Progress Report

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Title of Project: Investigating new genetic causes of muscular dystrophy

Summary:
This research project uses two approaches to help doctors diagnose the genetic mutations causing muscular dystrophy in different patients. The muscular dystrophies are a group of over 30 different conditions, each caused by mutations in a different gene. Muscular dystrophies are further grouped into different types depending on when symptoms first start and which muscles are most affected. One such category is Limb-Girdle Muscular Dystrophy (LGMD) and is used when muscle weakness begins after age 2 years mainly affects the large muscles around the shoulders and pelvis. There are over 20 different known causes of LGMD, which makes it a major challenge to identify the specific cause in each family.

We suspected that some patients who were given an overall diagnosis of LGMD by their doctors in fact had another condition called myotonic dystrophy type 2 (DM2), which can affect individuals in a very similar way but which requires a specific type of genetic test. DM2 is a common cause of muscle weakness in adults in some European countries but is not often diagnosed in Australia, perhaps because it is under-recognised. The first aim of this research project was to screen a large group of LGMD patients enrolled in INMR research studies who still didn't have a genetic cause identified for their muscle condition, for DM2. A research collaboration we developed with Professor Garth Nicholson, Concord Hospital has enabled us to screen many more LGMD patients than originally planned.

Muscles affected in LGMD

So far we have screened 158 LGMD patients for DM2 and two patients have tested positive (1.3%). These families have been grateful to find an answer for their muscle weakness. It is reassuring that Neurologists are not often missing this condition in their patients but it shows that sometimes DM2 is mistaken for LGMD, which is an important message for doctors.

The second part of this research study is to screen the DNA of patients with muscular dystrophy for mutations in two new genes that may be new causes of muscle disease. We are using both whole exome sequencing (in which all the regions of DNA that code for proteins are screened) and traditional gene sequencing

methods (Sanger sequencing) to screen patients with muscle weakness for mutations in these genes. We are excited to have recently found a second family with changes in one of the genes and we are performing further tests to confirm this finding.

What these research outcomes mean

If we are right, the finding of two families with mutations in the same gene makes it very likely we have found a new genetic cause of muscular dystrophy, which will enable further families with this condition to reach a genetic diagnosis. Finding the genes responsible for all genetic muscle conditions is a very important goal that will allow all families to receive accurate genetic counselling for their condition in the short term, and that in the long term will allow doctors and scientists to understand the basis of the muscle weakness in each disorder, and begin the task of developing treatments.