

# THE FAMILY GUIDE TO SMA RESEARCH



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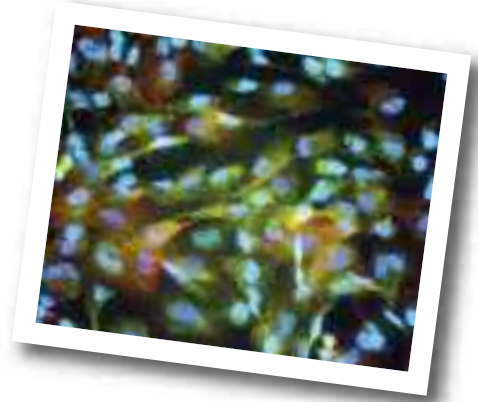
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# Introduction

## What is Spinal Muscular Atrophy?

SMA is often referred to by a number of terms, including "genetic disease", "autosomal recessive genetic disorder", "motor-neuron disease" or a "neuromuscular disease."



## SMA is a genetic disease

Genetic means relating to the genes. Each of us has about 25,000 genes that we inherit from our parents. These genes are responsible for the vast majority of our traits and our unique characteristics. In SMA, there is a mutation in a gene responsible for a protein that supports normal muscle movement and control of the limbs, abdomen, head and neck, chest and breathing muscles.

Researchers have a map of all genes in the body. They have been able to link SMA to chromosome #5 and a gene at this location called the "Survival of Motor Neuron" (SMN1) gene. It is the absence of or mutation in the SMN1 gene that causes SMA, which is the number one genetic cause of death in infants.<sup>1</sup>

## Acknowledgements

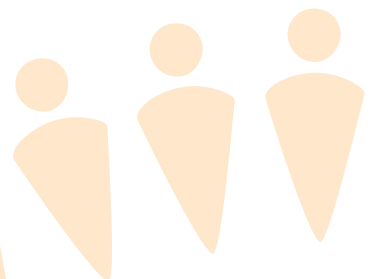
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## SMA is an autosomal recessive genetic disorder

Autosomal recessive refers to how the disease is inherited or passed down from the parents to their child. In SMA, the child who is affected by SMA inherits two copies of a mutated gene, one copy from each parent. While not typically affected by SMA, each parent carries a copy of the mutated SMA gene.



<sup>1</sup> See the FSMA booklet, *The Genetics of SMA* by Dr. Louise Simard for more background on genetic issues in SMA.



### **SMA is a motor-neuron disease**

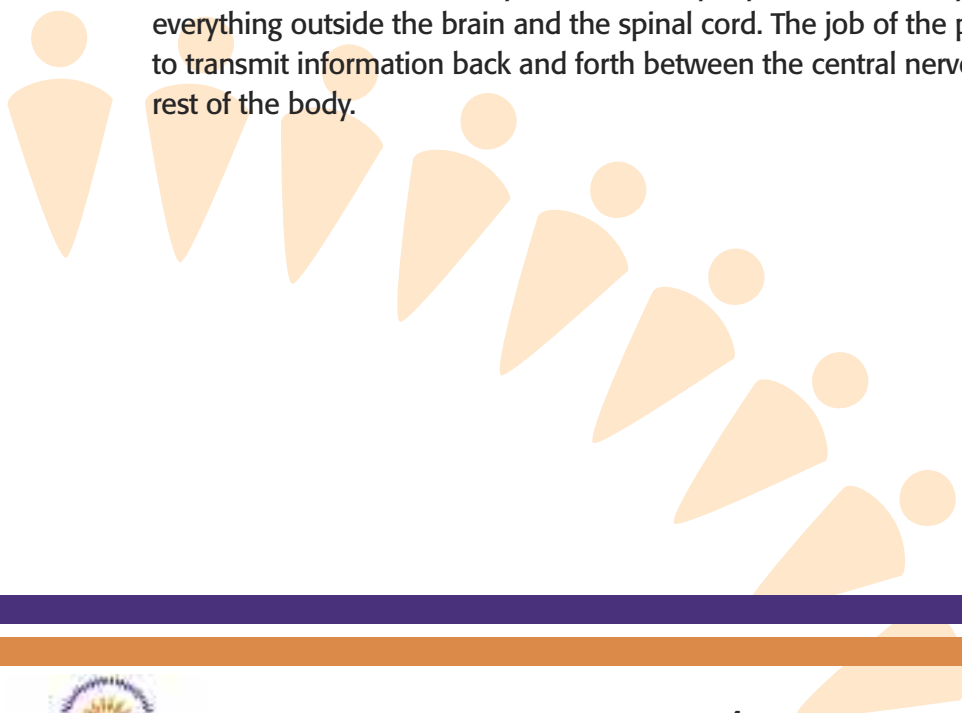
Motor-neuron refers to the type of neuron (or nerve) that is affected in SMA. A neuron is a nerve cell that sends and receives messages to and from parts of the body. A motor-neuron is like a wire that sends messages to and from muscles responsible for movement and control in the head, neck, chest, abdomen, legs, and limbs.



In SMA, the spinal motor-neurons do not have enough of a certain protein, called SMN protein. As a result, these motor-neurons do not function normally and may die, resulting in muscle weakness and atrophy (shrinkage).

### **SMA is a neuromuscular disease**

A neuromuscular disease (NMD) is a disease that affects the peripheral nervous system, which includes the motor neuron cell body (located within the spinal cord), motor neuron axons, neuromuscular junctions (the connection between the nerves and muscles), or the muscles themselves. The central nervous system includes the brain and the spinal cord. The peripheral nervous system includes everything outside the brain and the spinal cord. The job of the peripheral system is to transmit information back and forth between the central nervous system and the rest of the body.



