

Microbiology: Up to Date

“Molecular Detection Panels”

รองศาสตราจารย์แพทย์หญิง นันตรา สุวันทรัตน์
วิทยาลัยแพทยศาสตร์นานาชาติจุฬาภรณ์ มหาวิทยาลัยธรรมศาสตร์
โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

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M.Sc (Health Science Education)

Emerging and Re-emerging Infectious Diseases:
A Continuous Challenge

11 October 2020



Microbiology: Up to Date

“Molecular Detection Panels”

- What is it?
- Syndromic testing
- Which one should we use?
 - Respiratory panel/ Pneumonia panel
 - GI panel
 - Meningitis panel
 - Sepsis panel (Bacteremia)
- Summary

No disclosure

ห้องปฏิบัติการเทคนิคการแพทย์

เปิดการทดสอบด้านชีวโมเลกุล

1. ชุดตรวจ Respiratory Panel ประเภท Film Array
2. ชุดตรวจ Pneumonia Panel ประเภท Film Array
3. ชุดตรวจ Meningitis/ Encephalitis Panel ประเภท Film Array
4. Respiratory Panel ประเภท Multiplex real time RT-PCR
5. ชุดตรวจ Respiratory ประเภท Molecular Rapid Test ประกอบด้วย
 - ☐ Influenza A&B2
 - ☐ RSV
 - ☐ Strep A

FilmArray®
The fastest way to better results.



bioMérieux



เริ่มให้บริการ

ตั้งแต่ 1 เมษายน 2563

Film Array GI panels



Verigene Sepsis panels

วารสาร Tham Lab ฉบับที่ 1 ปีที่ 7 เดือน พฤษภาคม 2563

Diagnosis: Clinical Reasoning



- **Community acquired pneumonia (CAP) : Pathogens**
Lobar pneumonia, bacterial pneumonia → *Streptococcus pneumoniae*
Atypical pneumonia, or viral pneumonia → *Mycoplasma*, *respiratory viruses*
- **Hospital associated pneumonia (HAP) : Nosocomial Pathogens**
Pseudomonas aeruginosa, *Acinetobacter baumannii*, MRSA

Molecular Detection Panels = Syndromic Testing
Multiplex PCR/ Real-time PCR



BIO FIRE[®]
A BIOMÉRIEUX COMPANY

Syndromic Testing: The Right Test, The First Time
Respiratory • Blood Culture Identification • Gastrointestinal • Meningitis/Encephalitis

biofiredx.com

Molecular
Detection Panels

“Syndromic
Testing”

Based-on Diagnostic
Stewardship

Based-on Diagnostic Stewardship

Ordering (Preanalytic)

- Test only when pretest probability moderate to high for ≥ 2 targets on the panel
- when results will influence management

Collection (Preatalytic)

- Use recommended collection and transport conditions to reduce contamination and optimized yield

Processing (Analytic)

- Follow stringent contamination prevention guidance in the laboratory to avoid false-positive results

Reporting (Postanalytic)

- Selective suppression of results for tests on panel if other testing approach used in the laboratory
 - eg. *C. difficile* testing on stool pathogen panel (*C. difficile* = nosocomial infection/ not bacterial diarrhea/ community case)
- Text interpreting results discussing colonization



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22
PATHOGENS
45 min

Clinical Impact of the FilmArray® Respiratory Panels*

*Includes FilmArray® Respiratory Panel (RP)
FilmArray® Respiratory Panel 2 (RP2)
FilmArray® Respiratory Panel 2 plus (RP2plus)

FilmArray RP Pathogens

VIRUSES

Adenovirus
Coronavirus 229E
Coronavirus HKU1
Coronavirus NL63
Coronavirus OC43
Human Metapneumovirus
Human Rhinovirus/Enterovirus
Influenza A
Influenza A/H1-2009
Influenza A/H3
Influenza B
Middle East Respiratory Syndrome (MERS-CoV)*
Parainfluenza Virus 1
Parainfluenza Virus 2
Parainfluenza Virus 3
Parainfluenza Virus 4
Respiratory Syncytial Virus

BACTERIA

Bordetella parapertussis†
Bordetella pertussis†
Chlamydia pneumoniae
Mycoplasma pneumoniae

*Additional target on the FilmArray Respiratory Panel 2 (RP2)

†Additional target on the FilmArray Respiratory Panel 2 plus (RP2plus). RP2plus is currently under FDA review. For use when MERS infection or exposure is suspected.

