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Methods of efficacy measurement
– strength versus function
Dystrophin localisation and function

- Costamers: subsarcolemmal protein assemblies which couple force generating sarcomere with sarcolemma.

- Laterally transmission of force to sarcolemma and ECM

- Increased permeability and instability of plasma membrane with eccentric exercise when costamers perturbed
Dystrophin absence
= Mild / moderate less
tetanic force
+ 10 x decrease in strength
following lengthening
Strength vs function, take home message

• Depending on different stages of disease, function changes with little strength change or strength may change significantly with little change in function
• The concept requiring both strength AND function as co-primary endpoints only serves to dilute statistical power
• Clinically meaningful changes in function are preferable and more meaningful to patients and their family members
• Therapeutics with different mechanisms of action may preferentially create more changes in either strength or function but not necessarily both at a particular stage of disease
• There may be therapeutics targeting particular stages of the disease where an argument could be made for strength as a sensitive endpoint (as long as it correlates with function or has predictive ability as a surrogate endpoint), but this does not apply to the majority of current developments