

**Appendix e-1: Methods:**

**Standard protocols, registrations, and patient consents.** Participants included three siblings seen under the approved by NINDS IRB protocol at the National Institutes of Health for neuromuscular diagnostic evaluation. Written parental consent and appropriate assent was obtained from all patients.

**Imaging:** Muscle ultrasound (with Siemens Acuson S2000), muscle MRI of the lower extremities (on 1.5 Tesla or 3 Tesla MRI), and brain MRI was performed.

**Muscle histology:** Muscle biopsy cryosections were stained with hematoxylin and eosin, ATPase, and a panel of antibodies as described by Moore, *et al* [e1]. Primary antibodies included carboxy terminus dystrophin (rabbit polyclonal, Abcam), alpha-dystroglycan [IIIH6 and VIA4-1, Developmental Studies Hybridoma Bank (DSHB)], beta-dystroglycan (DSHB).

**Molecular investigations:** DNA was extracted from blood. *GMPPB* sequencing was performed by PreventionGenetics (Marshfield, WI, USA) based on standard procedure on P1, and targeted analysis was performed on the two siblings and mother. on the two siblings and mother.

**Reference**

[e1] Moore SA, Shilling CJ, Westra S, et al. Limb-girdle muscular dystrophy in the USA. J Neuropathol Exp Neurol 2006; 65:995-1003.