE, MEANING KINDNESS OR CHARITY:** This demands that the study's expected benefits outweigh any harm that may occur. It also demands that researchers minimize the possible risks, and that they disclose if the same benefits are available through other means.
3. **JUSTICE:** This rule demands that study subjects be treated fairly. This means that they should be chosen with care to ensure that those who are vulnerable, such as prisoners, the elderly, or those with financial problems, are not consistently chosen or denied the right to enroll unless there are valid reasons for doing so.

An Institutional Review Board (IRB) is a group charged with guarding the welfare of research participants and making sure that federal rules are followed. An IRB is required to review all studies that involve people. IRBs are often made up of doctors, researchers and lay people. Any researcher who wants to conduct a study must submit a description or plan of action (also called the study protocol) for IRB review. The IRB then decides whether the study's benefits outweigh the risks that may be involved and whether the risks have been minimized. The IRB reviews the informed consent to make sure that it is correct, easy to understand, and explains the risks and benefits as well as other possible treatments or experimental protocols (which could include the use of placebo medications⁶).



FORGING PARTNERSHIPS FOR A CURE

WHY IS PARTICIPATING BENEFICIAL?

- ☐ To help advance scientific knowledge about Alpha-1. Progress can lead to better treatments and/or even a cure.
- ☐ To potentially gain access to new treatments not otherwise available to Alphas.
- ☐ To help you and others who are affected by giving scientists a better understanding of the disease.



HOW CAN I DECIDE WHETHER TO ENROLL?

Speak to the person in charge of the study, known as the Principal Investigator, or other research staff. Find out specifically what will be required from you in terms of time, effort, activities, and medical tests. Ask about the risks and the benefits, possible treatment options outside of those proposed in the study, and what compensation, if any, is being offered.

Discuss these options with your doctor, family, and friends to find out what they think. Their points of view may be helpful to your decision-making process.

Afterward, you will be able to weigh the risks and benefits of being in the study. Again, only you can decide whether or not you should participate.

About the cover illustration: This original artwork depicts the sun reflecting optimism. The human figure atop the DNA evokes the hope and expectation that research will lead to a cure for Alpha-1.



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ABOUT THE ALPHA-1 FOUNDATION

The Alpha-1 Foundation is a not-for-profit organization dedicated to providing the leadership and resources that will result in increased research, improved health, worldwide detection and a cure for Alpha-1 Antitrypsin Deficiency (Alpha-1). The leading experts in the field of Alpha-1 research collaborate with the Foundation through their participation on the Board of Directors, as members of the Medical and Scientific Advisory Committee (MASAC), directing Clinical Resource Centers, as members of Working Groups, or as participants at Foundation-sponsored scientific conferences and workshops. These experts, together with respected members of the Alpha-1 medical, professional, scientific, and patient communities, are teaming up with the Alpha-1 Foundation to identify the most critical areas of research and support the development of new therapies. Importantly, the Alpha-1 Foundation has also formed collaborative relationships with government and industry to promote needed research and create awareness of this genetic disorder.

ABOUT THE ALPHA-1 ASSOCIATION

The Alpha-1 Association is a member-based not-for-profit organization founded in 1991 to identify those affected by Alpha-1 Antitrypsin Deficiency and to improve the quality of their lives through support, education and advocacy. The Association has a network of over 60 volunteer-led support groups throughout the United States.

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