‡Nationally notifiable conditions. Refer to your state health lab for requirements pertaining to state-reportable pathogens.

Overall Performance of the FilmArray RP2¹

- 97.1% Sensitivity
- 99.3% Specificity

Sample Requirements:

0.3 mL of nasopharyngeal swab specimen stored in transport medium

~ 4000 bath / test

TAT 45-60 min



TEST REPORT			
Patient ID	Sample ID	MX19002728	Test Time 2019-01-28 13:44
Pathogens detected <ul style="list-style-type: none"> Human Metapneumovirus A+B Mycoplasma pneumoniae Parainfluenza virus 3 			
User	KKH	Test Status	Completed
		Internal Controls	Passed
RESULT DETAILS			
Others			
Not detected	Adenovirus	-	-
Not detected	Bordetella	-	-
Not detected	Bordetella pertussis	-	-
Not detected	Coronavirus 229E	-	-
Not detected	Coronavirus HKU1	-	-
Not detected	Coronavirus NL63	-	-
Not detected	Coronavirus OC43	-	-
Not detected	Human Metapneumovirus A+B	30.7 / 134,998	-
Not detected	Influenza A	-	-
Not detected	Influenza A/H1N1	-	-
Not detected	Influenza A/H1N1 pdm09	-	-
Not detected	Influenza A/H3	-	-
Not detected	Influenza B	-	-
Not detected	Legionella pneumophila	-	-
Not detected	Mycoplasma pneumoniae	32.2 / 291,476	-
Not detected	Parainfluenza virus 1	-	-
Not detected	Parainfluenza virus 2	-	-
Not detected	Parainfluenza virus 3	30.5 / 295,518	-
Not detected	Parainfluenza virus 4	-	-
Not detected	Respiratory Syncytial Virus A+B	-	-
Not detected	Respiratory Syncytial Virus B	-	-
Not detected	Respiratory Syncytial Virus C	30.5 / 192,817	-
TEST DETAILS			
User	KKH	Cartridge SN	180243242
Assay	RP2	Cartridge LOT	180243
Sample	Swab	Expiration Date	2019-06-27
		SN Operational module	000001024
		SN Analytical module	1182
		Error code	None

Respiratory Panel V2

2000-3000 bath / test

Report TAT 90 min

Sensitivity 97.3
Specificity 98.4





QIAstat-Dx Respiratory Panel V2

The next generation of syndromic insights

The QIAstat-Dx® (EtiogCORE) Respiratory Panel V2 utilizes proven QIAGEN® sample and assay technologies to provide clinical insights for patients with suspected upper respiratory infections.



 FilmArray Respiratory Panel 2			
www.biofirmedx.com			
Run Summary		Run Date: 18 Jan 2017	
Sample ID: RP2ex_33_Equiv		5:21 PM	
Detected: Adenovirus		Controls: Passed	
Equivalent: Influenza A			
Result Summary			
		Viruses	
✓ Detected	Adenovirus		
Not Detected	Coronavirus 229E		
Not Detected	Coronavirus HKU1		
Not Detected	Coronavirus NL63		
Not Detected	Coronavirus OC43		
Not Detected	Human Metapneumovirus		
Not Detected	Human Rhinovirus/Enterovirus		
➤ Equivalent	Influenza A		
Not Detected	Influenza B		
Not Detected	Parainfluenza Virus 1		
Not Detected	Parainfluenza Virus 2		
Not Detected	Parainfluenza Virus 3		
Not Detected	Parainfluenza Virus 4		
Not Detected	Respiratory Syncytial Virus		
		Bacteria	
Not Detected	Bordetella parapertussis (IS1007)		
Not Detected	Bordetella pertussis (pdtP)		
Not Detected	Chlamydia pneumoniae		
Not Detected	Mycoplasma pneumoniae		
Run Details			
Pouch: RP2 v1.1	Protocol: RP2 v1.1		
Run Status: Completed	Operator: JDOE		
Serial No.: 0026525	Instrument: TMCCF3		
Lot No.: 161013E			

