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Office of Technology Management

GENE-SPECIFIC THERAPY TREATMENT FOR PREDICTING LIMB-GIRDLE MUSCULAR DYSTROPHY

Haller, Gabriel, Li, Chengcheng, Weihl, Conrad

Hardin, Clyde "Frank"

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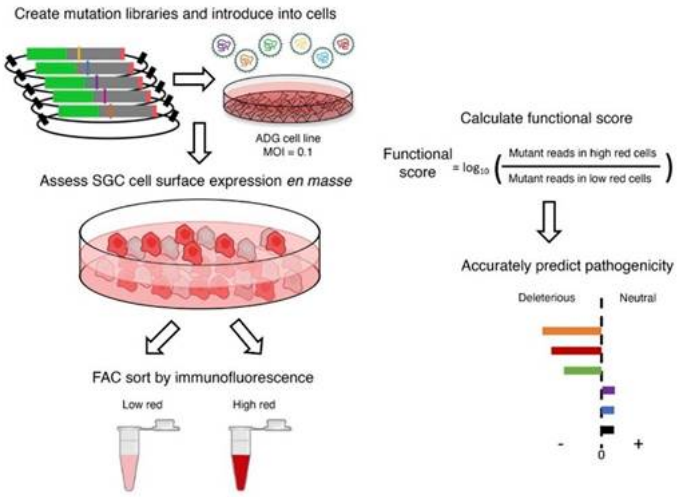
Value Proposition: *Method that uses gene-therapy to detect limb-girdle muscular dystrophy (LGMD) type 4R/2E.*

Technology Description

Researchers at Washington University in St. Louis have developed a method of predicting limb-girdle muscular dystrophy (LGMD) type 4R/2E. LGMD Type 4R/2E is caused by mutations in β-sarcoglycan (SGCB) which results in muscle wasting, progressive weakness, degeneration of skeletal muscle and often premature death. SGCB is a key component of the dystrophin-associated protein complex (made up of 4 sarcoglycan subunits, α, β, γ, δ) which localizes to the plasma membrane and connects the intracellular cytoskeleton to the extracellular matrix, allowing for coordinated force production in muscle. Clinical diagnosis of sarcoglycan-deficient LGMD currently requires histopathologic assessment of a patient's muscle biopsy for cell-surface localized sarcoglycan complex proteins or biochemical assessment of the protein's presence.

This method generates disease predictions for all possible protein-altering single nucleotide variants in the SGCB gene which causes recessive LGMD R4/2E. This information could be used to predict which patients could benefit from gene-specific therapies.



Above figure: Deep mutational scanning (DMS) was used to measure the effects of all possible missense variants of the SGCB gene and demonstrate that high-throughput function assays can accurately measure the effect of protein-coding genetic variation in the SGCB gene.

Stage of Research

Early stage of development

Publications

Li C, Wilborn J, Pittman S, Daw J, Alonso-Pérez J, Díaz-Manera J, Weihl CC, Haller G. Comprehensive functional characterization of SGCB coding variants predicts pathogenicity in limb-girdle muscular dystrophy type R4/2E. J Clin Invest. 2023 Jun 15;133(12):e168156. doi: 10.1172/JCI168156. PMID: 37317968; PMCID: PMC10266784.

Applications

- Gene therapy treatment
- Predicting limb-girdle muscular dystrophy
- Rare disease detection

Key Advantages

- LGMD protein-altering missense mutations that can be used predict pathogenicity of missense SGCB mutations
- Can accurately predict which patients could benefit from gene-specific therapies

Patents

Patent application filed

Related Web Links – Gabriel Haller Profile; Haller Lab