

Point-of-Care Diagnostic Technologies of the Future

Michel G. Bergeron, MD, FRCPC

Professor and Chairman
Division of Microbiology and
Infectious Diseases Research Center
2705, Boul. Laurier, Québec (Québec) G1V 4G2
Canada

Tel.: 418-654-2705

E-mail: Michel.G.Bergeron@crchul.ulaval.ca

AACC 21st International Symposium
Québec City, September 28, 2006



**Centre de recherche en infectiologie
Université Laval**

Michel G. Bergeron (Michel.G.Bergeron@crchul.ulaval.ca)

Infectious diseases : Number one cause of mortality worldwide

Diseases	Death per year (Million)	Percent (%)
INFECTIONS	17.0	30
Cardiovascular	11.0	20
Cancer	7.0	12
Others and accidents	10.5	19
Unknown	10.5	19
TOTAL	56.0	100

Mortality from infectious diseases (WHO Health report 2004)

	Death (Million) (Yearly)
Lower respiratory tract infections (Influenza, Pneumococcus, SARS)	4.0
HIV / AIDS	3.0
Vaccines preventable childhood diseases *	3.0
Diarrhea (<i>E. coli</i> , Salmonella, Cholera)	2.0
Tuberculosis	1.6
Malaria	1.2

* Pertussis, Poliomyelitis, Diphtheria, Measles (1/2 deaths), Tetanus, Meningitis and hepatitis B
Mathers, C.D., et al. Deaths and Disease Burden by Cause: Global Burden of Disease Estimates for 2001 by World Bank Country Groups 2003. World Bank Washington, D.C.

Infectious Diseases : America has its share !

HIV/AIDS

SARS

Clostridium difficile

Influenza (Flu)

MRSA (Antibiotic resistance)

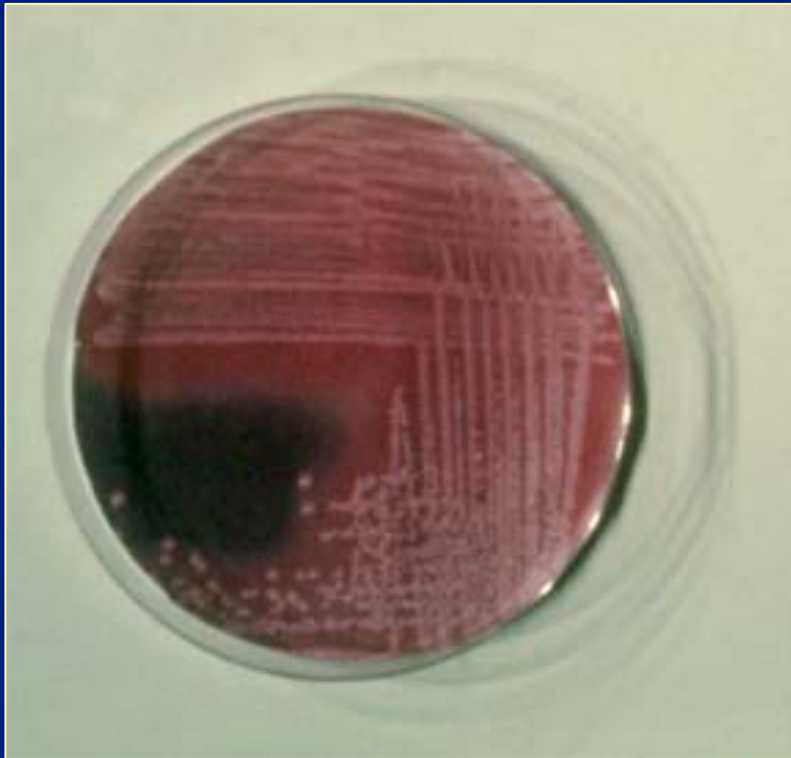
“Walkerton *E. coli* episode”

