

# MOLECULAR MARKERS FOR TRACKING SKELETAL MUSCLE FUNCTION IN DUCHENNE MUSCULAR DYSTROPHY

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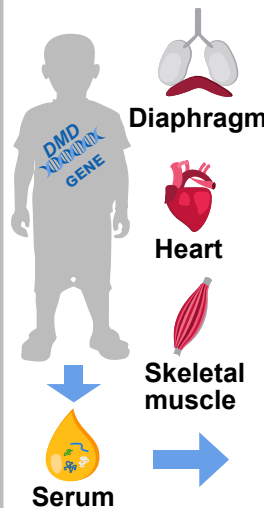
## SUMMARY

The use of sensitive, accurate and specific blood-derived biomarkers can improve assessment of disease progression and therapeutic effects in DMD. Using parallel reaction monitoring mass spectroscopy (PRM-MS) and quantitative immunoassays, we have developed a pipeline to analytically validate blood biomarker candidates for DMD using longitudinally collected serum or plasma. This was illustrated for carbonic anhydrase 3, with high agreement between both methods.

## CONCLUSIONS

1. Orthogonally validated 4 of 10 biomarker candidates for DMD using PRM-MS.
2. Developed quantitative immunoassay for **carbonic anhydrase 3 (CA3)** with high correlation to PRM-MS.
3. Proof-of-concept for **analytical validation** of biomarker candidates for DMD

## BACKGROUND



**Duchenne muscular dystrophy (DMD)** is caused by a mutation in the *DMD* gene, which results in the lack of expression of the muscle protein dystrophin.

The lack of dystrophin expression causes fatal, progressive muscle wasting. Development of dystrophin-restoring therapies are ongoing. The use of sensitive, accurate and specific blood biomarkers to assess therapeutic outcome could aid in this development.

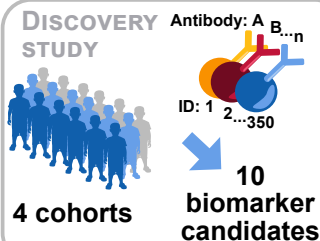
Proteins from dystrophic tissues leak into the blood stream.

Many blood biomarker candidates have been described in literature, but none clinically validated

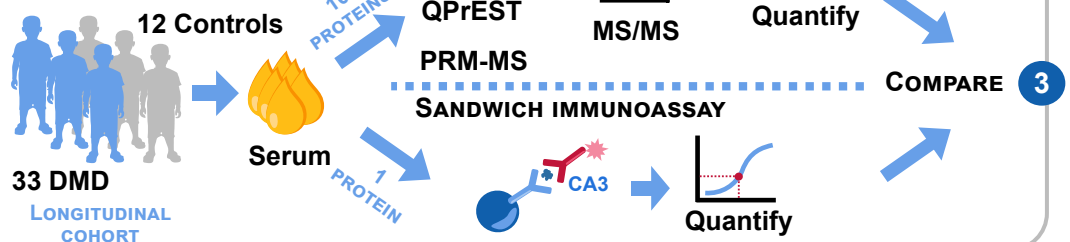
**This study focuses on analytical validation** of a subset of blood biomarker candidates. The aim is to define a pipeline for analytical validation ahead of clinical validation.

## METHODS

### DISCOVERY STUDY

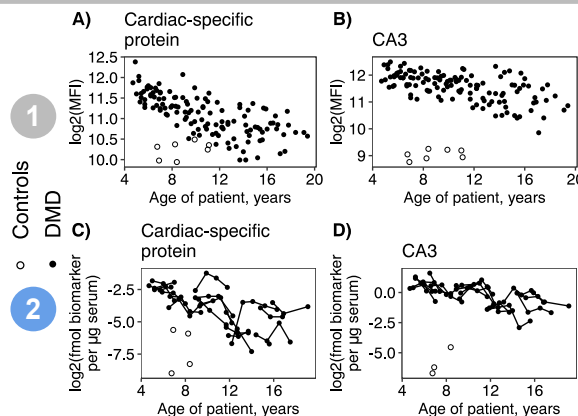


### ANALYTICAL VALIDATION STUDY



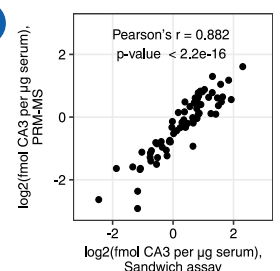
## RESULTS

Absolute quantification in a longitudinal DMD serum cohort was obtained for five of 10 targets. Four proteins followed trends seen in the discovery data. Figure exemplifies two proteins detected in (A-B) discovery study with antibody suspension bead array (relative signal), (C-D) in PRM-MS (absolute quantified)



One biomarker candidate, CA3, was further quantified with a sandwich immunoassay, with the same capture antibody as used in discovery study.

The two quantitative assays, which were performed in different labs, had high agreement



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CURE THROUGH INNOVATION