Mucopolysaccharidoses (MPS) disorders are a category of lysosomal storage diseases that result in a disruption of the catabolism of glycosaminoglycans (GAGs), macromolecules consisting of long polysaccharide chains. There are a total of seven MPS disorders, with MPS I and II on the (Recommended Uniform Screening Panel) RUSP.

Primary screening for MPS diseases is accomplished through enzyme activity testing, however, additional methods are required to identify false positives.

Second tier tests have traditionally relied on elevations of broad classes of GAGs such as dermatan sulfate and keratan sulfate. This approach cannot differentiate between MPS I and MPS II disorders.

Recent discovery of terminal non-reducing fragments cleaved from GAGs within affected patients presented us with an opportunity to investigate the utility of measuring these markers in specific MPS disease subtype.

MATERIALS AND METHODS

**MPS I**
- Whole blood DBS enriched with fibroblast generated MPS I biomarker served as the positive control (GelbChem)
- Presumed normal whole blood DBS served as the negative control
- MPS II
  - MPS II positive patient urine served as the positive control during validation studies carried out and shown in Figure 1.
  - Whole blood DBS enriched with fibroblast generated MPS II biomarker was implemented as the positive control for clinical samples.

**MPS II**
- Presumed normal whole blood DBS served as the negative control.
- Both biomarkers used Chondroitin disaccharide d4 as the IS (Cayman Chemical) and 1-phenyl-3-methyl-5-pyrazoline (PMP) (Sigma-Aldrich) as the derivatizing agent.

**MPS I**
- MPS I Patient set
  - 25 apparently normal
  - 27 MPS I pseudo-deficient or carrier
  - 4 MPS I IVUS
  - 3 known MPS I positive

**MPS II**
- MPS II Patient set
  - 25 apparently normal
  - 4 known MPS II positive in treatment
  - 3 known MPS II positive not in treatment

**Control**

**MPS I**
- MPS I Positive Control @ 80°C
  - t = 0
  - t = 1 month
  - t = 2 months
  - t = 3 months
  - t = 5 months
  - t = 6 months
  - t = 10 months

**MPS II**
- MPS II Positive Control @ 80°C
  - t = 0
  - t = 1 month
  - t = 2 months
  - t = 3 months

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2. Saville et al., Genetics in Medicine, 2008, 10 (2), 75-82.

Applicable to federal and/or state laboratory requirements, PerkinElmer Genomics establishes and verifies the accuracy and precision of their testing services.

**SPECFICITY OF MPS I & II MARKERS**

The markers of interest in this study are isobaric species of unknown structure. Extracts of positive controls containing each marker were combined to optimize chromatography conditions and achieve separation.

**CONCLUSION AND NEXT STEPS**

- Our validated methods allow for increased specificity between MPS I and MPS II disease subtypes from measuring a characteristic fragment of accumulated GAGs compound.
- The MPS I marker test was performed retroactively on a set of samples that tested low for DUA during primary newborn screening yet were confirmed unaffected by gene sequencing. The MPS I marker was found to be within normal limits for all 28 samples tested in this set, further supporting the benefit of performing this second-tier test as part of a newborn screening algorithm.
- Continuation of the MPS I allele study to further elucidate any possible correlation with genotype and MPS I marker ratios.
- An allele and biomarker correlation study for MPS II.
- Validation of MPS I and II biomarkers in urine samples.