Team Titin information sheet

This letter is for families with variant(s) in the Titin gene (TTN). Changes in a gene are called mutations or variants. These changes may cause muscle weakness as well as heart problems. You will need to discuss with your medical team to see if and how your Titin variant affects your health.

What is Titin?
Titin is a very large protein. It’s huge! In fact, Titin is the largest protein in the human body. The Titin protein is located in muscle cells in our bodies. It is also found in the heart, which is a specialized muscle. Muscles need Titin in order to work and move. You can learn more about Titin here: http://titinmyopathy.com.

Titin abnormalities can cause a wide spectrum of muscle disorders called “Titinopathy”. These disorders may be also called a “myopathy” or a “dystrophy” including limb-girdle muscular dystrophy (LGMD) and tibial muscular dystrophy. Some forms of titin-related myopathies may include centronuclear myopathy, multi-minicore myopathy, hereditary myopathy with early respiratory failure, Salih myopathy, core myopathy with heart disease, Emery-Dreifuss-like phenotype without cardiomyopathy and likely more. Muscle weakness may start in childhood or come on later as an adult. Weakness can range from mild to severe.

How to make sense of your Genetic Test Results for Titin
Some variants in a gene may lead to health problems, while others may not. Not all variants are equally problematic. Many truncating titin variants are clearly associated with a high risk of heart or muscle disease, and these are often classified as “pathogenic” or “likely-pathogenic” in the clinical genetic test report. On the other hand some variants are clearly not harmful and are classified as “benign” or “likely-benign”. Often however, there is insufficient information about variants to tell if they are harmful and these are classified as “variants of uncertain significance” (VUS or VOUS). These variants need follow up by experts (see resources).
## Resources

### Research

<table>
<thead>
<tr>
<th>For all people with Titin related muscle weakness:</th>
<th>For help with diagnosis:</th>
<th>Gene and heart disease research:</th>
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</table>
| **Beggs Laboratory**  
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BeggsLabGC@chidlrens.harvard.edu | **Prof Bjarne Udd, MD, PhD**  
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**Victor Chang Cardiac Research Institute and St Vincent’s Hospital, Australia**  
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| Study of atypical titinopathies, including persons with skeletal or cardioskeletal symptoms and single TTN variants. | Some Genetic testing options: | Please enroll in **The Congenital Muscle Disease International Registry!**  
http://www.cmdir.org |
| Jen Roggenbuck, MS, CGC  
**Ohio State University**  
Jennifer.Roggenbuck@osumc.edu | **Free program** via Patient Insights Network  
**Paid genetic testing** program through Invitae  
**GeneDx** genetic testing  
The **Lantern Project** | |

### Connect with families/resources

| Team Titin on **Facebook**  
**Private discussion group** for families  
**Public Facebook page** | **Sarah Foye, Titin Family Advocate**  
FoyeSarah@gmail.com  
973-797-9305 | **Titin Information Website** link |
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| **ZNM - Zusamment stark! e.V.**  
An association for centronuclear myopathies in Germany, the Netherlands and Austria. | **Recessive** titinopathy fact sheet for families. | |

### Care

| **Heart health information**  
DCM Foundation  
https://dcmfoundation.org/ | **The Care of Congenital Myopathy: A guide for families** link | **Summary of Evidence-based Guideline for patients and their families** Limb-Girdle and distal muscular dystrophies link |
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