West Nile

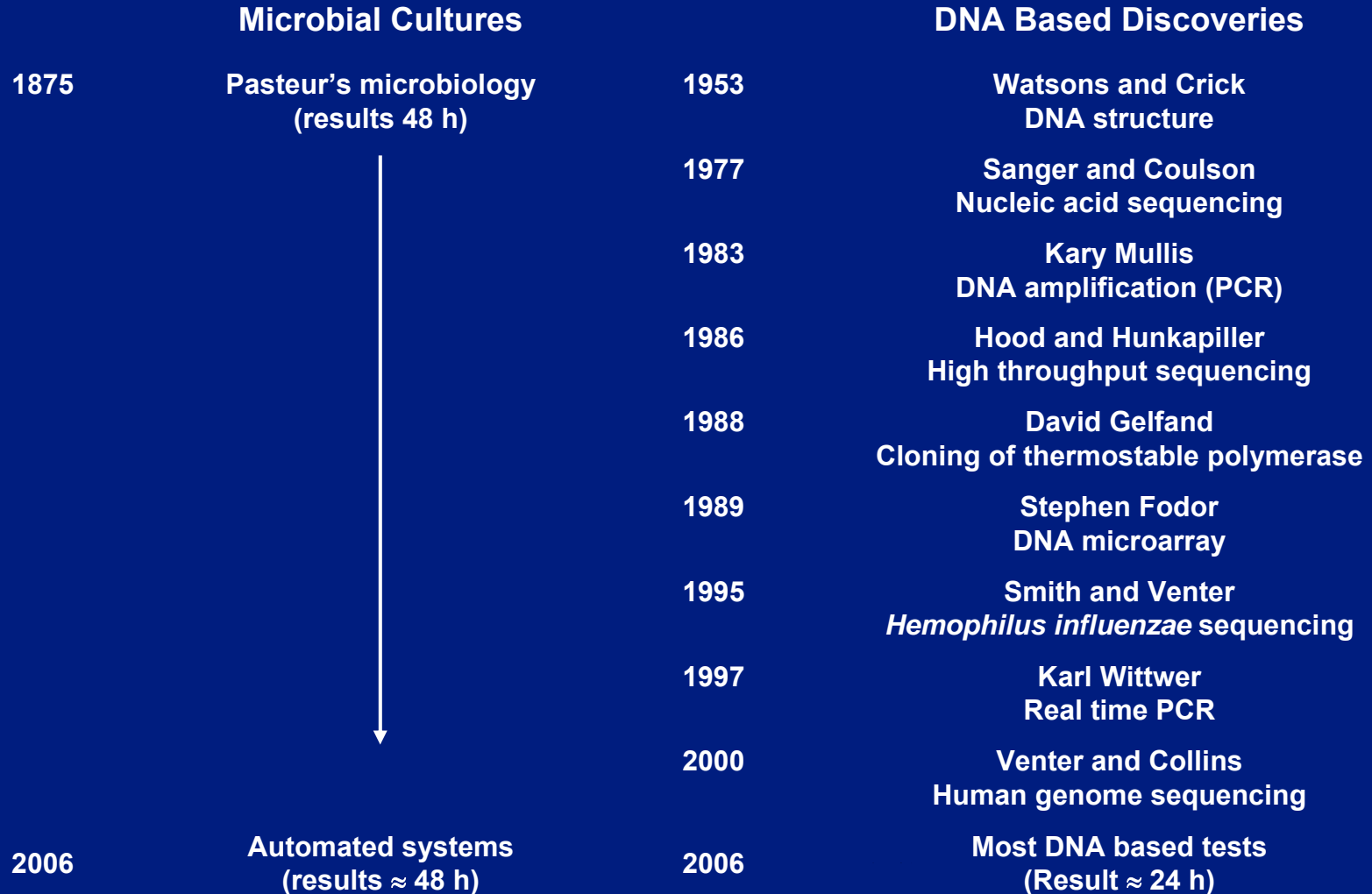
Mad cow diseases

Pasteur's Microbiology

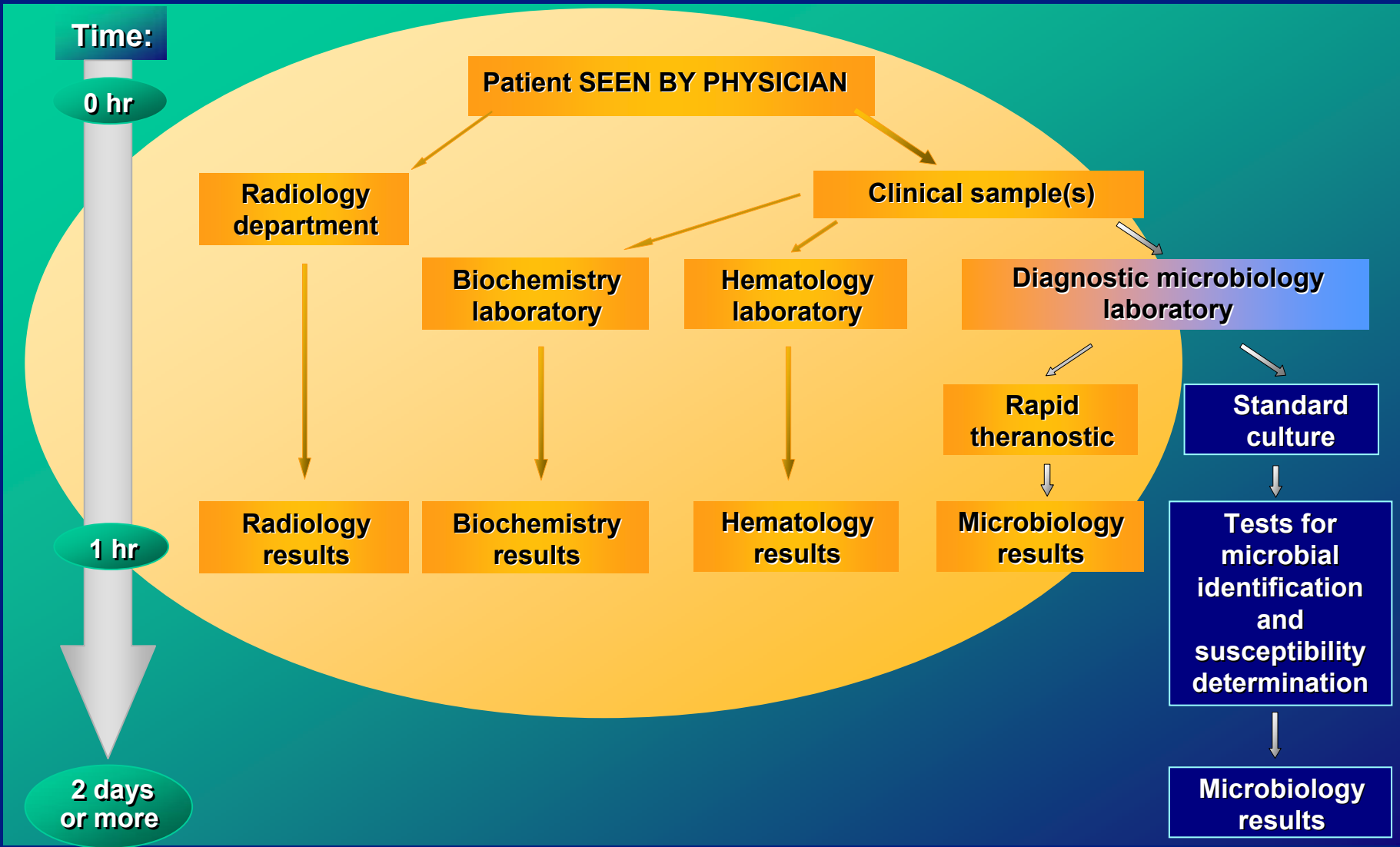
2 days to 2 weeks to identify microbes



Technologies Will Revolutionize Diagnostics



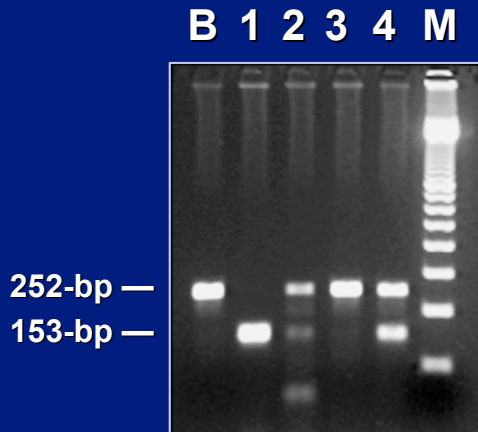
Why Rapid (<1h) Molecular Theranostics In Infectious Diseases?



Preventing meningitis using Rapid (<1h) Group B *Streptococci* GBS) test

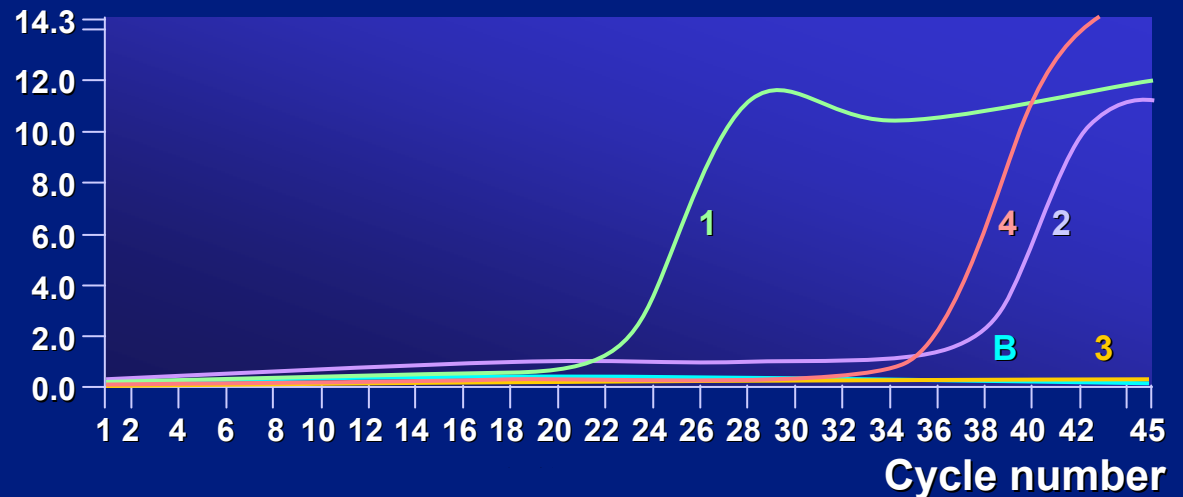
- Specific DNA sequences (finger prints) of the bacteria
- Lysis solution to crack open bacteria and extract DNA
- Protocols to appropriately eliminate inhibitors in clinical samples
- Simultaneous amplification (PCR) and detection of DNA target

Conventional PCR



Real-time PCR

Fluorescence ratio



Source: Bergeron et al, NEJM 343:175-179, 2000

Top ten discovery of the year of Quebec science 2000

November 18, 2002

FDA CLEARS NEW LAB TEST FOR GROUP B STREP IN PREGNANT WOMEN

The Food and Drug Administration today cleared for marketing a new laboratory test for Group B Streptococcus in pregnant women.

The new test, the IDI-Strep B test, made by Infectio Diagnostic, Inc., of Quebec, can provide results in one hour, if facilities can provide round-the-clock testing. In contrast, the standard method of culture testing takes 18 to 48 hours for results. The new test is performed using a Cepheid Smart Cycler instrument on a swab sample taken from the vagina and rectum.