## What are the key areas of SMA research?

### Basic Science Research

Basic science research looks at the fundamental building blocks of life, including molecules, proteins, cells and genes. Often referred to as “lab” or “bench” research, basic science research is carried out in a laboratory by researchers using microscopes and petri dishes. Other types of research, like *translational* research (see next section) or clinical research, are based on the findings and clues offered by basic science research.

Basic science research plays a critical role in the discovery and testing of chemical or biological materials that have the potential to become SMA drugs and therapies; and the identification of existing drugs with potential in SMA. Testing at this stage is conducted on proteins, cells, and in living animals, but not in humans.

Critical questions in SMA biology, including what is going wrong in the body to cause SMA, are answered by basic science research. It gives researchers many seed ideas or clues that lead to more advanced research.

### Drug Research—Translational Research

Drug research tests chemical and biological materials to see if they can be turned into drugs and therapies.

The National Institutes of Health (NIH) defines translational research as...*“the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans.”*<sup>2</sup>

This early phase is called the drug discovery phase. Researchers also work on drugs that are already approved for use in different diseases and conditions to see if they can help people with SMA.

### Two Major Classes of SMA Drugs

**FDA-Approved Drugs Used  
for Other Diseases.**

Re-purposed for SMA

**Novel Drugs-Not Yet  
Approved by the FDA.**

Designed for use in SMA

<sup>2</sup>From the NIH Roadmap: <http://nihroadmap.nih.gov/clinicalresearch/overview-translational.asp>



Translational research means taking something that we learn in one area of research and applying it to another area of research; as in applying the clues from basic research to the later stages of SMA drug making. Researchers are translating basic research discoveries from the laboratory into new drugs and therapies that can be tested in clinical trials with human subjects.

### **Clinical Research**

Clinical research is patient-oriented research, conducted with human subjects or human tissues. The investigator (the researcher) directly interacts with his subjects during the research project. Patient-oriented research can study a) the mechanisms (methods and parts of how something works) of human disease, b) therapeutic (used to treat disease) interventions, c) clinical trials, and d) the development of new technologies. (source: NIH)

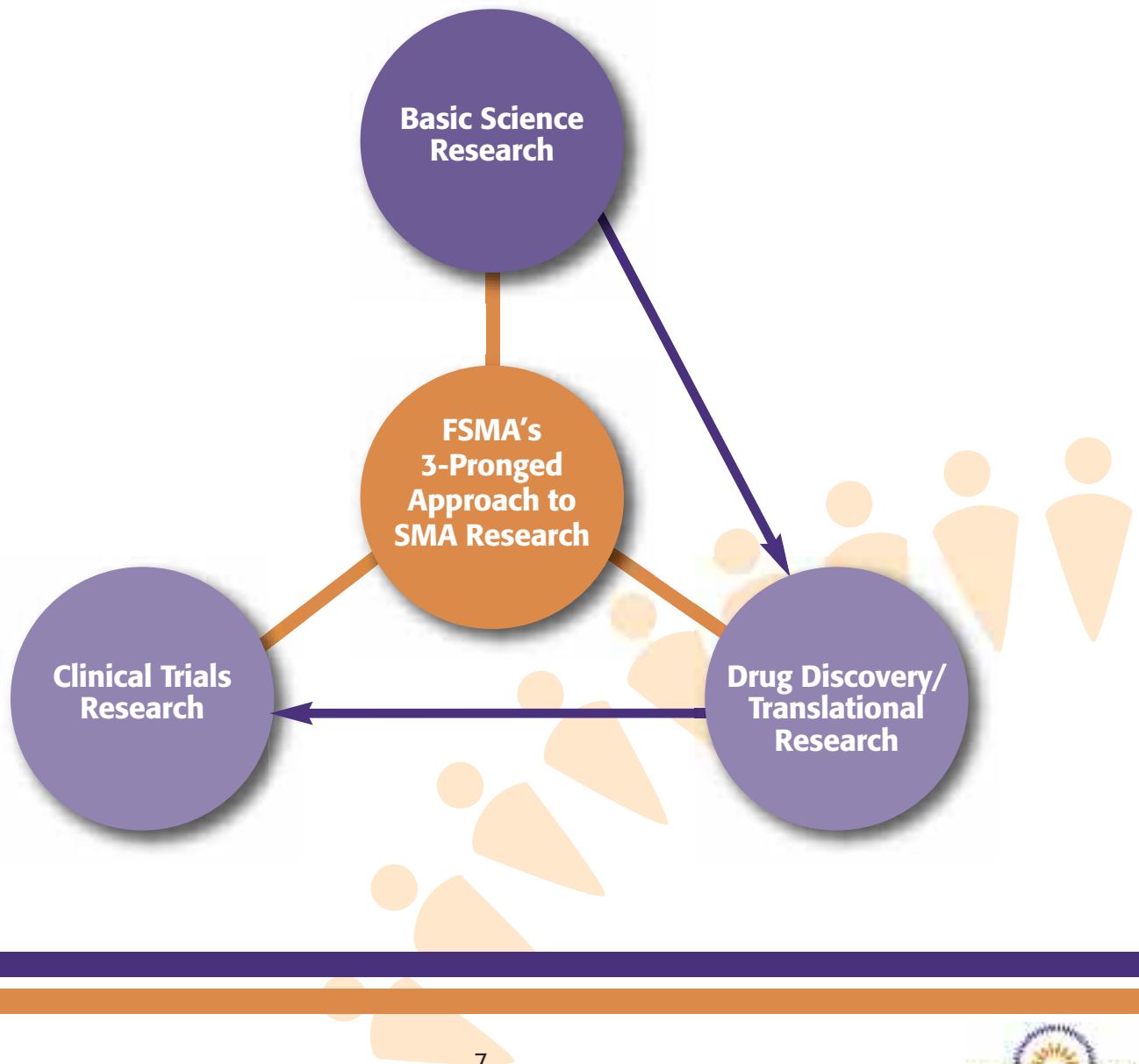


## What are FSMA's and FSMAC's research goals?

FSMA's main research goal is to accelerate the discovery of effective treatments and a cure for SMA, with a 3-pronged approach:

1. Basic Science Research to learn more about what causes and influences SMA at the most fundamental levels of life in the genes and DNA, in proteins, and in the cells of the body.
2. Translational Research to develop and then test chemical or biological materials in animal models of disease to see if they can work as SMA therapies.
3. Clinical Trials Research to study and test new treatments on human subjects.

