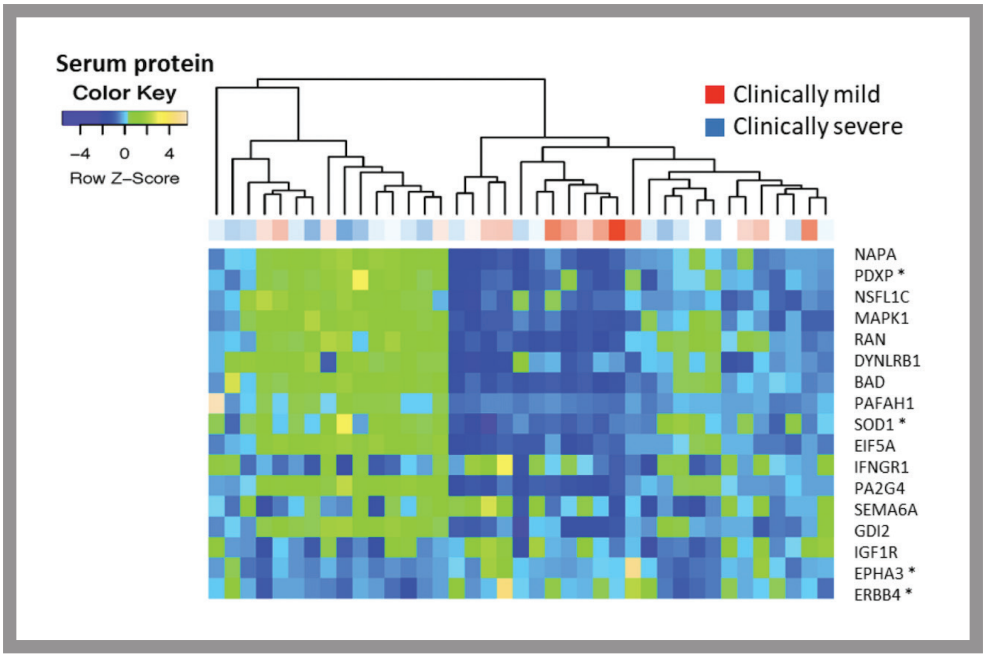
Serum Biomarkers and Clinical Severity in Young Steroid-Naïve Duchenne Muscular Dystrophy Boys



Abstract

Duchenne muscular dystrophy (DMD) is caused by loss of dystrophin in muscle, and while all patients share the primary gene and biochemical defect, there is considerable patient–patient variability in clinical symptoms. We developed multivariate models of serum protein biomarkers that explained observed variation, using functional outcome measures as proxies for severity. Serum samples from 39 steroid-naïve DMD boys 4 to <7 years enrolled into a clinical trial of vamorolone (NCT02760264) were studied. Weighted correlation network analysis was used for unsupervised clustering of 1305 proteins quantified using SOMAscan® aptamer profiling to define highly representative and connected proteins. Multivariate models of biomarkers were obtained for time to stand performance (strength phenotype; 17 proteins) and 6 min walk performance (endurance phenotype; 17 proteins) including some shared proteins. Identified proteins were further tested with associations of mRNA expression with histological severity of muscle from dystrophinopathy patients (n = 28) and normal controls (n = 6). We show that performance of DMD boys was effectively modeled with serum proteins, proximal strength associated with growth and remodeling pathways and muscle endurance centered on TGFβ and fibrosis pathways in muscle.

When

Thursday, October 14, 2021 at noon

Zoom

Please request Zoom details by e-mailing healthsciences@carleton.ca

Presenter

Dr. Utkarsh J Dang, Assistant Professor, Department of Health Sciences, Carleton University

healthscienceCU

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