Group B strep is a leading cause of illness and death among newborns in the United States. It can be acquired during birth from mothers who unknowingly have the organism. An estimated 10 percent to 30 percent of pregnant women have Group B strep. However, antibiotic treatment of the mother during labor can prevent transmission to the newborn.

Pregnant women are typically screened for Group B strep two to four weeks before labor begins using the standard culture method, as recommended by the Centers for Disease Control and Prevention (CDC). If the test is positive for Group B strep, the woman is given four hours of antibiotic treatment during labor.

Use of this standard screening method has led to a 70 percent decline in the incidence of Group B strep during the past decade. However, because of the time needed to culture samples and the four hours needed for antibiotic treatment, it is only useful for women who are tested at least several days before labor begins--not those who start labor early, or who do not have the advantage of pre-natal care. The new IDI-Strep B test, with timely results, could be particularly beneficial for these women when they first go into labor.

FDA cleared the IDI Strep B test based on clinical studies conducted by the manufacturer of 802 women at five medical centers in the United States and Canada. The studies showed that the test detected approximately 94 percent of Group B strep in pregnant women.

The IDI-Strep B test is the first non-culture test that meets the performance criteria recommended by CDC guidelines--at least 85% sensitive compared to culture methods. Because of this, it can be used instead of standard culture methods.



