

Recent Research Developments



Supported by the
Muscular Dystrophy
Association

MDA Research Advances Rapidly

This pamphlet lists highlights from among hundreds of major [research](#) breakthroughs made in recent years by MDA-funded scientists around the world. MDA, the world's largest private-sector supporter of research on [neuromuscular diseases](#), annually awards grants to nearly 350 physicians and scientists.

2009:

Injections of Utrophin Help Mice Missing Dystrophin

MDA-supported researchers modify utrophin protein molecules to enter and benefit muscle fibers in mice with a disease similar to [Duchenne muscular dystrophy](#). Utrophin can partially substitute for the missing muscle protein dystrophin, and may be less likely to cause an adverse immune response than dystrophin in boys with DMD. Previously, utrophin has been given to mice as a gene but not as a protein. Delivering utrophin as a protein may pose fewer safety concerns than utrophin gene injections.

LGMD Gene Transfer Trial Exceeds Expectations

Positive results are seen in an MDA-supported clinical trial to test the safety of transferring alpha-sarcoglycan genes to three people with type 2D [limb-girdle muscular dystrophy](#). Not only was the strategy safe, but all participants produced four to five times the amount of alpha-sarcoglycan protein in their gene-injected foot muscle as in the untreated corresponding muscle on the other foot.

Second DMD Exon Skipping Trial Restores Dystrophin

[AVI BIONPharma](#) of Portland, Ore., announces its experimental compound AVI4658 restored production of the muscle protein dystrophin in 10 boys with [Duchenne MD](#) in the United Kingdom. Developed by an international team including two MDA-supported investigators, AVI4658 is a laboratory-engineered molecule that coaxes muscle cells to "skip" a flawed section (exon) of the dystrophin gene. AVI begins a systemic trial of exon skipping.

Intravenous Exon Skipping Improves Function in DMD Dogs

Three dystrophin-deficient dogs with a disease resembling human [Duchenne MD](#) are successfully treated with an intravenous "cocktail" of molecules that cause exon skipping, a strategy that changes the way cells read genes. Intravenous delivery allows the therapy to reach many muscles at once. The dogs run faster after treatment, while untreated littermates become slower over the same time period. The study was supported in part by MDA.

Two CMD Treatment Possibilities Identified

An MDA-supported group finds the antibiotic doxycycline increased survival time, improved growth and delayed the onset of paralysis in mice with a disease resembling [congenital MD](#). Another MDA-supported group reports a protein called laminin 111 restored post-injury muscle repair capability to mice with a different CMD-like disease.

Potential 'Muscle Repair' Stem Cells Identified

A new type of stem cell that may have implications for treating several muscle diseases is identified by MDA-supported scientists. The stem cell appears to be specifically programmed to become a "satellite" cell, which carries out muscle repairs when needed.

ALS Fatigue Fighter

MDA-supported researchers report that the drug modafinil (Provigil), approved to treat narcolepsy, seems promising for the treatment of excessive fatigue in people with [amyotrophic lateral sclerosis](#).

2008:

MDA Funds Lithium Trial in ALS

After a small study in Italy suggests the psychiatric drug lithium carbonate may slow the progress of [amyotrophic lateral sclerosis](#), MDA begins funding a multicenter clinical trial of the drug in some 100 ALS patients.

Nervous System 'Support' Cells Contribute to ALS

MDA-supported researchers discover that support cells called astrocytes in the nervous system likely play a larger role in [amyotrophic lateral sclerosis](#) than previously believed, opening new targets for therapy.

'Read-Through' Drug Restores Dystrophin in DMD-Affected Boys

The experimental medication PTC124, developed by [PTC Therapeutics](#) of South Plainfield, N.J., with MDA support, restores production of the needed protein dystrophin in six boys with [Duchenne muscular dystrophy](#) who took it at a high dose for a month. Earlier, about half of 26 boys with DMD who took PTC124 at a lower dose also began making dystrophin. The drug is designed to make muscle cells ignore an aberrant molecular "stop sign" in the dystrophin gene.

Exon-Skipping Compound Restores Dystrophin Production in DMD

Four boys with [DMD](#) who received muscle injections of an exon-skipping compound called PRO051, developed by the Dutch company [Prosensa](#) and by an MDA-supported scientist at Leiden (Netherlands) University, begin making the needed protein dystrophin in a leg muscle.

Gene Therapy Safe in Six with DMD

Six boys with [Duchenne muscular dystrophy](#) who received arm-muscle injections of miniaturized dystrophin genes encased in adeno-associated viral transporters have no serious adverse reactions to the procedure. The gene therapy compound, called Biostrophin, was developed by [Asklepios BioPharmaceutical](#) of Chapel, Hill, N.C., with substantial support from MDA. Plans advance for a gene therapy trial in [limb-girdle MD](#).

New SMA Gene Identified

MDA-supported researchers identify an X-chromosome gene that causes a rare form of [spinal muscular atrophy](#). The finding may yield additional information about all forms of this disease.

High-Dose Vitamin C to be Tested in CMT

An MDA-supported trial will test the hypothesis that high-dose vitamin C may help patients with type 1A [Charcot-Marie-Tooth disease](#), a disorder of peripheral nerves, after studies in mice with a CMT-like disease appear promising.

2007:

300 ‘Antisense’ Compounds Developed for Possible Use in DMD

An MDA-funded team in Australia develops some 300 “antisense” compounds that can coax muscle cells to skip over errors in the dystrophin gene and produce functional dystrophin protein molecules. Dystrophin is needed but missing in [DMD](#). One such compound is already being tested in boys with the disease.

