Implementation of Sequencing in a Newborn Screening Laboratory

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First – Questions About a New Condition

- What is known about the methods?
- What is being done in NBS?
- Will 2\textsuperscript{nd} tier even be needed?
- What is the anticipated volume of a 2\textsuperscript{nd} tier test?
- Think about the future:
  - Where are you headed?
  - Multiplexing?
  - Platforms?
What Types of Molecular Testing are Available?

- What is the specificity of the biochemical test?
- Will detection of pseudodeficiency alleles decrease referrals?
- Common early / late onset mutations; is a targeted panel sufficient?
- Is Sanger sufficient or should Next Gen sequencing be used after a positive biochemical result?
Space and Infrastructure

- Construction?
- More space needed?
- Work done in program?
- Workflow, need post both clean and dirty PCR areas
Staffing

- Expertise in house?
- Added burden to overworked staff?
- Ability to hire higher level staff?
- Willingness of staff – cross training?
- Willingness of staff – stay on to finish?
- Follow-up to handle new referrals?
- Training of follow-up staff to report?
- Medical providers acceptance/education of sequence results?
Follow-up

- Engage and involve state specialty care center directors early; form task force with all stakeholders for reporting
- Find the condition experts and engage them
- Develop short-term follow-up plan
  (dx guidelines; management guidelines; case definitions – feeds back to interpretations)
- Decide on long-term follow-up plan
- Train follow-up staff for reporting information
Quality Control

• Maintenance of Instrumentation
• Fancy, Finicky, and Costly
• Reagents and Lot to Lot Testing
  • Working with Vendors
  • Standing Orders
• PCR and Contamination Controls
Quality Controls and Quality Assurance

- Work with advocates; referral centers; other states; CDC; APHL
- Quality assurance materials; reference materials; system for proficiency testing
- Consent to use specimens
- IRB approval required
- Can help with refinement of biochemical test
- Heterozygous controls
- Synthetic controls or transformed cell lines can be used
Proficiency Testing

- College of American Pathologists
- CDC NBS Quality Assurance Program; Now Incorporates DNA
- Sample Exchange with Colleagues
- Blinded In-House Proficiency Testing
Reporting

• Genotype

• Methodology Employed

• Interpretation: References; Database Information

• Recommendation for Clinical Follow-up

• Disclaimers
Information and Reporting

- Systems to Handle:
  - Multiple Mutations
  - Multiple Interpretations
  - More than 1 Analyte for Determination

- Pediatrician Education
- Specialist Education
- Follow-up Staff Education
- Reporting Requirements for DNA-Based Tests
Other Considerations

- Inform all (hospitals; public)
- Website (yours and others), brochures, fact sheets
- Impacts on timeliness
- Timing of test, thus result release
- Reporting system (merge/mailers)
- LIMs to handle interpretations
- Systematic approach to query resources for interpretations
Thank you! Next up Jersey Boy—Dr. Scott Shone