**Graphic 1: FSMA's 3-Pronged Approach to SMA Research**



### **What are the major SMA research questions?**

Research questions define the unsolved mysteries of SMA and what causes the disease. Every research project involves one or more research questions. Some of the the leading research questions about SMA include:



### **What role does SMN protein play in causing SMA?**

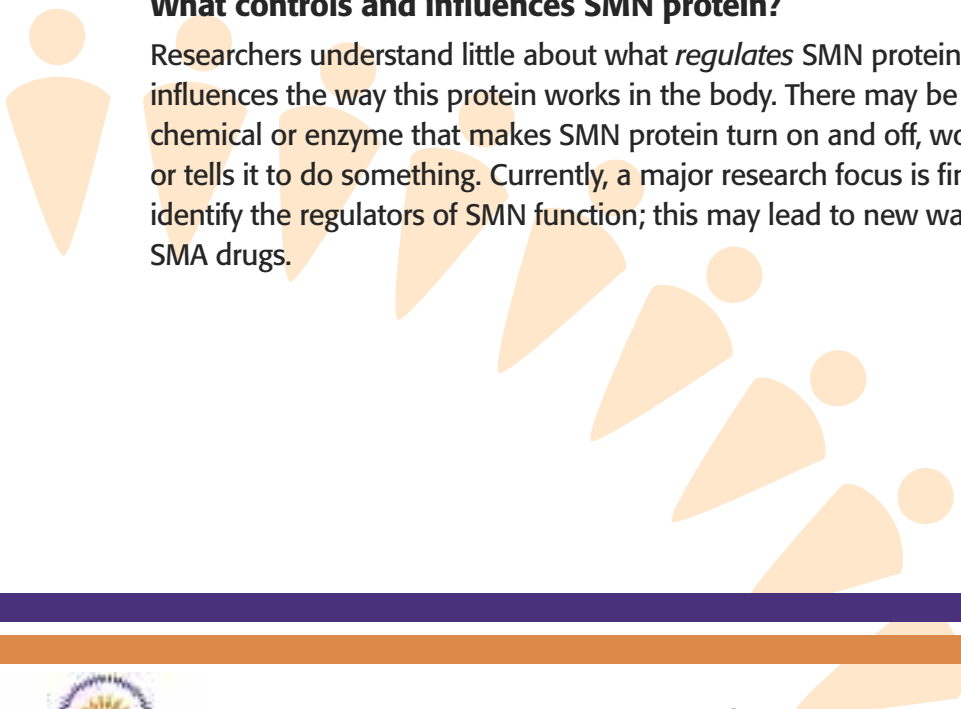
The SMN protein has multiple functions. Researchers still do not understand which of these functions is the most important in actually causing SMA. In addition, researchers do not know exactly what part of the SMN protein is needed for particular SMN functions. Therefore, they still do not completely understand the job that SMN protein performs in a healthy body. Put simply, it is unclear why and how SMN protein deficiency leads to the degeneration and death of motor neuron cells.

### **Is SMA only a motor-neuron disease?**

Researchers still do not know if there are problems in other areas of the body, like the bones and muscles, in people with SMA. A specific type of nerve cell called the motor-neuron is most affected in SMA. Recent studies have shown that replacing SMN solely in the nervous system can prevent most SMA disease symptoms. However, there are clearly problems in other organ systems in the body that may be directly or indirectly caused by SMN protein deficiencies.

### **What controls and influences SMN protein?**

Researchers understand little about what *regulates* SMN protein; that is, what influences the way this protein works in the body. There may be something like a chemical or enzyme that makes SMN protein turn on and off, work better or worse, or tells it to do something. Currently, a major research focus is finding ways to identify the regulators of SMN function; this may lead to new ways of making SMA drugs.





### What is the definition of a treatment?

A treatment for SMA could do one of several things. First, it could slow down the progression of the disease or how fast it develops. Secondly, it could stop the progression of the disease; this means to stop it from becoming any worse.

By definition, a treatment will only work as long as the treatment is given. It does not put an end to the disease or mean that the patient is disease free.

### What is the definition of a cure?

A cure means that the patient is disease free and able to function like someone without SMA. A cure can reverse the effects of a disease.

### What is the definition of prevention?

Prevention is a way to avoid an illness or disease from happening in the first place—as in preventing the flu by getting a flu shot or preventing polio with a polio vaccine. A treatment is used *after* someone has a disease or illness. Prevention or a preventive measure is used *before* someone has a disease or illness. It prevents the illness from starting in the first place.

### Approximate Costs of SMA Research

\$100,000	Cost of one basic research grant to one researcher per year.
\$2,000,000	Cost for a clinical trial to test a re-purposed drug for SMA.
\$10,000,000	Cost of taking a new drug candidate to the start of human clinical trials.

# SMA Researchers



## How many SMA researchers are there?

FSMA estimates that there are 300 to 400 individuals at the M.D. or Ph.D. level doing SMA research in the U.S., and about 600 researchers worldwide.

