

## President's Letter (2015 Conference)

**Dear Scientists,**

A decade. How do I assess whether or not we are making a difference? We have made progress in some areas and we had limited success in others, but have we come far enough in this long span of time? From my family's perspective, we have not. It has been excruciating to watch people we care dearly about, go from walking to wheelchairs and become dependent on caregivers around the clock just to do basic daily activities. My personal desperation to find the cure is no less today than it was 10 years ago. In fact, the quest to cure dysferlinopathy has become personal for the entire foundation team, as they embed themselves into the business of discovery and as they navigate the complexities of developing and delivering therapies to the patients that we have begun to consider family.

Ten years ago, many of us sat next to each other at the first dysferlin conference in Bermuda breathing in the tropical air and feasting our eyes on the aquamarine waters. We were a new community just beginning to explore and engage. Since that time, we have built trust through candid conversations where nothing is off limits and all pride is checked at the door. You have collaborated when you may have been vulnerable. You called and updated us when you may not have felt it necessary. Your research these last 10 years has elucidated the biology of dysferlin, provided valuable ideas and tools for designing platforms to test drugs and has helped define the clinical aspects of the disease. You have continued to grow as scientists and have stayed committed to our cause and now I hope that the mission to cure dysferlinopathy is as much yours as it is ours.

Your results are the basis of two drug screening platforms that we continue to use in our search to find the first therapy for dysferlin deficiency. At our last conference, we described the development of a high throughput *in vitro* screening assay. Using this platform, we have now tested over 1700 FDA approved and known drugs. Almost one hundred "hits" resulted from this screen and we are now looking for ways to validate and test these in order to arrive at the best candidates to take forward toward the clinic. We seek your involvement in finding ways to design additional sieves for high throughput drug screening. We also reported a method to reliably measure the deterioration of muscle in live dysferlin deficient mice. We have now tested seven drugs with this platform, but have yet to see a significant improvement in the mice. We continue to test drugs with this system, but are also looking for ways to make this platform more robust, sensitive and efficient.

Unraveling the biology and the role of dysferlin and finding treatments will not benefit patients unless they are diagnosed — people with dysferlin deficiency have never even heard of dysferlinopathy or LGMD2B. Therefore, our mission must also include finding and diagnosing as many dysferlinopathy patients as possible worldwide. Toward this end and using the power and low cost of next generation sequencing, we are identifying LGMD patients (not just LGMD2B) at a faster rate than ever before. We helped engage Genzyme, a Sanofi Company, to spread the word of our diagnostic program to over 10,000 neurologists in the US via their sales force and have

formed partnerships with other LGMD foundations so that patients that suffer from all subtypes of LGMD can find help and hope. Our estimate is that less than 10% of patients suffering with dysferlinopathy are currently diagnosed. Therefore, we have a long way to go and additional challenges to overcome to diagnose all patients with this rare disease.

My team at the Foundation also continues to “get the ducks in a row” to run successful clinical trials. We are searching for reliable biomarkers of disease progression and we have begun evaluating data from our *Clinical Outcome Study*. We anticipate that the results from this three-year study will provide specific outcomes that can be used to monitor the effectiveness of drugs and therapies in a clinical trial setting.

I am confident that getting so many bright and creative minds from around the world together to focus on this disease will inevitably produce the great ideas we so desperately need. I’d like to return to Bermuda with all of you as a celebration of our great accomplishment once we have cured this devastating disease. Perhaps we can get there sooner rather than later.

We will use the next four days to pave the way towards a speedy attainment of our goal.

**Plavi Mittal, PhD**

President & CEO, Jain Foundation