

# You Can Do It Yourself! Molecular Testing for Community Pathologists

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# Disclosure

- Dr. Kant has no conflicts of interest to disclose which relate to material which will be presented in this course; he is an elected member of the Association for Molecular Pathology Council
- Acknowledgment: Thomas Williams MD, Omaha, Nebraska (Member, CAP Education Committee)

# Course Objectives

- Explore questions which arise for community pathologists who consider doing molecular (nucleic-acid based) testing in-house
- Factors which make one hesitant; assess whether these are real issues or not
- Resources, instruments/assay platforms, local factors which facilitate/impede successful implementation
- How to design appropriate validation and quality control protocols for in-house molecular assays
- Review of normal and aberrant assay results for common conditions
- Advise clinical and laboratory staff on proper procedures for collection, preparation, and storage of samples for molecular testing

# Agenda

Topic	Time
Overview/Questions – Dr. Kant	8:30 – 8:55
Case studies - Dr. Hyder	8:55 – 9:25
Case studies - Dr. Kaul	9:25 – 9:50
Discussion	9:50 – 10:00
<b>Break</b>	<b>10:00 – 10:30</b>
Case studies - Dr. Kaul	10:30 – 10:55
Case studies - Dr. Hyder	10:55 – 11:30
Selected technical issues / sendout testing - Dr. Kant	11:30 – 11:45
Discussion	11:45 – Noon

# Faculty and Background

- Dan Hyder
  - Modest-sized community hospital system, Pacific West
- Jeffrey Kant
  - Academic Medical Center, mid-East
- Karen Kaul
  - Large 'community' health system affiliated with academic center, mid-West

# University of Pittsburgh Medical Center – Molecular Diagnostics

- Division of Molecular Diagnostics
  - ~60 assays, 30,000 samples (Microbiology, Genetics, Hemepath)
  - ‘Common’ to esoteric reference tests, simple PCR to sequencing
  - Vast majority of tests are laboratory-developed
  - PhD Lab Manager, 2 semi-‘dedicated’ development staff,
  - Research faculty participate in service signout
  - ACGME-accredited MGP Fellowship
- Division of Molecular Anatomic Pathology
  - <1,000 samples/year
  - Microsatellite analysis (identity, LOH), MSI, some sequencing
- Virology Laboratory
  - CT/NG, quantitative CMV, SARS, influenza, respiratory panel pending
- Magee Women’s Hospital
  - Most STD (CT/NG, HPV, several other viruses)
- Children’s Hospital of Pittsburgh
  - Quantitative EBV, enterovirus, pertussis

# Questions from Community Pathologists

# Do I need specialized Training – to start/expand?

- No/depends
  - Support staff available – to be discussed
- How much/where?
  - National Meeting courses
  - Practicum (VCU)
  - Visits, formal MGP Fellowship training
  - Manufacturer training/'turn-key' systems
- Molecular Resources for Community Pathologists
  - Association for Molecular Pathology Website, membership (CHAMP listserve)
  - CAP Website, Mol Path course – more, regulatory
  - Journals (J Molec. Diagnostics, Clin. Chem, J. Clin Micro, Diag Mol Path, Archives Path/Lab Med., specialty journals)
  - Texts – see reference list

# How do I determine what tests to do scientifically?

- Clinical Utility
  - User requests/needs
    - Real need vs. marketing initiatives
    - 'Fit' for your system/situation
  - Implies clinical validity, analytic robustness
- Platform(s) available locally
  - Match to reagents
- New platform potential vs. capital available

# Do I need a savvy PhD? Why? Why not? When?

- Background/resourcefulness of Lab Director/staff
- Laboratory-developed testing
  - This means from scratch, not commercial ASR reagents
- Economics – lab-developed tests, prior experience, relationship with clinicians to discuss alternative or sequential testing

# What design issues are important for setting up a molecular laboratory?

- Do I need two (or more) rooms?
  - PCR amplification
  - Open/closed systems
- Centralized vs. 'distributed' molecular testing
- LIS for reporting?

# Does molecular testing differ from general laboratory testing?

- If so, in what way(s)?
  - Nucleic acid chemistry – sample types
  - RNA
  - Genetic testing
- What preanalytic process are most crucial to monitor?
  - Fixation (not) for tissue
  - Anticoagulant
- Are there unique issues associated with quality control or proficiency testing?
  - Alternate assessment
  - ‘Match’ of PT programs to platform in your laboratory

# Which Methods Should I Use?

- IVD vs. ASR vs. Other
- Existing platform(s) in laboratory?
  - What tests are available/planned on platform
  - Robustness of assays
  - Needs (e.g. analytic sensitivity)
  - Intended purpose (screening/diagnostic)
- Automation
- Track record of vendor including support
- Experience of other users

# Can I do ASR (lab-developed) or RUO assays?

- ASR (Analyte Specific Reagent)
  - The original rule
  - IVD (FDA-cleared)
  - RUO (“not for diagnostic purposes”)
- Disclaimer
  - “This test was developed and its performance characteristics determined by [Laboratory Name]. It has not been cleared or approved by the U. S. Food and Drug Administration.”
- Current status of FDA proposed guidelines to clarify original rule
- Issues with RUO assays

# Are there federal or state regulatory issues which impact decisions?

- Where/How does one find out this information?
  - e.g. Informed consent for genetic testing
- Pharmacogenetic assays – FDA and relabeling of drug package inserts

# Can you trust what vendors tell you?

- No different than other lab areas - Homework
  - Other users (vendor-provided +)
- Stability
  - History of 'churning' instruments/assays
- Support
  - Sendout TAT – commercial/boutique
  - True level of support for difficult cases
- In lab demo/trial periods
- ROI spreadsheets – examine vendor assumptions carefully
- Status of assay vs. FDA (e.g. ASRs)

# Bring in/send out molecular tests?

## Costs and other issues

- Volume
  - Do high/easy, send out low/complex?
- Savings can be significant
- Impact on laboratory staff
- Workflow
  - Centralized vs. Distributed Approaches
- Support issues to prepare for
- More on this in my 2<sup>nd</sup> brief presentation

# Economics

- How do I determine which tests make sense economically?
- Complexities of CPT coding
- Opportunities for niche testing and consultation?
- TAT (batched/panels vs. small runs or even individual samples)

# Genetic Testing

- How do I determine if a genetic test is appropriate before proceeding?
- How do I deal with issues that relate to genetic counseling?
- What if there is a separate CLIA specialty for genetic testing?

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