## Where do SMA researchers work and what is their training?

SMA researchers work in laboratories at universities and medical centers, in biotechnology and pharmaceutical companies, and in clinics.

SMA research is usually done by individuals with M.D.'s, and/or Ph.D.'s, or who are working toward their Ph.D.'s, often in the fields of genetics, neurobiology, biochemistry and cellular biology. M.D.'s are medical doctors who go to college, then medical school, then into residency and sometimes into fellowship programs. Individuals with Ph.D.'s go to college, then graduate school for 5-6 years, then do a post-doctoral research fellowship for 3-5 years, then take a job doing research in academia or industry.



# Drug Research

## What is the drug discovery and development process?

The goal of SMA drug research, and the drug discovery and development process, is to find a new chemical or an existing drug that will work as an effective treatment or cure for SMA.

Drug research includes many stages and phases. A drug candidate (a possible drug) needs to pass each stage before it can move on to the next.

Drug discovery refers to the process of how drugs are discovered and designed. This phase tests raw chemical compounds and turns the most promising chemicals into SMA drug candidates. Once a chemical compound passes the early tests, it moves into the drug development stage.

Drug discovery includes: **1)** identifying chemicals that could potentially work as SMA drugs; **2)** medicinal chemistry to turn these compounds into drugs; and **3)** the early studies in animals on the newly identified compounds. Medicinal chemistry refers to making many different versions of a chemical, each time trying to improve its properties as a drug.

Researchers usually screen thousands of chemical compounds just to find one candidate that has the potential to be a SMA drug. Currently, most drug discovery efforts in SMA focus on identifying compounds that can boost the amount of SMN protein made from the low-producing SMN2 back-up gene found in all SMA patients. Other programs focus on neuroprotective compounds that more generally prevent motor neurons from dying.

Finding answers to the following questions is part of the drug research process:

- Can the chemical compound reach a high enough concentration to do what it needs to do in the human body?
- Will it travel all the way up to the brain (cross the blood-brain barrier) and work effectively there?
- Can it be made into a pill, an injection, or into another acceptable form?

Drug research is a very high risk process. On average, 90% of neurological drugs fail to pass through all the clinical trial phases needed for approval by the Federal Drug Administration (FDA).

*See Graphics #2 and #3 for an explanation of the drug discovery and development stages.*



## Graphic 2: How SMA Drugs Begin...The Drug Discovery Process

### 1. Target Identification

Researchers try to identify targets in SMA. The targets are then used in the Assay and Screening steps ahead. In SMA, one example of a target is the SMN2 gene. Researchers want to find a chemical that causes the SMN2 gene to become more active and increase production of protein.

### 2. Assay Development to Screen Chemicals

An assay is a test used to screen various chemicals and chemical compounds to see if they are able to activate the target; for instance, activate the SMN2 gene.

### 3. Screening of Chemical Compounds to Find "Hits"

Compounds that pass the assay or screening tests are called "hits".

### 4. "Hit" Testing for Bioactivity

Hits undergo further testing (in petri dishes) to see if they have "bioactive" properties. This means, do they have the potential to work on living organisms and tissues?

### 5. Lead or "Hit" Optimization

Researchers create chemical relatives, like brothers and sisters, of the best performing "hits" to see if they work even better than the originals.

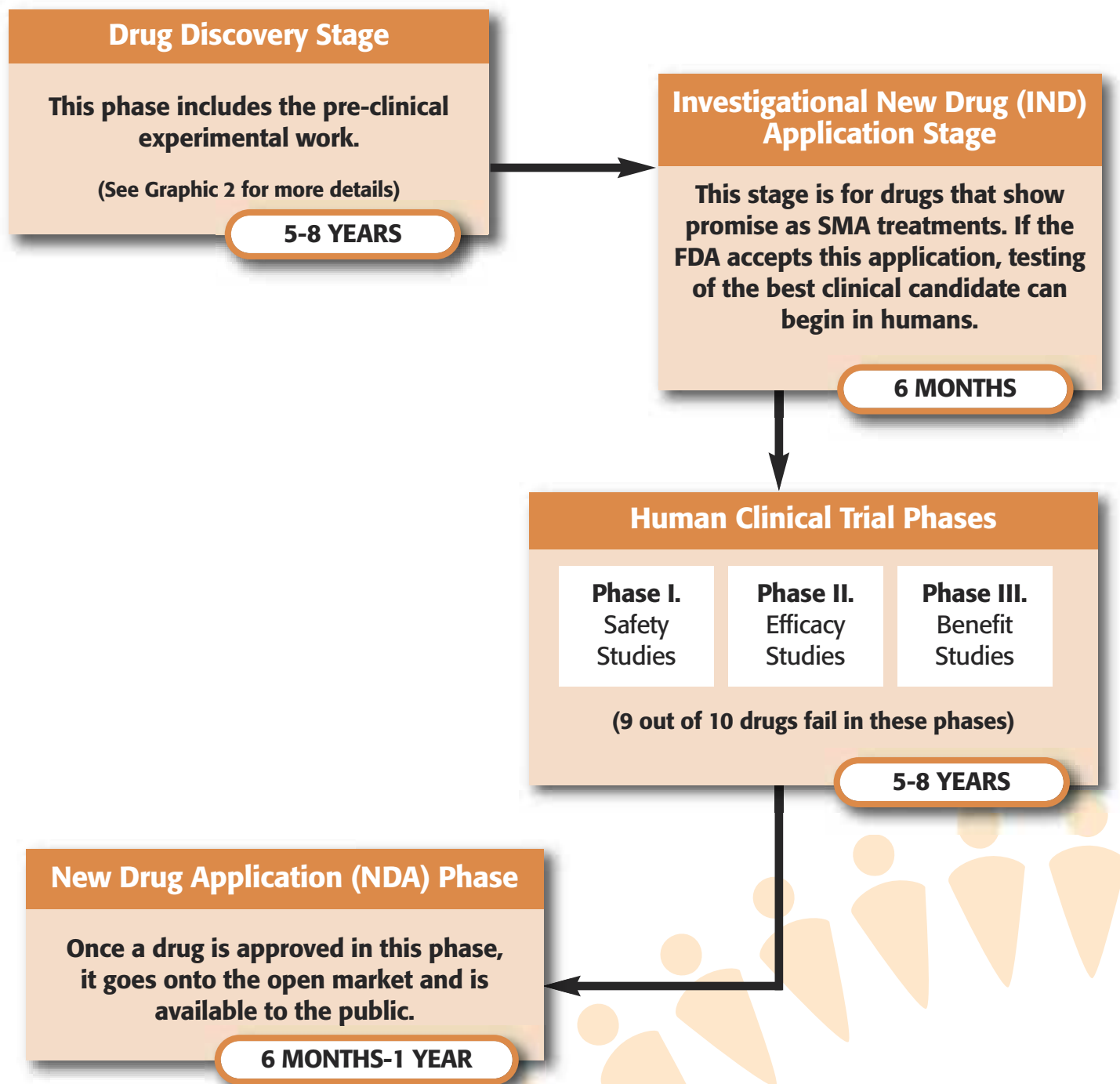
This helps the researchers find compounds with the most bioactivity, drug-like qualities, and best safety profile.