TEST REPORT			
Patient ID	Sample ID	MX19002728	Test Time 2019-01-28 13:44
Pathogens detected <ul style="list-style-type: none"> Human Metapneumovirus A+B Mycoplasma pneumoniae Parainfluenza virus 3 			
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Others			
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Not detected	Bordetella	-	-
Not detected	Bordetella pertussis	-	-
Not detected	Coronavirus 229E	-	-
Not detected	Coronavirus HKU1	-	-
Not detected	Coronavirus NL63	-	-
Not detected	Coronavirus OC43	-	-
Not detected	Human Metapneumovirus A+B	30.7 / 134,998	-
Not detected	Influenza A	-	-
Not detected	Influenza A/H1	-	-
Not detected	Influenza A/H1N1 pdm09	-	-
Not detected	Influenza A/H3	-	-
Not detected	Influenza B	-	-
Not detected	Legionella pneumophila	-	-
Not detected	Mycoplasma pneumoniae	32.2 / 291,476	-
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Not detected	Parainfluenza virus 2	-	-
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Not detected	Parainfluenza virus 4	-	-
Not detected	Respiratory Syncytial Virus A+B	-	-
Not detected	Respiratory Syncytial Virus C	30.5 / 192,817	-
Not detected	Respiratory Syncytial Virus D	-	-
Not detected	Respiratory Syncytial Virus E	-	-
Not detected	Respiratory Syncytial Virus F	-	-
Not detected	Respiratory Syncytial Virus G	-	-
Not detected	Respiratory Syncytial Virus H	-	-
Not detected	Respiratory Syncytial Virus I	-	-
Not detected	Respiratory Syncytial Virus J	-	-
Not detected	Respiratory Syncytial Virus K	-	-
Not detected	Respiratory Syncytial Virus L	-	-
Not detected	Respiratory Syncytial Virus M	-	-
Not detected	Respiratory Syncytial Virus N	-	-
Not detected	Respiratory Syncytial Virus O	-	-
Not detected	Respiratory Syncytial Virus P	-	-
Not detected	Respiratory Syncytial Virus Q	-	-
Not detected	Respiratory Syncytial Virus R	-	-
Not detected	Respiratory Syncytial Virus S	-	-
Not detected	Respiratory Syncytial Virus T	-	-
Not detected	Respiratory Syncytial Virus U	-	-
Not detected	Respiratory Syncytial Virus V	-	-
Not detected	Respiratory Syncytial Virus W	-	-
Not detected	Respiratory Syncytial Virus X	-	-
Not detected	Respiratory Syncytial Virus Y	-	-
Not detected	Respiratory Syncytial Virus Z	-	-
TEST DETAILS			
User	KKH	Cartridge SN	180243242
Assay	RP2	Cartridge LOT	180243
Sample	Swab	Expiration Date	2019-06-27
		SN Operational module	000001024
		SN Analytical module	1182
		Error code	None

Specification Comparison	FilmArray	QIAstat-Dx
Pathogens Detection	21 types (18 viruses/ 3 Bacteria) (- Legionella, + Chlamydia) +/- MERS-CoV +/- SARS-CoV2	21 types (18 viruses/ 3 Bacteria) (- Chlamydia, + Brocavirus, Legionella) +/- MERS-CoV +/- SARS-CoV2
Sensitivity (Overall)	97.1%	97.3%
Specificity (Overall)	99.3%	98.4%
Report TAT (turn around time)	45-60 min	70-90 min
US FDA Cleared	YES	NO (RUO, Research Use Only)
CE-IVD Cleared	YES	YES
Price per test	4000 bath (Sell price = ?)	2000 - 3000 bath (Sell price = ?)
Biosafety/ Labs workflow	Comparable	Comparable
Available to set up at your hospital / comfortability of the Labs	?	?

