Serum biomarkers in Duchenne muscular dystrophy: a leap toward precision diagnostics

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I was interested to read the article by Dowling *et al.*[1] in the European Journal of Translational Myology, where the authors provide a comprehensive review of serum biomarkers for Duchenne Muscular Dystrophy (DMD), a devastating early-onset muscle wasting disease. The emphasis of research on liquid biopsy-based approaches, with the application of Mass Spectrometry (MS)-based proteomics for the identification of novel biomarkers like carbonic anhydrase CA3, fatty acid binding protein FABP3, and titin fragments, represents a revolutionary step towards minimally invasive diagnostics. As a neurologist and clinical pharmacologist working in Uganda, where diagnosis of DMD is delayed owing to the limited access to invasive tests, I find the prospects of these biofluid-based markers not only intriguing but also of immense worth in advancing precision medicine in resource-poor settings.

The detailed consideration of muscle-derived protein markers, such as Creatine Kinase (CK), Myoglobin (MB), and novel candidates like sarcomeric proteins (e.g., myosin light chain, troponin), underscores their utility in mirroring DMD's complex pathophysiology, myonecrosis, and reactive myofibrosis. The potential to resolve specific proteoforms and peptide fragments by MS-based proteomics is particularly exciting, considering the urgent need for DMD-specific biomarkers with minimal overlap with other neuromuscular disorders.[2] That the CA3/MB ratio can resolve skeletal muscle versus cardiac involvement is ground-breaking, and this will be a valuable addition to the daily clinical practice to refine differential diagnoses in those patients where cardiac complications are prevalent in DMD.[3]

Nonetheless, the article raises a number of considerations for clinical translation. Firstly, although MS-based proteomic surveys offer high sensitivity, their expense and technical sophistication are likely to hinder uptake in resource-poor environments such as Uganda. Might more straightforward, affordable assays, *i.e.*, Enzyme-Linked Immunosorbent Assays (ELISA) against CA3 or FABP3, be created to close this divide? Second, the article highlights the potential of biomarkers in therapeutic monitoring, for instance, for novel exon-skipping treatments and gene editing.[4] In my own practice, where DMD patients present late with advanced myofibrosis, the inclusion of these biomarkers in routine monitoring would guide personalized treatment planning, for example, the optimization of corticosteroid regimes or the assessment of the efficacy of novel drugs like ataluren.

Clinically, the proposed biomarker signature can revolutionize DMD management in disease-prevalent but diagnostically underserved areas. CK and CA3 levels in combination in newborn screening programs, for instance, can enable earlier detection with interventions in a timely manner to avert multisystem complications like cardiorespiratory failure.[5] The identification of fibrosis-associated markers like fibronectin and matrix-metalloproteinases also offers possibilities for assessing antifibrotic therapies, which are critical for lessening disease progression in DMD.[6]

Future research should seek to validate these biomarkers in diverse populations to capture genetic and environmental variabilities, which can influence serum protein profiles. Longitudinal studies that correlate biomarker levels with clinical endpoints, such as loss of ambulation or respiratory decline, would also establish their prognostic value. In addition, the exploration of the utility of these biomarkers for monitoring toxicity of new therapies, such as adeno-associated virus-based gene transfer, would enhance patient safety.[7]

In conclusion, the work of Dowling *et al.*[1] opens a new era for DMD diagnostics with the power of liquid biopsies. Its promise to improve early diagnosis, differential diagnosis, and therapeutic monitoring is huge, particularly for resource-scarce regions. I commend the authors for their rigorous proteomic approach and advocate for ongoing innovation of scalable and low-cost biomarker assays to make DMD care accessible globally.

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Conflict of interest

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