### 6. Safety Studies on the Best Hits

The lead or best chemical "hit" from Step 5 becomes a "clinical candidate" (possible drug). The drug goes through a series of studies that look at safety in animals. If this drug candidate passes the safety studies, it goes on to the IND phase (see next chart).

This flow chart shows the steps that researchers take before a drug can go into clinical trials with humans.

**Graphic 3: Stages of the Drug Research Process**



\* Approval of drugs for orphan diseases is sometimes shortened on a case by case basis.



## How long is the drug research process?

It can take 10-15 years for a drug to go through the entire drug development process and gain FDA approval for marketing. The time required for all three phases of human clinical trials can range from 5-8 years.

## What is the investigational new drug (IND) application stage?

This is a very detailed stage in the drug development process that requires meetings with the Federal Drug Administration (FDA). It is a part of the drug approval process that opens the door for clinical trials in humans. Bringing a drug to this point is considered a big achievement, it means that a chemical compound has been discovered that may be viable as a treatment and can be constituted into a drug for human consumption. Once the FDA accepts the IND application, the human clinical trials can begin.



## What is the human clinical trials stage?

The FDA requires three phases of clinical trials that involve human subjects. A new drug needs to pass all three of these clinical trials before it can be approved and released to the public. Each phase is designed to test different aspects of the drug.

The four phases of clinical trials for new drugs are called Phase I, Phase II, and Phase III, and Phase IV. *Please see the section on Clinical Trials for more details on each phase.* Some steps in the clinical trials process can be shortened for orphan diseases<sup>3</sup>, like SMA, and where there are no available drug treatments.

## What is a drug pipeline?

A “drug pipeline” is just a way of saying that we have multiple drug candidates moving forward at the same time. Because so many drugs fail when going through the different test phases, it is important to have new ones always coming up for consideration. With a drug pipeline, when one drug candidate drops out, another one will always be there.

A major goal at FSMA is to build a drug pipeline for SMA. This will increase the chances of successfully developing a treatment for SMA.

<sup>3</sup> Orphan disease: a rare genetic or infectious disease that affects less than 5 per 10,000 people in a particular country or region; and has a prevalence of fewer than 200,000 affected individuals in the United States.

# Gene Therapy

## What is gene therapy?

Gene Therapy is an approach to treating diseases by either modifying the expressions of an individual's genes or by correction of abnormal genes. Gene therapy works by administration of DNA rather than a drug. Many different diseases are currently being investigated as candidates for gene therapy. These include cystic fibrosis, cardiovascular disease, infectious diseases such as AIDS, cancer and SMA.<sup>4</sup>

## How can gene therapy work in SMA?

In the case of SMA, gene therapy could take several approaches. The most likely approach would be to replace the lost SMN1 gene in cells. A second approach could be to use small pieces of genetic material, called oligonucleotides, to improve the functioning of the back-up SMN2 gene. A third approach could be to use gene therapy to deliver neuroprotective proteins like growth factors to motor neurons to help keep them alive and well functioning.

The challenge with gene therapy for SMA is to find a way to deliver the genetic material to the spinal cord. In most cases, these materials will not cross the blood brain barrier. Currently, a number of viruses are being studied for their ability to safely and effectively carrier the genetic material across the blood brain barrier, where they will be needed to treat a disease like SMA.

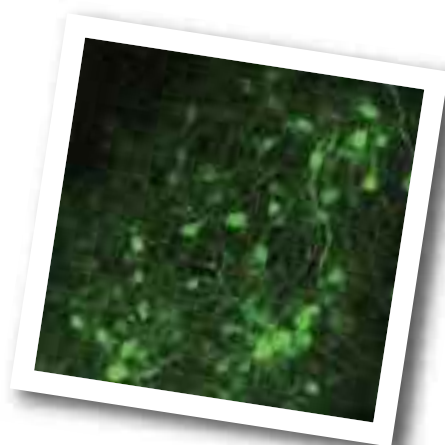
## What will it take to make gene therapy work in humans?