FilmArray Pneumonia Panel Plus
"1 Test, 34 Targets. All in about an hour."

The FilmArray Pneumonia Panel will test for a comprehensive set of 27 pathogens and 7 antibiotic resistance markers. The FilmArray Pneumonia Panel will identify the most common bacterial, viral, and fungal pathogens associated with various types of community/hospital-acquired pneumonia. Quickly identifying the probable causative agent helps determine how a healthcare provider chooses to treat a lower respiratory tract infection.

Panel Menu

Bacteria
Semi-Quantitative Bacteria
Acinetobacter calcoaceticus-baumannii complex
Serratia marcescens
Proteus spp.
Klebsiella pneumoniae group
Enterobacter aerogenes
Enterobacter cloacae
Escherichia coli
Haemophilus influenzae
Moraxella catarrhalis
Pseudomonas aeruginosa
Staphylococcus aureus
Streptococcus pneumoniae
Klebsiella oxytoca
Streptococcus pyogenes
Streptococcus agalactiae

Atypical Bacteria
Qualitative Bacteria
Legionella pneumophila
Mycoplasma pneumoniae
Chlamydia pneumoniae

Antimicrobial Resistance Genes
mecA/C and MREJ
KPC
NDM
Oxa-48-like
CTX-M
VIM
IMP

Viruses
Influenza A
Influenza B
Respiratory Syncytial Virus
Human Rhinovirus/Enterovirus
Human Metapneumovirus
Parainfluenza virus
Adenovirus
Coronavirus
Middle East Respiratory Syndrome Coronavirus



Pneumonia Panel
VIRUS
Atypical bacteria
Bacteria
MDR genes detection

6-8000 bath / test
TAT 1 hr , sensitivity

Hausen's Real time PCR Solution



RP – 33
Virus + Bacteria

Real-time PCR
(ready to use test
Vs traditional version)

Price bath / test

Report TAT

Sensitivity
Specificity

Labs expertise

Labs biosafety level

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No disclosure

FilmArray Meningitis/Encephalitis Panel

"1 Test, 14 Targets, All in about an hour."

The FilmArray Meningitis/Encephalitis (ME) Panel tests cerebrospinal fluid (CSF) for a variety of pathogens including bacteria, viruses, and fungi. The integrated FilmArray system yields sample to results in about an hour, with only 2 minutes of hands-on time.

Panel Menu

Bacteria

Escherichia coli K1
Haemophilus influenzae
Listeria monocytogenes
Neisseria meningitidis
Streptococcus agalactiae
Streptococcus pneumoniae



Viruses

Cytomegalovirus (CMV)
Enterovirus
Herpes simplex virus 1 (HSV-1)
Herpes simplex virus 2 (HSV-2)
Human herpesvirus 6 (HHV-6)
Human parechovirus
Varicella zoster virus (VZV)



Yeast

Cryptococcus neoformans/gattii



Meningitis Panel

~ 6000 bath / test

TAT 1 hr

Meningitis Panel: Traditional RT-PCR
or
Small multiplex PCR panels
(such as only HSV, enterovirus)

Price, TAT, instruments, Labs expertise
TAT 1 hr

THE BIOFIRE GI PANEL MENU

Overall 98.5% Sensitivity and 99.2%

Specificity³

Sample Type: Stool in Cary Blair medium

BACTERIA:

Campylobacter (jejuni, coli, and upsaliensis)
Clostridium difficile (toxin A/B)
Plesiomonas shigelloides
Salmonella
Yersinia enterocolitica
Vibrio (parahaemolyticus, vulnificus, and cholerae)
Vibrio cholerae

DIARRHOEAGENIC E. COLI/SHIGELLA:

Enteraggregative E. coli (EAEC)
Enteropathogenic E. coli (EPEC)
Enterotoxigenic E. coli (ETEC) *stx1/stx2*
Shiga-like toxin-producing E. coli (STEC)
E. coli O157
Shigella/Enteroinvasive E. coli (EIEC)

PARASITES:

Cryptosporidium
Cyclospora cayentanensis
Entamoeba histolytica
Giardia lamblia

VIRUSES:

Adenovirus F40/41
Astrovirus
Norovirus GI/GII
Rotavirus A
Sapovirus (I, II, IV, and V)

GI Panel

~ 5000 bath / test

TAT 1 hr

GI Panel
Traditional RT-PCR
Small multiplex PCR

• *C. difficile* result need to be suppressed

(Use specific test for *C. difficile* PCR)

The FilmArray BCID Panel

Simultaneous detection of 27 targets:

Gram + Bacteria <ul style="list-style-type: none"> <i>Staphylococcus</i> <i>Staphylococcus aureus</i> <i>Streptococcus</i> <i>Streptococcus agalactiae</i> 	<ul style="list-style-type: none"> <i>Streptococcus pyogenes</i> <i>Streptococcus pneumoniae</i> <i>Enterococcus</i> <i>Listeria monocytogenes</i>
Gram - Bacteria <ul style="list-style-type: none"> <i>Klebsiella oxytoca</i> <i>Klebsiella pneumoniae</i> <i>Serratia</i> <i>Proteus</i> <i>Acinetobacter baumannii</i> <i>Haemophilus influenzae</i> 	<ul style="list-style-type: none"> <i>Neisseria meningitidis</i> <i>Pseudomonas aeruginosa</i> <i>Enterobacteriaceae</i> <i>Escherichia coli</i> <i>Enterobacter cloacae</i> complex
Fungi <ul style="list-style-type: none"> <i>Candida albicans</i> <i>Candida glabrata</i> 	<ul style="list-style-type: none"> <i>Candida krusei</i> <i>Candida parapsilosis</i> <i>Candida tropicalis</i>
Antibiotic Resistance <ul style="list-style-type: none"> <i>mecA</i> <i>vanA / vanB</i> 	<ul style="list-style-type: none"> <i>KPC</i>

Blood c/s GP
Blood c/s GN

Flu A(H3, H1)
Flu B
RSV



Fig. 3. Nanosphere Verigene system. Verigene processor on the right, reader and cartridges on the left. Instrument footprints in inches: Processor, 7.6 width × 18.7 height × 22.9 depth; reader, 11.7 width × 12.4 height × 20.5 depth. Processors are stackable. No computer is required for operation. (Courtesy of Nanosphere, Northbrook, IL; with permission.)

Rapid Diagnostics in Clinical Microbiology and ASP

Direct Testing from BC Bottle	Mortality Benefit	Change in LOS	Cost saving per patient (\$)	AS Intervention
FISH probes	ND	2 d less	4005 <small>Plot Area</small>	YES
FISH probes	ND	2.2 d more	ND	NO
FISH probes*	ND	ND	1729	YES
FISH probes	16.8% vs 7.9%	2 d less**	19,441**	NO
GeneXpert MRSA/SA	18% vs 26% **	6.2d less	21,387	YES
MALDI-TOF	5.6% vs 10.7%**	1.8d less	19,547 **	YES
MALDI-TOF	12.7% vs 20.3%	2.8 d less **	ND	YES
Verigene #	NO	21.7d less	60,729	YES

* = Yeast only; ** = difference was not statistically significant; # = enterococci

Kothari A, et al. 2014; CID 59:272-8

Limited data in Thailand

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Molecular Detection Panels = Syndromic Testing

Multiplex PCR/ Real-time PCR

Respiratory (RP & RP2plus) Panel  22 Targets • 4 bacteria • 18 viruses	Blood Culture Identification (BCID) Panel  27 Targets • 19 bacteria • 5 yeast • 3 antibiotic-resistance genes	Gastrointestinal (GI) Panel  22 Targets • 13 bacteria • 5 viruses • 4 parasites	Meningitis/Encephalitis (ME) Panel  14 Targets • 6 bacteria • 7 viruses • 1 yeast
Immunocompromised host Critical ill Viral, atypical bacteria • Not for only SARS-CoV2 test (less sensitive in multiplex panel)	Severe sepsis? MDR pathogens	Chronic diarrhea? Not for only C. difficile test	HSV Enterovirus

Questions
and
Discussion



Thank you for your attention

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