Evaluation of a Flexible Molecular System for the Detection of Respiratory and Gastrointestinal Pathogens

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Revised Abstract

Background: In our clinical lab, molecular tests are used to detect respiratory pathogens. Molecular tests, culture, immunoassays and microscopic exam are used to detect gastrointestinal pathogens. The BioCode MDx-3000 (Applied BioCode Inc, Santa Fe Springs, CA) (ABC) allows users to perform the BioCode Respiratory Pathogen Panel (RPP) and BioCode Gastrointestinal Pathogen Panel (GPP) simultaneously. The MDx-3000 offers flexible ordering and reporting capabilities.
Methods: The MDx-3000 uses Barcoded Magnetic Bead (BMB) technology to integrate and automate PCR, post-PCR sample handling and detection in a 96-well format. Contrived and clinical stool samples in Cary-Blair media (N=100) and nasopharyngeal samples (N=48), supplied by ABC, were tested by GPP and RPP. For samples extracted on the bioMerieux easyMAG, testing included runs of 24, 48 and 96 samples for GPP alone, 24 and 48 samples for RPP alone and combined runs of 24 GPP and 36 RPP and 36 GPP and 48 RPP samples. Sample results were compared to expected results. Workflow analysis included hands on time (HOT), turn-around time (TAT), ability to include different assays in one run, ease of use and flexibility in regards to clinical utility. A combined run of 36 GPP and 48 RPP samples was extracted on the Roche MagNA Pure 96 and included for workflow analysis.
Results: For EasyMag extracted samples, the GPP positive and negative agreement was 99.4% (178/179) and 99.8% (3348/3355) when compared to expected results. The RPP positive and negative agreement was 100% (117/117) and 99.1% (2058/2076). HOT and TAT were superior to tests currently in use. Reproducibility was evaluated with pooled NATtrol Controls (Zeptometrix). For RPP, 5 pools were assayed per run, all targets detected (4/4 per organism), no false positives (0/20). For GPP, 4 pools were assayed per run, all targets detected (5/5 per organism) with 1 false positive for Campylobacter (1/20).
Conclusion: GPP and RPP on the MDx-3000 displayed a high level of agreement with expected results and showed good reproducibility. The MDx-3000 was easy to use with the flexibility to run multiple assays on different sample types in one run. Flexible ordering and reporting allows clinicians to order only necessary tests and additional tests can be ordered and resulted without performing additional assays.

Background

The focus of the test utilization committee at Cleveland Clinic is to offer high quality laboratory testing by providing tests that are are clinically relevant and cost effective. One way is to eliminate ordering of unnecessary tests. Syndromic testing with highly multiplexed test can decrease turn around time but often clinicians do not want the full panel of tests for all patients due to cost and reimbursement issues.

Examples

- Multiplex respiratory panel can be ordered for hospitalized, immunocompromised patients.
- Multiplex GI panel requires approval from Infectious Disease physicians.

Methods

- 100 clinical and contrived stool specimens in Cary-Blair medium for the presence of GI pathogens.
- 48 clinical and contrived NPS specimens were evaluated for respiratory pathogens.
- Extracted for total nucleic acids by easyMAG.

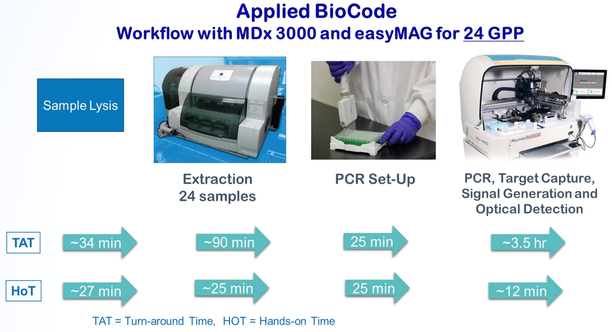


Figure 1: Workflow for BioCode MDx-3000

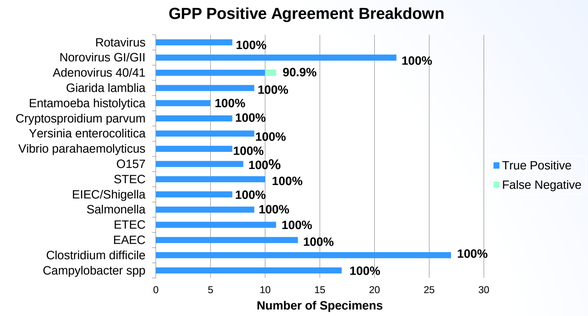
Following extraction with easyMAG, total nucleic acids were transferred to a PCR plate with an 8-channel pipettor. Mechanical lysis step is required only for stool samples but not for NPS.
MDx-3000 performs PCR, target capture, liquid handling and detection steps. The system is designed to simultaneously run up to 3 different BioCode panels in one run.