Currently there are no FDA approved gene therapy products in the United States. Gene therapy products are still being studied to assess their safety and efficacy in a wide variety of diseases. The main challenge in developing gene therapy approaches for all diseases is how to effectively deliver the genetic material into a human.

Gene Therapy and Cell Therapy are overlapping fields of research with similar goals. Gene Therapy can be defined as the use of genetic material to manipulate a patient's cells for the treatment of an inherited or acquired disease. Cell Therapy can be defined as the infusion or transplantation of whole cells into a patient for the treatment of an inherited or acquired disease.

<sup>4</sup> Source: American Society of Gene Therapy website at [http://www.asgt.org/about\\_gene\\_therapy/defined.php](http://www.asgt.org/about_gene_therapy/defined.php)

# Stem Cells



## What are stem cells?

Stem cells are living cells that have the remarkable potential to develop into many different types of cells in the human body. In many living tissues, stem cells serve as a kind of internal repair system. They are able to divide over and over again and replenish (rebuild, renew) other cells as long as the person (receiving them) is alive. When a stem cell divides, each new cell has the potential to remain a stem cell or become another type of cell with a more special function, such as a muscle cell, a red blood cell, or a motor-neuron cell.

## What are human embryonic stem cells (hESCs)?

Human embryonic stem cells (hESCs) are cells from early stage human embryos that have the potential to form the 200 different human cell types. hESCs can be grown in lab dishes, where they can continue to divide.

## What are adult stem cells?

Adult stem cells primary role is to maintain and repair the tissues in which they are found, which include tissues that have already developed. The most common source of adult stem cells is the bone marrow, a soft substance in the middle of some bones. However, adult stem cells can also be found in many other organs and tissues, including the brain, blood vessels, skeletal muscles, and skin. Like embryonic stem cells, adult stem cells may also have the potential to form into other types of cells. Researchers are actively exploring how adult stem cells work in the body and comparing their function to embryonic stem cells. (Source: International Society of Stem Cell Research, NIH Stem Cell Resource Information)  
<http://www.isscr.org/science/faq.htm>

## What are induced pluripotent stem cells (iPS)?

*Pluripotent* means many (pluri) potentials (potent). In other words, these cells have the potential of taking on many fates in the body, including all of the more than 200 different adult cell types. Induced pluripotent stem cells can come from skin or other types of adult cells that are treated and turned into pluripotent cells. These induced cells can be taken from skin tissue in a child or adult and modeled to become any stem cell type.

## What will it take to make stem cells work in humans?

Given their unique regenerative (ability to grow again) abilities, stem cells offer new potential for treating such diseases as Parkinson's, diabetes, heart disease, and SMA. However, much work remains to be done in the laboratory and the clinic to understand how to use these cells for *cell-based therapies*.

To realize the promise of novel (not yet approved by the FDA) cell-based therapies for debilitating diseases, researchers must be able to manipulate stem cells so that they have necessary characteristics.

Researchers will have to learn how to make stem cells do the following in order to successfully bring cell-based therapies, like stem cell treatments, to patients in the clinic:

1. Grow and multiply extensively and generate sufficient quantities of tissue.
2. Turn into the desired cell type.
3. Survive in the patient after transplant.
4. Become part of the surrounding tissue after transplant.
5. Function appropriately for the duration of the recipient's life.
6. Avoid harming the patient in any way.

Stem cells offer exciting promise for future therapies, but many technical hurdles remain that will only be overcome through more intensive research.

## How can stem cells be used in SMA?

Stem cells can be used in SMA for two essential purposes:

1. **To advance research.** Stem cells that are turned into SMA-like motor-neuron cells can be used for SMA research. Researchers can study these SMA motor-neurons to learn more about what goes wrong in them; and use them for testing new drugs that may correct the problems.
2. **As a therapy for people with SMA.** Healthy motor-neuron stem cells could replace defective motor-neuron cells in the body. These new motor-neuron cells could also help to provide support to sick motor-neurons, and make them function better.

# Clinical Trials

## What is a clinical trial?

A clinical trial is a study conducted to evaluate a new drug (or other treatment) with human subjects. With any new drug there are benefits as well as possible risks. Clinical trials help us find out if promising new treatments are safe and effective for patients.<sup>6</sup>

In the United States, an independent committee of physicians, statisticians and members of the community must approve and monitor the protocol. This is called an Institutional Review Board (IRB). They make sure that the risks are small and are worth the potential benefits.<sup>7</sup>

## What are the phases of clinical trials?

Clinical trials are conducted in phases. The trials at each phase have a different purpose and help scientists answer different questions:

In **Phase I trials**, researchers test an experimental drug or treatment in a small group of people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.

In **Phase II trials**, the experimental study drug or treatment is given to a larger group of people (100-300) to see if it is effective (does what it is intended to do) and to further evaluate its safety.

In **Phase III trials**, the experimental study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.

In **Phase IV trials**, post-marketing studies delineate additional information including the drug's risks, benefits, and optimal use. These studies are done after the drug has been approved and made available to the public.

For an orphan disease, trial size often can be smaller than the average numbers presented above.

<sup>6</sup> Sources for information in these sections on clinical trials: Basic Questions and Answers on Clinical Trials, U.S. Food and Drug Administration (<http://www.fda.gov/oashi/clinicaltrials/clintrialdoc.html>); and ClinicalTrials.gov, a service of the National Institutes of Health (<http://www.clinicaltrials.gov/>)

<sup>7</sup> Source: National Institutes of Health (NIH).







### **Who can participate in a clinical trial?**

All clinical trials have guidelines about who can participate that helps to produce reliable results. These guidelines are based on such factors as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. Before joining a clinical trial, a participant must qualify for the study. Some research studies seek participants with illnesses or conditions to be studied in the clinical trial, while others need healthy participants.