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Genomics at the service of Infectious Diseases : A New Reality

Researchers from Université Laval have developed the:

- First rapid DNA-based FDA approved real-time (< 60 min) PCR assays now commercialized by BD Diagnostics - GeneOhm

- IDI-StrepB™
- IDI-MRSA™
- IDI-VRE™



Identification systems currently available :

Number of technical steps and time-to-results

SYSTEMS EXAMPLES	NUMBER OF TECHNICAL STEPS	TIME TO RESULTS (hours)
Phenotypic identification		
Manual (API galleries and others)	15 - 25	48 – 72
Automated (Vitek, Microscan)	10 – 20	30 – 54
Genotypic identification (Directly from clinical samples)		
Roche Cobas Amplicator for <i>Chlamydia</i>	59	22
Bayer HIV/ β DNA analyser	71	30
IDI* Strep B™ (Group B Streptococcus)	6	<1
IDI* MRSA™ (Methicillin-resistant <i>S. aureus</i>)	6	<1
IDI* VRE™ (Vancomycin-resistant enterococci)	6	<1

* BD Diagnostics – GeneOhm (www.bd.com)



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Optimal Point-Of-Care Tests (POCTs)

Definition

Simple (single step), rapid (<15 minutes) and affordable tests at point of care that give a clear answer and which are supported by a handheld device

**Examples: Pregnancy tests
Glucose Tests**

GeneXpert[®] from Cepheid



Real-time PCR results in 75 minutes

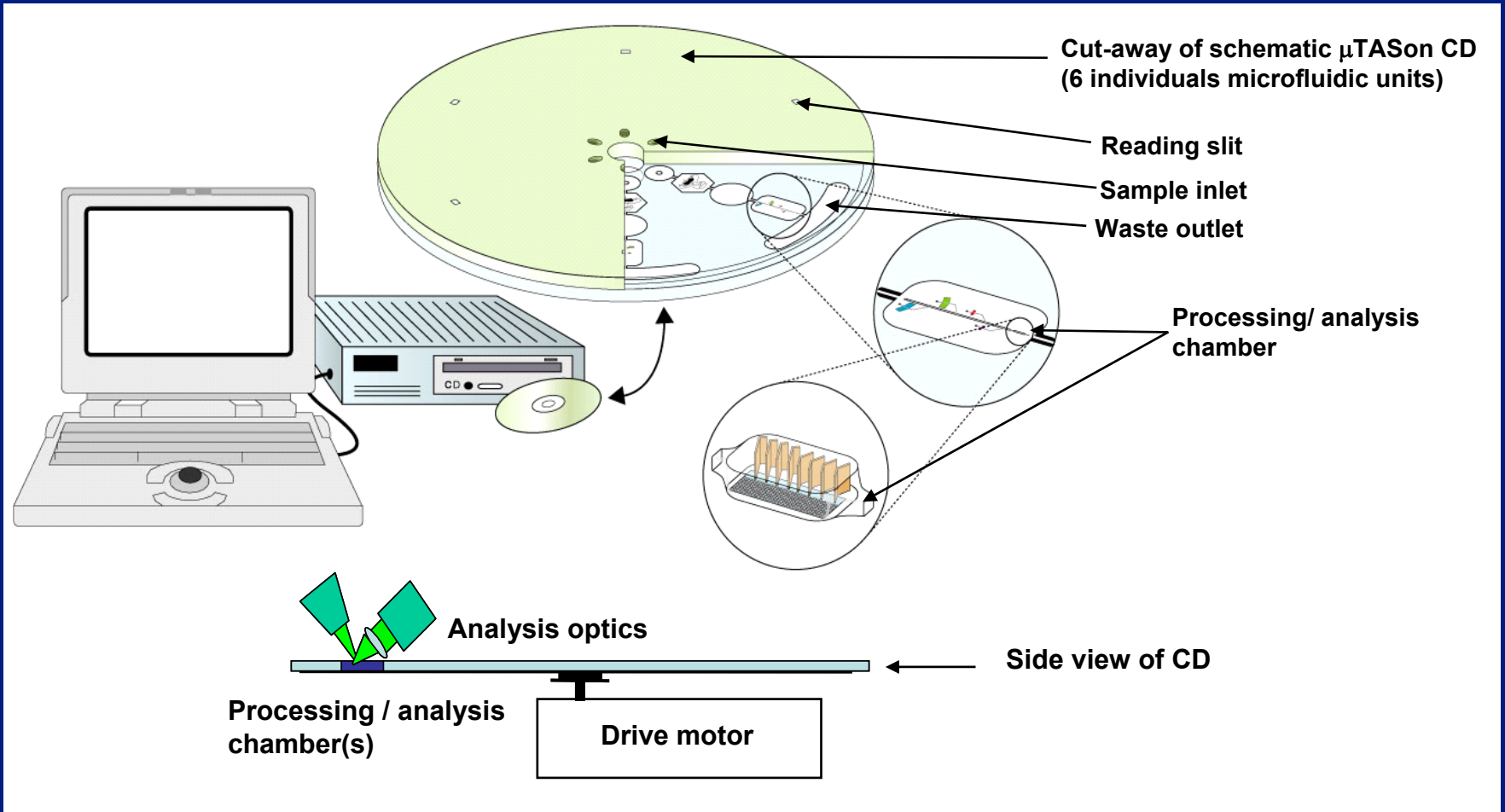
Source: www.cepheid.com/gbs/cepheid_gbs_microsite_9.html

From Real-Time PCR to Rapid (<15min) Nucleic Acid-Based Microfluidic-Microarray Point-Of-Care Tests (POCT) on Compact Disc (CD)

- Most infectious diseases are caused by several pathogens
- Real-time PCR can only detect few microbes (≤ 5)
- Combining:
 - Genomics
 - DNA microarrays
 - Innovative biosensors
 - Microfluidic technologies

We are developing Dx devices that will be merged into a lab-on-a-chip (μ TAS) that will identify multiple pathogens