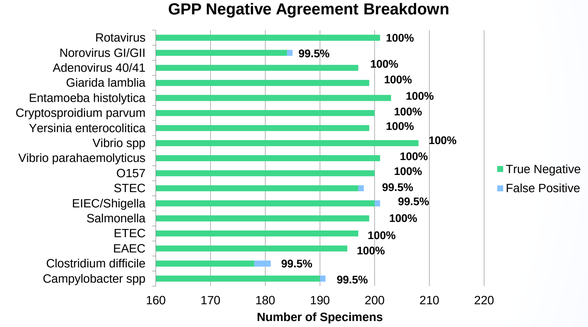
Table 1: Samples used to test for evaluation runs

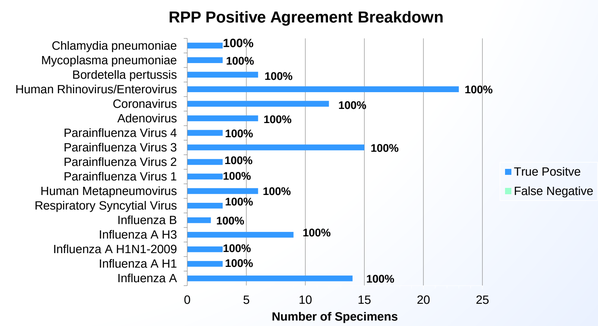
Run #	GPP wells	RPP wells	Total wells
CC eval1	24	0	24
CC eval2	48	0	48
CC eval3	96	0	96
CC eval4	0	72	72
CC eval5	24	36	60
CC eval6	36	48	84

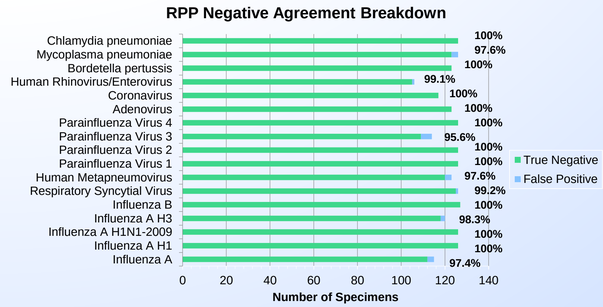
- Evaluation consisted of 6 runs (total of 384 wells)
- 2 of 6 runs had both RPP and GPP assays run concurrently
- NATtrol Controls were combined in pools or 3 to 5 organisms and included on each run (4 pools for GPP and 5 pools for RPP)

Results

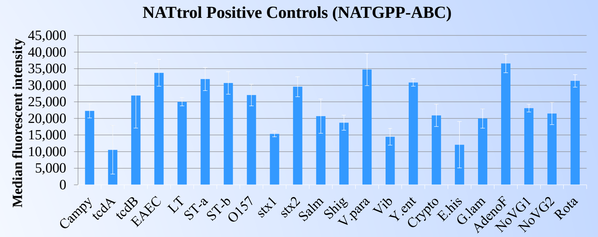


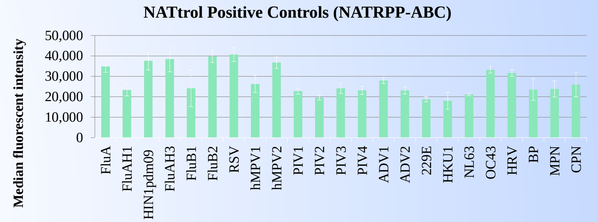






Results





Conclusions

- **Flexible**
  - Run up to 3 different panels and sample types on one plate.
  - Physician can choose which tests to order.
  - Customize reports and add on tests if requested.
- **Easy to use**
- **Highly reproducible**
- **Low Invalid rate (Internal control inhibition)**
  - RPP 0.8% (1/130). Sample valid on repeat.
  - GPP 0.0% (0/208).
- **Minimal training needed**
- **Intuitive deck/PCR set up**

Discussion

- BioCode MDx-3000 offers more flexible syndromic panel testing due to the data masking option which enables select target reporting based on clinician's order (only order necessary tests).
- Tests can later be unmasked if requested by physician. These additional results are reported without the need to collect another sample or perform additional testing.

Acknowledgements

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