

Missouri Krabbe Disease Screening

(4-17-15)



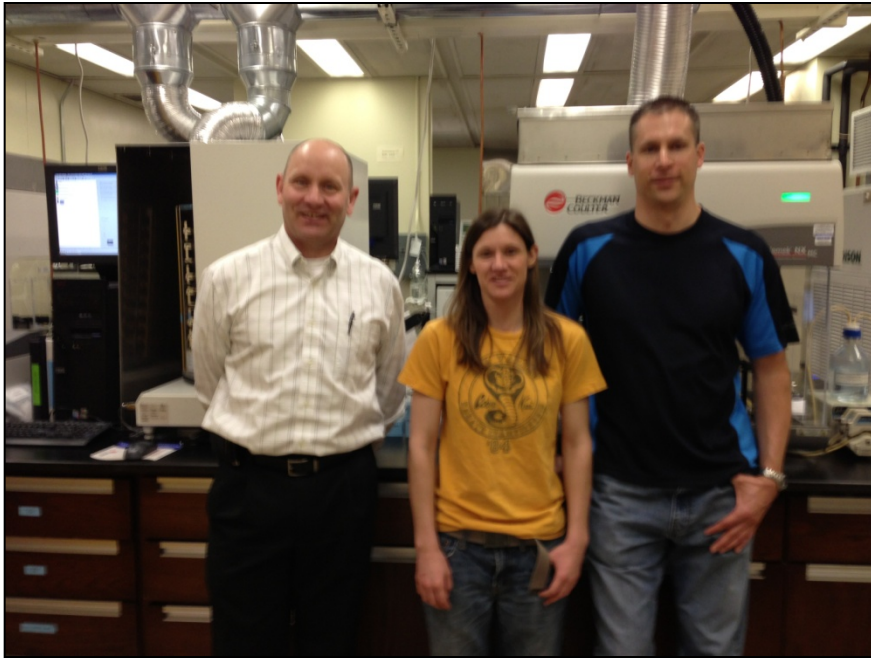
Missouri State Capitol



Missouri State Health Laboratory

Patrick Hopkins; Chief, Missouri Newborn Screening Laboratory

Thank You to New York's NBS Laboratory!



The Krabbe Screening Experts

The Screening Process

- Missouri sends samples to NY daily via overnight FedEx after all testing has been completed (7 days after received by MO).
- NY receives MO samples and tests them in the same manner as their own.
 - Retest anything $< 20\%$ of the GALC mean
 - Start DNA testing if first analysis is $< 12\%$
 - Continue DNA testing if average GALC is $< 12\%$
 - Notify MO for referral if mutation is found.
- NY sends samples and results back to MO

Missouri NBS Collection Cards Shipped

PLT. ORIGLES
PROG. ONE
SIDE ONLY

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Collected by: *[Signature]*

MO bar code ID

MO NBS lab ID

Positive Screens

- Email notification from NY if a screen is proceeding to DNA.
- Email notification from NY if DNA is mutation positive for referral or just Polymorphism.
- NY faxes report if positive referral for Krabbe.
- MO NBS lab responds back by email when fax is received.
- MO NBS lab refers the case to appropriate MO referral center and notifies MO follow-up.

Screening Stats to Date

- 235,191 Missouri samples screened by NY as of 3/31/15 (~204,000 births).
- ~40 with polymorphisms only (these are not at risk for Krabbe disease and are not referred).
- 45 referrals: 8 genotypes of unknown significance, 31 with one Krabbe mutation, 4 pending and 2 refusals to follow-up.

