Congenital Muscular Dystrophy Overview
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Subtypes of CMD of Known Cause

Classification schemes for the congenital muscular dystrophies historically began in the second part of the 20th century with the description of syndromic forms with brain malformations observed in discrete geographic populations (Fukuyama CMD in Japan, muscle-eye-brain disease in Finland) and a contrasting contracture phenotype with normal intelligence, initially labeled as classic or Occidental CMD.

In the 1990's, a major step forward came from the observation of differential merosin protein expression in patients with the classic form, leading to the designations "merosin-positive" and "merosin-negative" CMD. A subsequent discovery identified mutations in *LAMA2* as the causative agent for merosin-deficient CMD. Merosin was identified as a key ligand in the extracellular matrix and interactions with the dystroglycan-dystrophin complex. The gene product of *LAMA2* is laminin alpha 2, one of three chains that forms heterotrimeric structure known as laminin 211 (merosin).

Early in 2000, several extraordinary advances in gene discovery led to the re-classification of merosin-positive CMD along with improved understanding of the underlying pathologic mechanisms triggered by deficiencies in proteins involved in the extracellular matrix and dystrophin-dystroglycan complex. Additional work to identify the developmental role of specific protein deficiencies and the effect of their absence on brain, muscle, and heart development will contribute to knowledge gaps.

Extracellular matrix binding deficiencies may mediate fibrotic and apoptotic changes, while dystrophin/dystroglycan abnormalities may be implicated in impaired regeneration [Durbeej 2010] and in central nervous system development (cobblestone lissencephaly). Furthermore, abnormal glycosylation of alpha-dystroglycan may have a negative effect on merosin expression (secondary partial merosin deficiency); normal glycosylation is required for adequate attachment of the extracellular matrix to the dystroglycan complex through merosin.

Literature Cited

Durbeej M. Poster session. Santa Clara, CA: Annual SMA Conference; 2010.