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Newborn Screening for Pompe Disease in New York

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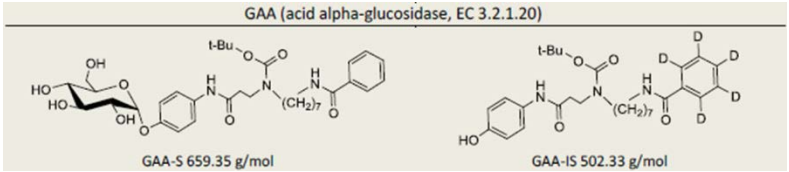
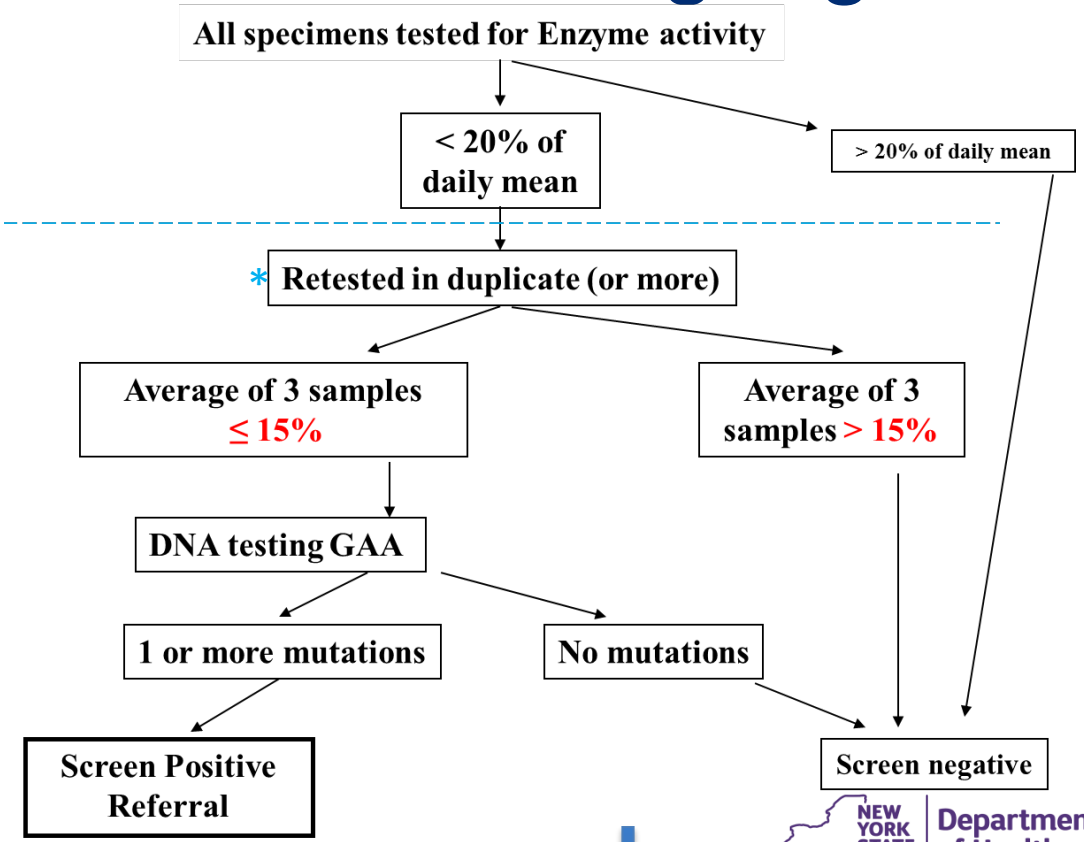
Methodology

1. MS/MS using CDC provided ASRs (Oct. ‘14- May ‘15)

2. MS/MS using Perkin Elmer ASRs with universal buffer



Cutoffs and Testing Algorithm



*Plan to perform retest with 6-Plex (FP)

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Screening Results

1. Infants screened: 330,000
2. 89 Infants with ≤ 15% (DNA tested)
3. 11 Infants with pseudo only (not referred, ~12-15%)
4. 18 Infants with other non-disease causing variants (not referred, 12-15%)
5. 60 infants referred (≥ 1 mut, 0.018% screen positive rate)

Follow-up results (60 referrals)

1. Infantile Pompe disease = 1 (<8%)
2. Infants with two “mutations”/low diagnostic enzyme = 28
   a. 11 with known pathogenic mutations (“probable cases”)
   b. 10 with 1 known pathogenic/1 VOUS (“possible cases”)
   c. 6 with two VOUS (activity above LOPD range at diagnostic lab)
   d. 1 referral - awaiting Dx lab results
3. Carriers: 31 (activities generally >12%, often premature infants – tend to have lower activity, dx lab activities in carrier range)
4. Current case classifications are internal, subject to change

*For more information on genotypes and diagnostic testing results see Poster: *“The LC-MS/MS Assay of Leukocyte Acid α-Glucosidase Activity Reliably Differentiates Early-onset and Late-onset Pompe Disease.” Chunli Yu, et al.*

Dried blood spot analysis: attenuated activity modes

Expected the unexpected

1. Only 1 infant in 330,000 detected with infantile Pompe disease. Lower than expected (reported incidence all forms 1/40,000).
2. 21 infants (1/15,714) with “potential” for LOPD. Higher than expected
3. Many cases with pseudo-deficiency alleles as background and other variants detected
4. Prediction of if/when infant will become symptomatic very difficult
5. Families responses vary (cultural, socio-economic, physician experience/knowledge)

Conclusions and improvement opportunities

1. Population dependence on screening results
2. Use of hard cutoffs in “single” enzyme analysis leads to higher positive rates – Exploring use of Region IV CLIR software*
3. Dx MS/MS leukocyte assay: more LOPD cases needed to better define
4. Need for improved genotype/phenotype correlations
5. Short-term follow-up is “long-term” follow-up when screening diseases with common late onset phenotypes

*CLIR: Collaborative Laboratory Integrated Reports.

No “cutoffs” uses ratios with other LSDs/markers

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Health research throughout the lifespan

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Thank You !!


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