friends of FSH research

2014
Case Statement

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Introduction

There is no cure or treatment strategy for patients with FSH Muscular Dystrophy (FSHD). This debilitating disease slowly consumes skeletal muscle, robbing people of the active, healthy, and independent years of their lives. For over a decade, Friends of FSH Research (*Friends)* has supported research studies that have contributed to our understanding of FSHD, offering the hope of treatment to the over 500,000 people living with the disease.

Friends was started by the family and friends of Terry and Rick Colella, whose son has FSHD. The goal of the organization was to stimulate research on FSHD in the Pacific Northwest. By reaching out to investigators at the University of Washington, Seattle Children's Hospital, and the Fred Hutchinson Cancer Research Center, we were able to provide seed monies for projects that would ultimately attract over $15 million dollars in funding. Although there now exists an impressive number of researchers supporting FSH research, there are even more projects that need to be funded in order to accelerate the goal to develop a treatment or cure.

Mission

The mission of the Friends of FSH Research is to accelerate the discoveries that will lead to treatments or cures for FSHD. To achieve our goal, we actively manage a portfolio of research that supports a pipeline for drug discovery. Our board, staff, volunteers, and world-class scientists are fully committed to transparent, reproducible, and transformative science that will inspire hope for people with FSHD.

The Research Landscape

The development of therapies for any disease takes a lot of work and can take a long time. *Friends* believes that by understanding the biology of the disease, we can strategize treatments and cures. A key aspect of developing therapies is funding researchers to conduct experiments that incrementally unravel the mysteries of the disease, and improve the technologies that will enable treatment.

There are a number of sources of funding for medical research; however, the process can be quite arduous and long. *Friends* leverages our small size and nimble review process to rapidly provide funding for innovative research required to build sustainable research programs in academic and industry settings.

Funding organizations are inherently risk averse, which often makes it difficult for researchers to find funding for new ideas. Friends of FSH Research de-risks projects by soliciting and reviewing proposals

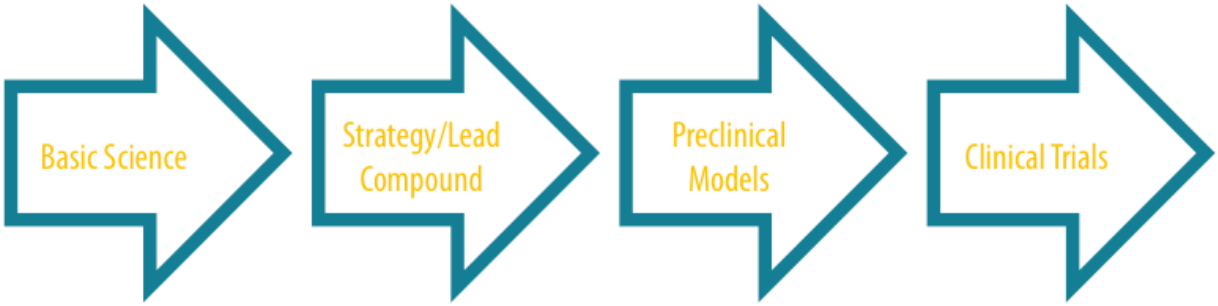
that support our pipeline, by having a quick turn-around time on the review process, and by having open communication about progress with our Scientific Development Director and our Scientific Advisory Board. By working together with groups of researchers, we establish the collaborative culture necessary to accelerate research.

Because our organization is highly risk tolerant we focus our funding efforts on transformative ideas that will attract additional outside funding and help build our knowledge base.

How we think about drug discovery

In order to support the most innovative research, *Friends* fosters projects that support the process of drug discovery (even though our strategies are not always focused on traditional pharmaceutical drugs). By encouraging collaboration, open communication, and focused direction, we are thinking forward about how the projects we fund will help researchers build robust programs that they need to cure the disease.

We think of drug discovery as having four steps that each flow into one another:



Basic Science is an all-encompassing term to cover basic discovery and research. In the context of a disease, we view this as focusing on "target" identification. Targets are any molecule, pathway or system that can be intervened with to reduce disease burden. Research has shown that the successful development of clinical interventions is dependent on a solid understanding of targets. Therefore, we do not shy away from projects that will help us understand more about the underlying mechanisms of FSHD. Basic Science projects are the most risky, and often require the most support to gain traction to continue down the pipeline.

Strategy/Lead Compound Identification is the process of building strategies and systems to neutralize or modify the target identified through basic research. For example, if gene *X* is defined as causing FSHD, we need to devise strategies to stop gene *X*. If gene *Y* is required for gene *X* to cause FSHD, we can also develop strategies around gene *Y*. The ultimate goal of this stage is to identify a compound or strategy that can be tested to prove whether it will have a beneficial effect on the disease.

Preclinical Models are designed to test the efficacy of compounds and strategies identified in animal models. This may seem like a superfluous or unnecessary step, but oftentimes compounds identified during the first stages need to be optimized to be able to work in people. Sometimes they can be very

toxic, and sometimes they just don't work. Preclinical work is very important to establish before investing in later stage clinical trials.

Clinical Trials are designed to prove that interventions actually work. They help establish standard of care and an in depth understanding of potential side effects and risk/benefit ratios. It goes without saying, that the more you know from stages 1-3, the better the chances are that the clinical trial will work.

Hope

Because of the contributions of our generous donors over the last decade, we have achieved unprecedented progress on our understanding of FSHD.

- ✓ Scientists have reached a consensus on the root cause of FSHD and have identified two molecular targets for intervening with the disease.
- ✓ Platforms have been developed for lead compound identification and scientists are now performing massive experiments to look for compounds. Other strategies, including viral gene therapy, are also showing great promise.
- ✓ Preclinical models of the disease have been developed, and are being used to test lead compounds and strategies.
- ✓ Clinical trial endpoints are being established so we know, when we find a therapy, whether it will work or not.

FSHD Champions

Friends of FSH is a member of the FSHD Champions; a concerted group of individuals and foundations that are working towards finding a cure for FSHD. Having multiple organizations supporting research and patient support for FSHD is critical for bringing treatments to patients. Having different approaches and geographical proximities diversifies the research being done and the investments being made. By working together with partnering organizations we can better understand the landscape for research on FSHD and can maximize our chances of success.

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Although the development of a therapy seems like a long road, each milestone that we achieve leaves an indelible mark on our knowledge. What we discover will never go obsolete, and will forever change the way we perceive and approach FSH.

- *Gregory Block, Scientific Development Director – Friends of FSH Research*