New Fluorometric Bench Assay for Krabbe

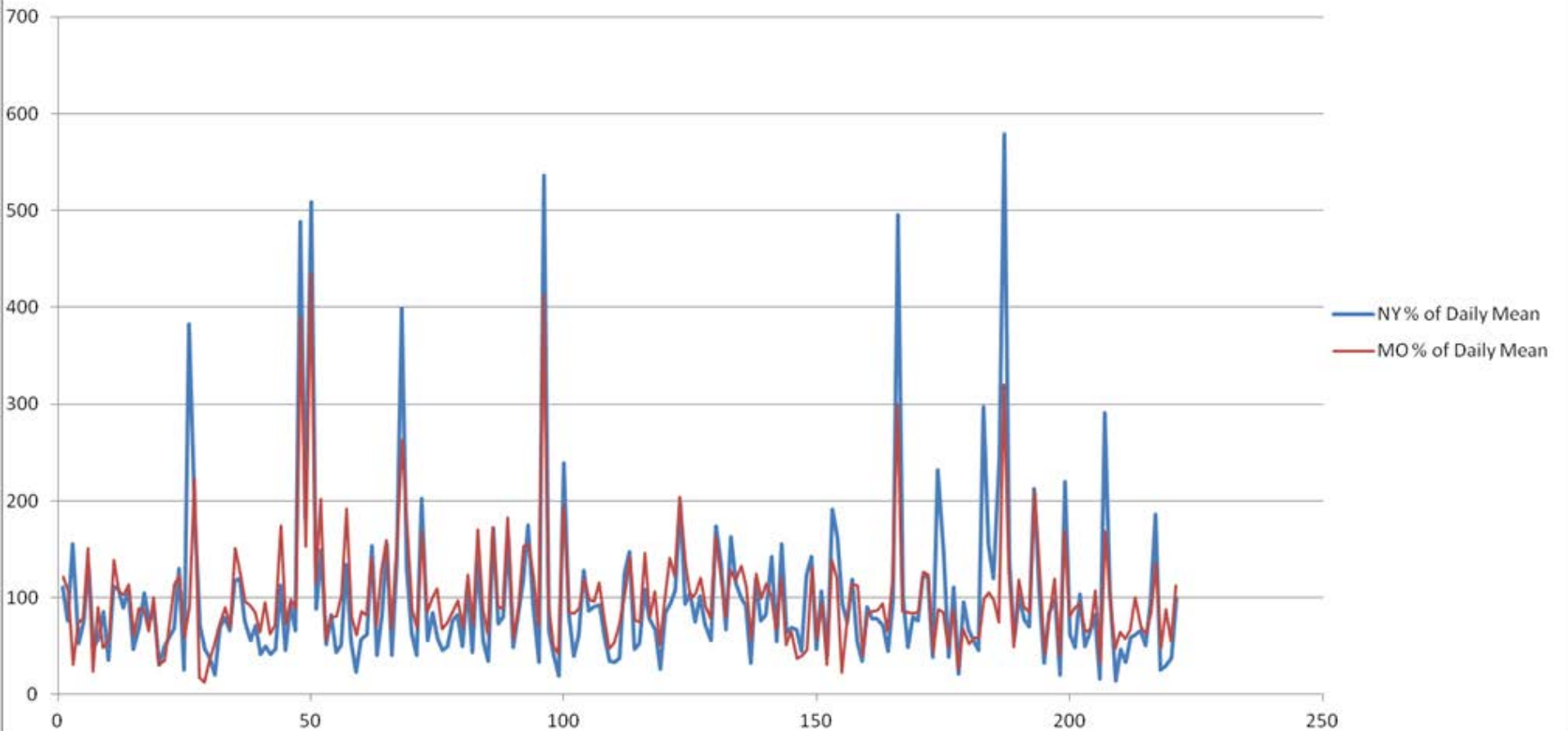
- Punch samples
- Add 100 ul of GALC Extraction Buffer to columns 2-12 of each plate
- Seal plates with adhesive cover and shake at room temperature for 1 hour
- Add 10 ul of GALC substrate to columns 2-12 of a black microtiter plate
- Transfer 10 ul of sample extract to black microtiter plate (add to GALC substrate already in wells)
- Seal plates with adhesive foil and place in humid chamber in 37°C incubator
- Incubate for 17 hours
- Add 70 ul of calibrants to column 1 of each plate
- Add 50 ul of stop buffer to columns 2-12 of each plate
- Read plates in fluorimeter

Implementation Plan

- Validation and verification of bench method
- Four month parallel testing with NY (Apr, May, Jun, Jul)
- MSPHL Molecular Unit conducts 2nd DNA testing for 30 Kb del.
- Discontinue sending samples to New York as Krabbe pilot continues in Missouri (July 31st, 2015).
- Missouri goes live with Krabbe testing

First Day to be Parallel Tested

NY and MO GALC % of the Daily Mean - Day 2015091



Acknowledgements

- Dr. Joe Orsini and the New York newborn screening team.
- Tracy Klug and the Missouri NBS laboratory staff.
- Jami Kiesling and the Missouri NBS follow-up program.
- The Missouri LSD Task Force.

**Special thanks to
Dr. Joe Orsini**

