Pietrofight.org FUNDED PROJECTS

The funds received through Pietrosfight.org are directed, in full, to Duchenne Muscular Dystrophy research. Pietro's Fight bases all decisions regarding the awarding of funds to research projects, after the project is submitted to the Duchenne Alliance review process which is rigorous and transparent. This process is led by our Director of scientificresearch, Dr. Carlo Rago. We also collaborate with other non-profit organizations which have similar goals to that of Pietro's Fight concerning current and promising advances being made in Duchenne research. These organizations also have scientific advisors who specialize in the field of DMD to determine the validity and potential of a given project. Pietrofight.org Policy on Donated Funds-Pietro's Fight Inc. contributes 100% of proceeds for programs, grants, and projects that support its mission to provide and appropriate funds that benefit the community for which it serves. Funds are not to be used for institutional, administrative, overhead, or indirect costs, only direct patient care or
research.

Project: Iowa State University

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Overview:

It has been apparent that increased expression of the protein utrophin will decrease the severity of DMD. Emerging evidence suggests that the same result may also be achieved by increasing mitochondrial biogenesis. The potential to target both of these outcomes simultaneously may lie with activation of two pathways originating with PGC-1alpha. This funded project supports research into the efficacy of a compound that can drive PGC-1alpha activity. Link

*This project is being funded in conjunction with other Duchenne Alliance Foundations.

Project: Duplication Study

Overview:

Dr. Kevin Flanigan's group at Nationwide Children's Hospital has developed a new mouse model for DMD that carries a duplication of exon 2. This is the most common single exon duplication in Duchenne patients. Preliminary studies show that these mice do not make dystrophin, and have significant muscle pathology. Dr. Flanigan and team have successfully generated mice carrying a duplication of exon 2 within the Dmd locus, and they are currently expanding their colony of this novel DMD mouse model. This expansion of the mouse colony is necessary to generate enough animals for meaningful analysis of any experiments.

*This project is being funded in conjunction with other Duchenne Alliance Foundations.

Project: Halo Therapeutics

Overview:

Halo Therapeutics which is beginning clinical trials in boys with DMD with their drug called HT-100. HT-100 is a powerful antifibrotic medication that presents great hope as a therapy for Duchenne Muscular Dystrophy and other diseases involving fibrosis. In animal models, HT-100 prevents and even reduces fibrosis, a major component in the pathology of Duchenne. Halo has reached a critical point: They have added tremendous value to the drug and its use in DMD, but now are on the cusp of translating that effort into something tangible for the boys—testing it in the clinic, and marching rapidly toward wide-scale testing and approval.

Project: Hugo W. Moser Research Institute at Kennedy Krieger

Overview:

Dr. Kathryn Wagner and colleagues in the Center's laboratory are focused on skeletal muscle regeneration. Muscle contains resident adult stem cells, which can be stimulated under the appropriate conditions to regrow injured muscle. However, in disease states, muscle frequently takes a non-productive path towards fibrosis or scar tissue instead of regeneration. Dr. Wagner and colleagues have shown that myostatin inhibition improves several of the features of the dystrophic mdx mouse model and that loss of myostatin in humans is associated with increased muscle mass. Furthermore, they have demonstrated that inhibition of myostatin stimulates muscle stem cells, dramatically improving muscle regeneration while reducing fibrosis. Their work has led to the development of myostatin inhibitors by several pharmaceutical companies. Current studies in the laboratory are centered on understanding the potential of myostatin to not only reduce, but reverse pre-existing fibrosis and the potential of myostatin and other factors to act synergistically. Active collaborations with colleagues in industry facilitate these studies and lead to the direct translation of mouse studies to human trials.

Project: Hugo W. Moser Research Institute at Kennedy Krieger

Overview:

Lobbying. Pietro's Fight has joined a number of foundations as part of the Duchenne Alliance in lobbying the FDA for accelerated approval of Eteplirsen. The drug has been in clinical trials in boy for over 2 years. It has shown that the patients have stabilized with no side effects. This is important because if granted accelerated approval it will change the pathway on getting therapies approved not only for DMD but all rare diseases. Funding has been provided for travel expenses, attorney fees, buying media, hiring or lobbyists etc.

Project: Dr. Louis Kunkel- Discovered the gene that causes DMD.

Overview:

Preclinical testing of a PDE9 inhibitor which nearly corrects all zebrafish for absent dystrophin in the zebrafish model. The correction with the PDE9A inhibitor is zebrafish was substantially better than parallel treatment with the PDE5 inhibitor sildenafil. The overall goal of this project is to determine whether PDE9A inhibition might ultimately be tested in human trials as to whether it ameliorates the muscle pathology in human DMD. Any drug developed will potentially be applicable to almost all patients with DMD.

Prject: Joshua Selesby- Iowa State University

Overview:

PGC-1α gene transfer effectively prevents and rescues dystrophic muscle from typical decline. Next, we found that quercetin, an orally available and safe agent, promotes PGC-1α activity in cell culture and *in vivo* models. In a quercetin feeding trial we found histological evidence of diaphragm rescue and heart preservation. We are currently performing a long-term feeding trial where respiratory and cardiac muscle function will be repeatedly measured, in vivo. Unknown, are the mechanisms by which quercetin protects dystrophic muscle. Further, the degree of protection against fatigue and contraction induced injury remain unknown.

Project: Dr. Jerry Mendel- Nationwide Children's Hospital for Milo Biotechnology

Overview:

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Project: Follistatin Gene Therapy Trial

Overview:

The trial is being led by Dr. Jerry Mendell, at Nationwide Children's Hospital. According to Mendell, "This is the first gene therapy clinical trial to demonstrate functional improvement in any form of muscular dystrophy, and a major advance for those suffering with muscle disease." The DMD trial is being funded by the Duchenne Alliance, which coordinated funding from 15 disease foundations from around the world.

Project: Development of SC-Prorelaxin for the Treatment of Duchenne muscular dystrophy

Overview:

University of Washington & ImmunoMod Jeffrey Chamberlain PhD Ronald Berenson MD Investigators: Jeff Chamberlain, PhD; Ron Berenson, MD; and Michael Regnier, PhD. Relaxin is a natural hormone, which has a number of biological effects that may be of benefit in Duchenne Muscular Dystrophy (DMD), including its ability to regenerate muscle, reduce scarring and improve cardiac function. Animal studies have shown that Relaxin promotes healing and increases strength of damaged skeletal muscle in young and aged normal mice. Additional rodent studies have shown that Relaxin reverses fibrosis in muscle as well as in many other tissues and organs. The hormone also has potent therapeutic effects on the heart, which have been demonstrated in several clinical trials in patients with heart failure. In mdx mice, a standard model of DMD, treatment with Relaxin was also shown to improve cardiac function in a recent unpublished study. Relaxin has been demonstrated to be safe and well tolerated in clinical trials, and it should be available for clinical studies.

Project: ReveraGen (VPB15)

Overview:

VBP15 may prove successful as a novel anti-inflammatory for many indications where pharmacological glucocorticoid steroidal drugs are currently standard of care. The improved safety of VBP15 may prove particularly important in the pediatric populations, where many of the side effects of prednisone can significantly reduce the quality of life of young patients. Key to the development of ReveraGen's lead compound, VBP15, was the recognition that there are sub-properties of glucocorticoids that are associated with either efficacy or side effects. ReveraGen's expertise in steroid chemistry was used to change the steroid chemistry to optimize for these sub-properties: transactivation.