Integrated Microfluidic-Microarray CD

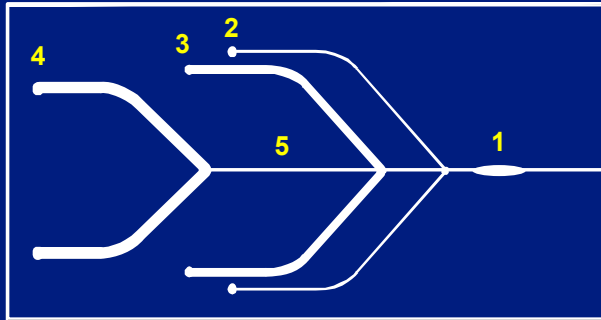


Sample Preparation and Nucleic Acid Extraction and Purification CD



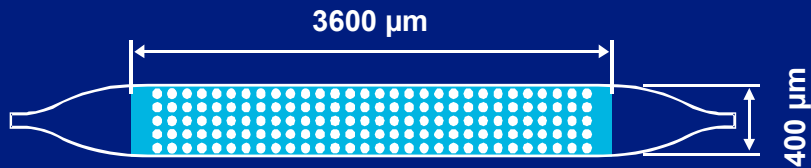
CD d'hybridation

A



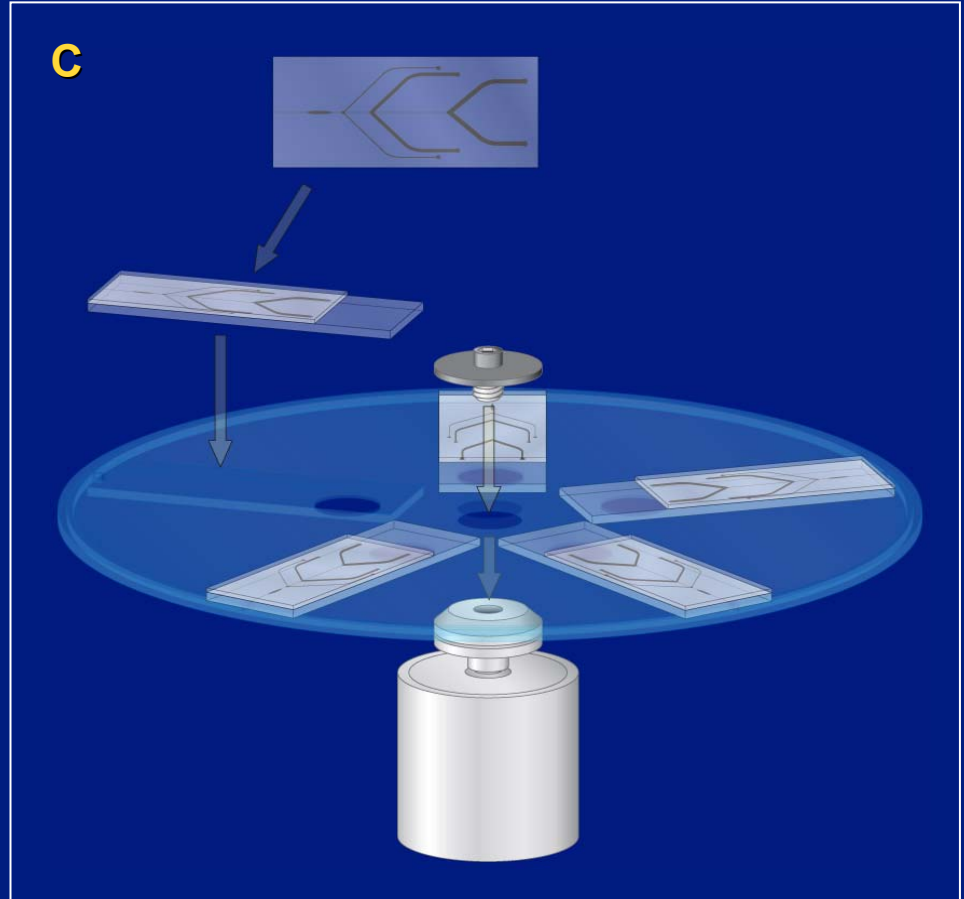
Microfluidic unit (2, 3, 4, 5)

B



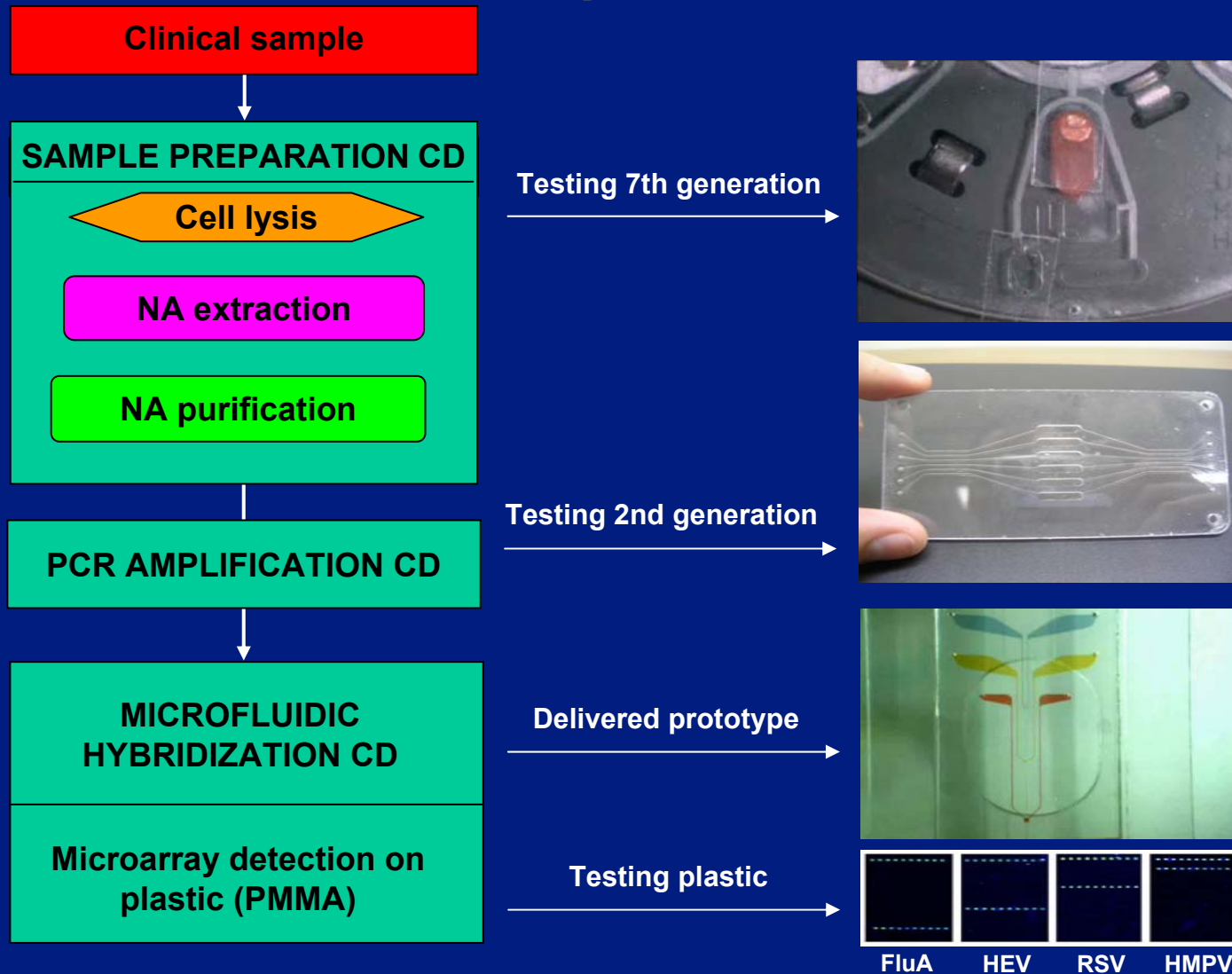
Microarray (1)