### **Who sponsors clinical trials?**

Clinical trials are funded by a variety of organizations or individuals such as physicians, medical institutions, non-profit organizations, foundations, voluntary groups, and companies, in addition to federal agencies such as the National Institutes of Health (NIH).

### **Where do clinical trials take place?**

Clinical trials take place in doctors' offices, other medical centers, community hospitals and clinics, in cities and towns across the United States and in other countries. Clinical trials may include participants at one or two highly specialized centers, or they may involve hundreds of locations at the same time.

### **Where can you find information about active clinical trials?**

You can search for clinical trials on your own at <http://clinicaltrials.gov>.

The FSMA website, [www.curesma.org](http://www.curesma.org) lists all active trials for SMA.

# Government Research on SMA

Multiple NIH groups fund SMA research. The main group is NINDS.

## What does the National Institute for Neurological Disorders and Stroke (NINDS) do in SMA?



The National Institute for Neurological Disorders and Stroke (NINDS) conducts research on SMA in laboratories at the National Institutes of Health (NIH) and also supports research through grants to major medical institutions across the country.

The NINDS believes that SMA is an ideal candidate for the development of targeted therapeutics for two reasons. First, because SMA is caused by a known gene mutation, and there is a known back up gene, there are easy to work with strategies for developing treatments. Second, SMA is the most severe of the common genetic neurological diseases and currently no effective treatment for SMA exists.

Here are examples of NINDS-funded research on SMA:

1. Basic research grants to university researchers;
2. Translational research grants to industry researchers working on SMA, like Paratek Pharmaceuticals;
3. The Spinal Muscular Atrophy (SMA) Project (see [www.smaproject.org](http://www.smaproject.org)), a collaborative program focused on the development of drug therapies for the treatment of SMA; and
4. Clinical trials in SMA, including the Neptune trial testing of sodium phenylbutyrate.<sup>8</sup>



<sup>8</sup> Source: SMA Fact Sheet, NINDS, National Institutes of Health

# U.S. Food and Drug Administration (FDA)



## What is the FDA?

The U.S. Food and Drug Administration (FDA) is an agency within the U.S. Department of Health and Human Services. The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

## How does the FDA address orphan drugs?

The term *orphan drug* refers to a drug that has been developed specifically to treat a rare medical condition. The condition is often referred to as an orphan disease. An orphan disease is a rare genetic or infectious disease that affects a relatively small number of people in the population.

According to the FDA, the term *rare disease* or condition means any disease or condition which (a) affects less than 200,000 persons in the U.S. or (b) affects more than 200,000 persons in the U.S., but for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such disease or condition will be recovered from sales in the U.S. of such drug.

Congress passed the Orphan Drug Act in 1984 and amended it in 1985 and 1988 to help improve the development and approval process for orphan drugs. The FDA runs the Office of Orphan Products Development (OOPD) and administers the OOPD Grants Program.<sup>9</sup>

<sup>9</sup> Source: FDA Office of Orphan Products Program Overview: <http://www.fda.gov/orphan/progovw.htm>

# FSMA's and FSMAC's Role in SMA Research

*See, also, FSMA and FSMAC Research Goals in the Introduction section.*

## How much research does FSMA fund?

Over the last 25 years, FSMA has funded \$50 Million in SMA research. These funds were generated through chapter fundraising events and private donations.

This funding has covered:

- More than 140 basic research grants at 70 institutions around the world,
- Two new drug discovery programs, and a motor-neuron (stem cell) replacement therapy for SMA,
- 5 clinical trials with existing drugs, and the SMA Clinical Trials Network, Project Cure SMA.

## How much does FSMAC fund?

Families of SMA Canada funds research right here in Canada. Funds are raised through fundraising events and individual donations. Since our inception in 2002, we have funded over 2.2 million in Canadian research projects. We work very closely with FSMA (USA), the same Scientific Advisory Board makes funding recommendations to FSMAC for research and trials held in Canada.

## What is the Scientific Advisory Board (SAB) and its role?

FSMA's Scientific Advisory Board (SAB) includes research experts who work in hospitals, clinics, biotechnology and pharmaceutical companies as professors, doctors, researchers, and company officers. Their expertise covers the fields of medical genetics, molecular and cellular biochemistry, motor-neuron biology, neurology, neuromuscular disease, and pediatrics.

The SAB directs FSMA's basic research agenda by setting directions and priorities; and organizes FSMA's Annual International SMA Research Meeting. Specifically, this group decides which research grants are funded in the FSMA grant application program. Each grant is assessed for its scientific merit and its alignment to the FSMA research goals. These goals include increasing the understanding of SMA disease pathology and accelerating the path to identifying a SMA treatment.



### What is Project Cure SMA?

Project Cure SMA is a Clinical Trials Network, developed in collaboration between Families of SMA and clinical investigators (researchers) in North America, including the U.S. and Canada. The Network includes 7 clinical testing sites at major universities and medical centers, and the entire supporting infrastructure needed to carry out multiple clinical trials for SMA. There are more than 30 professionals involved in Project Cure SMA in sites across North America. They are organized to facilitate the rapid translation of promising new therapies to individuals with SMA.

The network has conducted multiple clinical trials to date, including the Phase II CARNI-VAL trial in children with SMA type II and III, the Valiant Trial in ambulatory adults with SMA, and the CARNI-VAL Type I Trial in infants with SMA.

The existence of Project Cure SMA, and its ready-made network of clinical trial sites, is also very attractive to biotechnology and pharmaceutical companies looking to invest in SMA drug development.