Researchers Release Molecular ‘Brake’ on Protein that Could Help Treat DMD

MDA-supported researchers identify a molecule called ERF that keeps a potentially therapeutic protein, utrophin, confined to one small area of muscle fibers. Reducing ERF levels appears to release this “brake” on utrophin production, allowing it to be produced all over the fibers and opening up a possible new therapeutic pathway for [DMD](#).

Toxic Neighboring Cells Identified in ALS-Affected Nervous System

MDA-supported researchers find that nervous system cells called glia secrete an unknown toxic compound that kills neighboring motor neurons, the muscle-controlling nerve cells affected in amyotrophic lateral sclerosis. They say transplanting stem cells that become good glia into people with [ALS](#) might be beneficial.

Blocking Inflammation Pathway Helps in DMD

MDA-backed researchers confirm that blocking inflammation has significant benefits in [Duchenne muscular dystrophy](#). When they treated DMD-affected mice with an engineered molecule that blocks a specific part of the inflammatory pathway, the animals had more regeneration of muscle tissue

and more effective breathing muscles than untreated mice did. The researchers believe these findings may help unravel some of the underlying mechanisms involved in DMD and improve understanding and use of anti-inflammatory drugs, such as prednisone.

Researchers Identify New Type of Muscle Stem Cell

MDA-supported researchers in Italy announce they’ve identified a new type of muscle stem cell that they believe is highly promising for treatment of muscular dystrophies. These new stem cells, called “pericyte-derived,” are located around small blood vessels in muscle tissue. When injected into mice with [Duchenne muscular dystrophy](#), they matured into muscle fibers and improved the animals’ ability to grip a rod and stay on a treadmill.

Two Anti-Scarring Drugs Show Promise in Mice with DMD

An MDA research grantee is among the scientists who announced that two drugs, losartan and pirfenidone, have shown promise in reducing scar formation (fibrosis) in mice affected by [Duchenne muscular dystrophy](#). Scar formation resulting from excess deposits of connective tissue is a major factor in muscle damage in DMD and other muscle diseases.

Largest Ever ALS Drug Search Begins

MDA and the [ALS Therapy Development Institute](#) in Cambridge, Mass., launch the largest drug discovery project in [amyotrophic lateral sclerosis](#) in history. The three-year, \$36 million endeavor will attempt to identify biochemical targets and find drugs that work on them.

2006:

Lab-Made Enzyme Approved by FDA

[Myozyme](#), a laboratory-engineered enzyme patented by [Genzyme](#) and developed in part with basic research funded by MDA, is approved for use in children and adults with [acid maltase deficiency \(Pompe disease\)](#). It replaces the missing enzyme in this metabolic muscle disease.

Gene Therapy Trial for Duchenne Dystrophy Begins

Scientists and physicians launch the first U.S. human gene therapy trial directed at [Duchenne muscular dystrophy](#), with the support of a \$1.6 million grant from MDA. The first of six boys with DMD receives an injection of genes for dystrophin, the missing protein in DMD, in one arm and a placebo in the other. The scientists will later measure dystrophin production and monitor the effects of the gene transfer on the children.

Variants in ‘Detox’ Genes Found to Raise ALS Risk

MDA-supported investigators identify variations in and around genes known as PONs, whose normal role is to detoxify poisons such as pesticides and nerve gas, as risk factors for developing amyotrophic lateral sclerosis. The finding may help explain why Gulf War veterans have a higher than normal rate of ALS ([Lou Gehrig's disease](#)) occasionally have been identified.

2005:

Cardiac Stem Cells ID’d in Lab

MDA research grantees find cardiac muscle stem cells in the hearts of rodents and humans. They say the cells, identified by the presence of the protein islet-1, are likely to help researchers understand human heart muscle disease and may even lead to treatment strategies.

Sodium Phenylbutyrate Trial Begins in ALS

MDA researchers discover that sodium phenylbutyrate appears to interfere with a cell death program and extends the lives of mice with amyotrophic lateral sclerosis ([Lou Gehrig's disease](#)). In conjunction with the Veterans Administration, they begin a trial of the drug in people with [ALS](#).

Ceftriaxone Helps Mice with ALS

An MDA-supported research team reports that the drug ceftriaxone extends lives and prolongs strength in mice with [ALS](#). A clinical trial of the drug, which experts believe improves recycling of the potentially toxic chemical glutamate, is approved by the Food and Drug Administration in 2006.

2004:

Three MD Centers of Excellence Result from MDA-NIH Collaboration

Three new “centers of excellence” in muscular dystrophy research are established at the University of Washington in Seattle, the University of Pittsburgh and the University of Rochester (N.Y.), as a result of a collaborative funding arrangement between MDA and the [National Institutes of Health](#).

Key Mechanisms Found in Myotonic MD

MDA-funded groups discover that two types of proteins — transcription factors and muscleblind — are both interfered with in cells affected by [myotonic muscular dystrophy](#). The findings lead to additional investigations at the newly established muscular dystrophy center of excellence at the University of Rochester (N.Y.), co-funded by MDA and the [National Institutes of Health](#).

Gene Found for Rare Form of ALS

MDA-backed researchers find the gene for a rare, juvenile-onset form of [ALS](#). The gene, on chromosome 9, carries instructions for a protein called senataxin. The finding has clear implications for diagnosis of juvenile-onset ALS and may increase understanding of ALS in general.

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