C



Source: Peytavi, R. *et al Clin. Chem.* 2005. 51(10):1836-1844 Bioarrays news microarray Innovaters 2006

Rapid (<1h) Point-of-Care Diagnostics on Compact Disc



Disadvantages of PCR

Time consuming

Difficult to multiplex

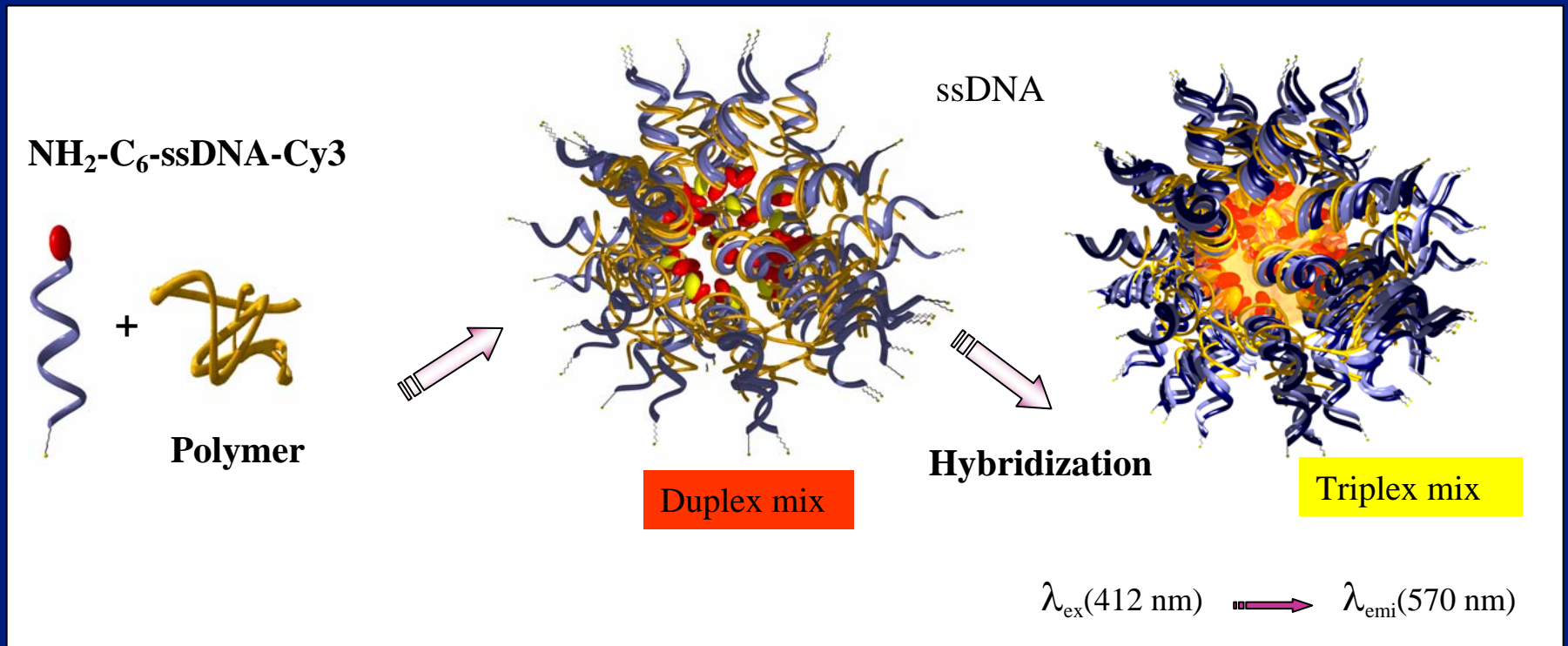
Sensitive to enzyme inhibitors

Expensive

Increase the complexity of the lab-on-chip

Towards Ultra Sensitive Polymeric Detection without PCR Amplification

Fluorescence Chain Reaction (FCR) in Liquid
Limit of detection: 5 DNA molecules

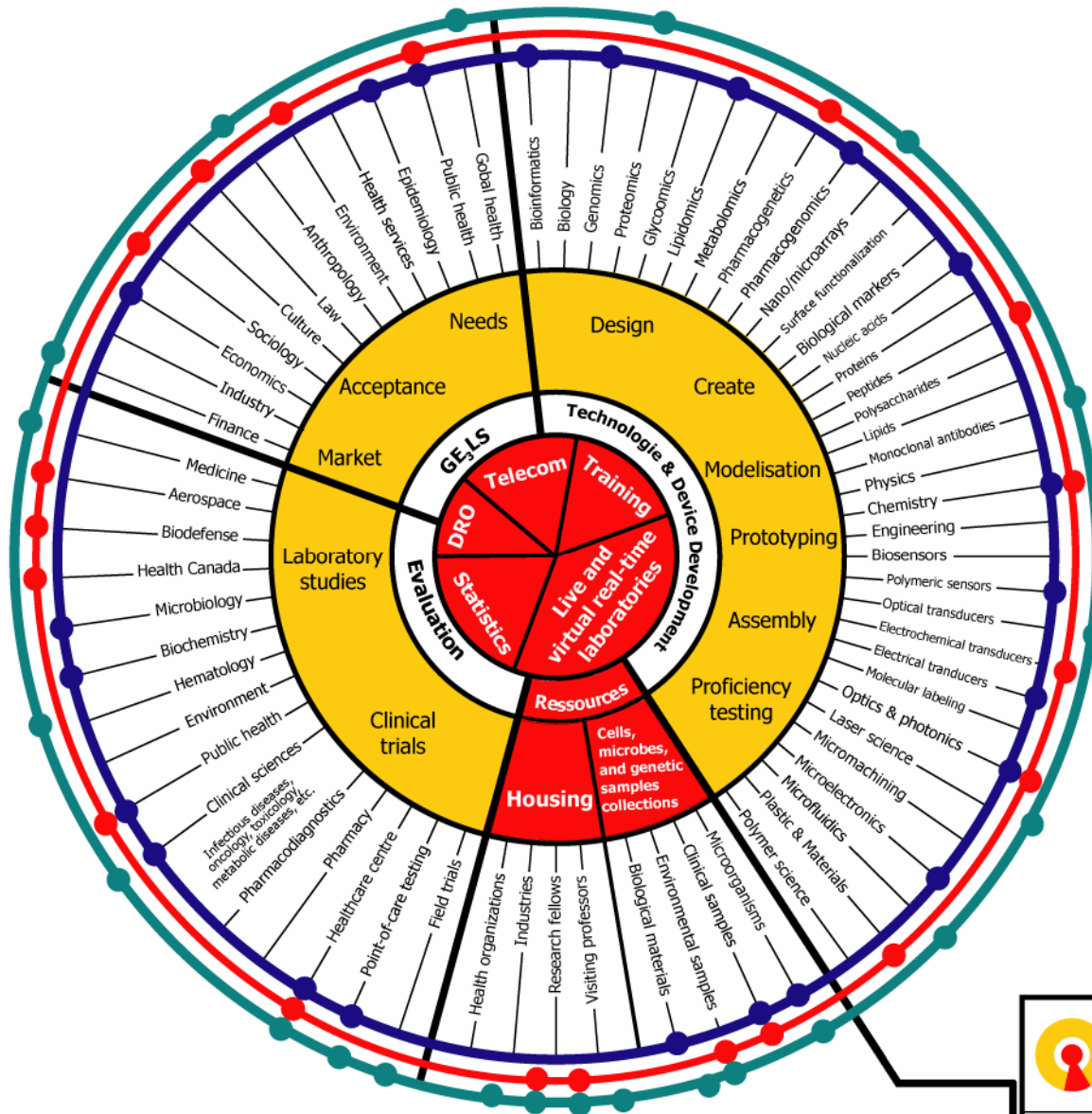


Ho et al. 2005, J Am Chem Soc **127**:12673-12676

Top ten discovery of the year of Quebec science 2000

Diagnostics for Life

"A new vision of global health through point-of-care testing (POCT)"



Universal Diagnostic Interactive/Integrative Station (UDIS) in Québec City

Satellites and collaborators

- : Québec City
- : Canada
- : International

20061016

Rapid (<1h) POCT Diagnostics Impact

- **HIV / AIDS:** Diagnostic takes several weeks
5 million new cases a year
- **Respiratory Tract Infections (TB, FLU, SARS) :** 70% of antibiotic use
(>100 million cases a year)
- **Malaria :** 400 million cases a year
- **Diarrheal Diseases :** 100 million cases a year
- **Sexually Transmitted Diseases :** 340 million cases a year
- **Septis:** 18 million cases a year
- **Meningitis :** 1.2 million cases a year
- **Antimicrobial Resistance :** Need rational use of antibiotics