### What is the SMA International Research Conference?

FSMA sponsors the largest Annual International SMA Research Conference in the world. Hundreds of dedicated researchers gather every June from around the world to share results and exchange ideas. This meeting fosters a spirit of cooperation and moves the entire SMA community closer to its goals of finding a treatment and a cure.



## Research Partners

Families of SMA partners and collaborates with researchers at universities, companies in the biotechnology and pharmaceutical industry, as well as government groups, to further SMA research and drug therapies.

Pharmaceutical and biotechnology companies develop and place drugs on the market that are licensed for use as medications, under the authority of the FDA (see the section on the FDA). Many laws and regulations on patents, testing, and marketing apply.

Historically, it has been difficult to attract major pharmaceutical companies to research projects on orphan diseases, like SMA, with small patient populations and consequently, small profit potential.

Families of SMA work hard to attract industrial partners (like pharmaceutical and biotechnology companies) to SMA drug research. We provide them with funding, research tools, and scientific expertise for the early phases of SMA drug development. Once they have the preliminary data, they are more able to use their own funding, including research funding from the federal government, for the later stages of SMA drug development.



# For More Information On Research

**FSMA website:** [www.curesma.org](http://www.curesma.org)

Research Section: <http://www.fsma.org/Research/>

(Find information here on basic research, drug discovery programs, stem cell research, Project Cure SMA, and more...)

**National Institute of Neurological Disorders and Stroke (NINDS)**

Spinal Muscular Atrophy Information Page:

<http://www.ninds.nih.gov/disorders/sma/sma.htm>

**Federal Drug Administration (FDA) Home Page:**

<http://www.fda.gov/>

**NIH Stem Cell Information Page:**

<http://stemcells.nih.gov/>

**NIH Clinical Trials Home Page:** <http://clinicaltrials.gov/>

(search here for clinical trials)

**NIH Genetics Home Reference: Your Guide to Understanding Genetic Conditions, What is Gene Therapy?**

<http://ghr.nlm.nih.gov/handbook/therapy/genetherapy>



# About Families of SMA Canada

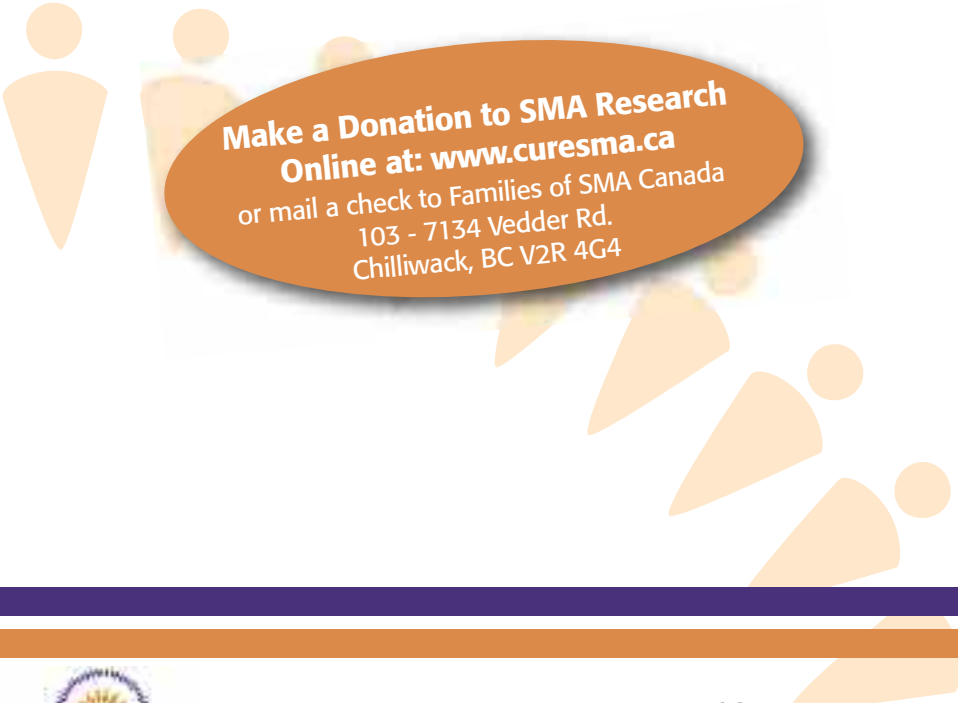
Families of SMA Canada is a non-profit organization dedicated to funding research and supporting Canadian families affected by Spinal Muscular Atrophy. We work closely with Families of SMA (USA) with a common goal of educating the public and professional community about SMA and networking families to gain mutual support. Our ultimate goal is to accelerate the discovery of an effective treatment and cure for Spinal Muscular Atrophy.



**Families of SMA Canada is dedicated to creating a treatment and cure by:**

- Funding and advancing a comprehensive research program;
- Supporting SMA families through networking, information and services;
- Improving care for all SMA patients;
- Educating health professionals and the public about SMA; and
- ***Embracing all touched by SMA in a caring community.***

**Our vision is a world where Spinal Muscular Atrophy is treatable and curable.**



**Make a Donation to SMA Research**  
**Online at: [www.curesma.ca](http://www.curesma.ca)**  
or mail a check to Families of SMA Canada  
103 - 7134 Vedder Rd.  
Chilliwack, BC V2R 4G4

# Contacting Families of SMA Canada

**Families of SMA Canada**

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Families of SMA Canada on the Web:  
<http://www.curesma.ca>

**Other booklets from Families of SMA Canada:**

- *Caring Choices: For Parents of Infants Newly Diagnosed with SMA*
- *Breathing Basics: Respiratory Care for Children with Spinal Muscular Atrophy*
- *The Genetics of SMA*
- *Understanding Spinal Muscular Atrophy*

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