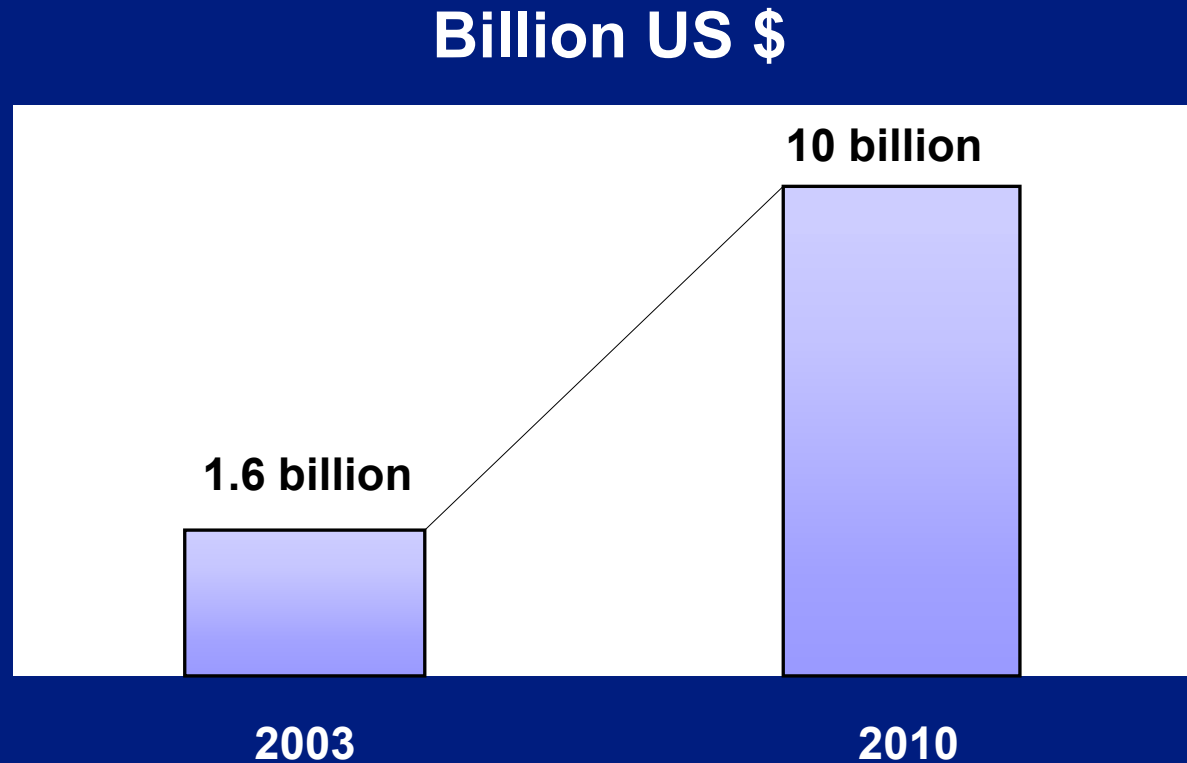
Priority of Mr. Harper's Canadian Government:

Reduce patients waiting time

Solution:

Rapid Point-of-Care Testing (POCT)
A powerful preventive tool

Market potential for infectious diseases diagnostics*



* Compounded Annual Growth Rate

Data from "Reuters Business Insight" and "European Diagnostic Manufacturers Association" adapted by IDI

Conclusion

Microbes are here to stay

Origin : 3.8 billion years (possibly 4.3 billion)

Ecology : 2-3 billion microbial species
0.5% identified
60% of earth's biomass

CONCLUSION

STAT DNA-based microbiology is here !

It will revolutionize the practice of medicine

Conclusion

POCT will require:

**A CHANGE IN CULTURE
WITHOUT CULTURE !!!**

Michel G. Bergeron

How to control infectious diseases

20th Century

Therapy

21st Century

Prevention

Public and Private Research Funds Relating to Prevention

VACCINES:	15%
DIAGNOSTICS:	3,5%
MICROBICIDES:	0,01%

Acknowledgement for financial support

Canadian Institutes of Health Research (CIHR) (Octroi PA-15586)

Genome Canada – Genome Quebec

Fond de recherche en santé du Québec (FRSQ)

Canadian Department of National Defence

Chemical, Biological, Radiological or Nuclear Research and
Technology Initiative (CRTI)

National Institutes of Health (NIH)

Canadian Foundation for Innovation (CFI)

BD Diagnostics - GeneOhm

Genomics – Microfluidics – Microarrays - Biosensors

Multidisciplinary Team for Rapid Nucleic Acid Detection

Université Laval



Dr. Guy Boivin



Dr. Michel G. Bergeron



Dr. Marc Ouellette

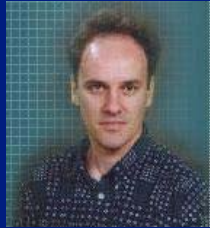


Dr. Paul H. Roy

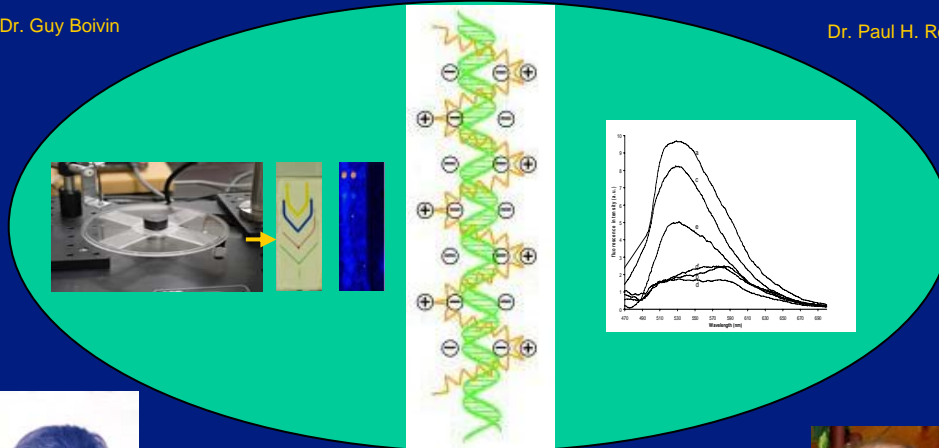
Université Laval



Dr. Mario Leclerc



Dr. Denis Boudresu



Dr. Marc Madou



Dr. Jean-Pierre Gayral



Dr. Michel Dumoulin



Dr. Teoder Veres



Dr. André Nantel



Dr. Benoît Simard

UCI

NRC

Collaborator
BD Diagnostics - GeneOhm



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Centre de recherche en infectiologie
Université Laval

Michel G. Bergeron (Michel.G.Bergeron@crchul.ulaval.ca)



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Michel G. Bergeron (Michel.G.Bergeron@crchul.ulaval.ca)

Site of *Diagnostics for Life* Infectious Diseases and Human/Microbial Genomics Research Center

May 2006



May 2007





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**Centre de recherche en infectiologie
Université Laval**

Michel G. Bergeron (Michel.G.Bergeron@crchul.ulaval.ca)