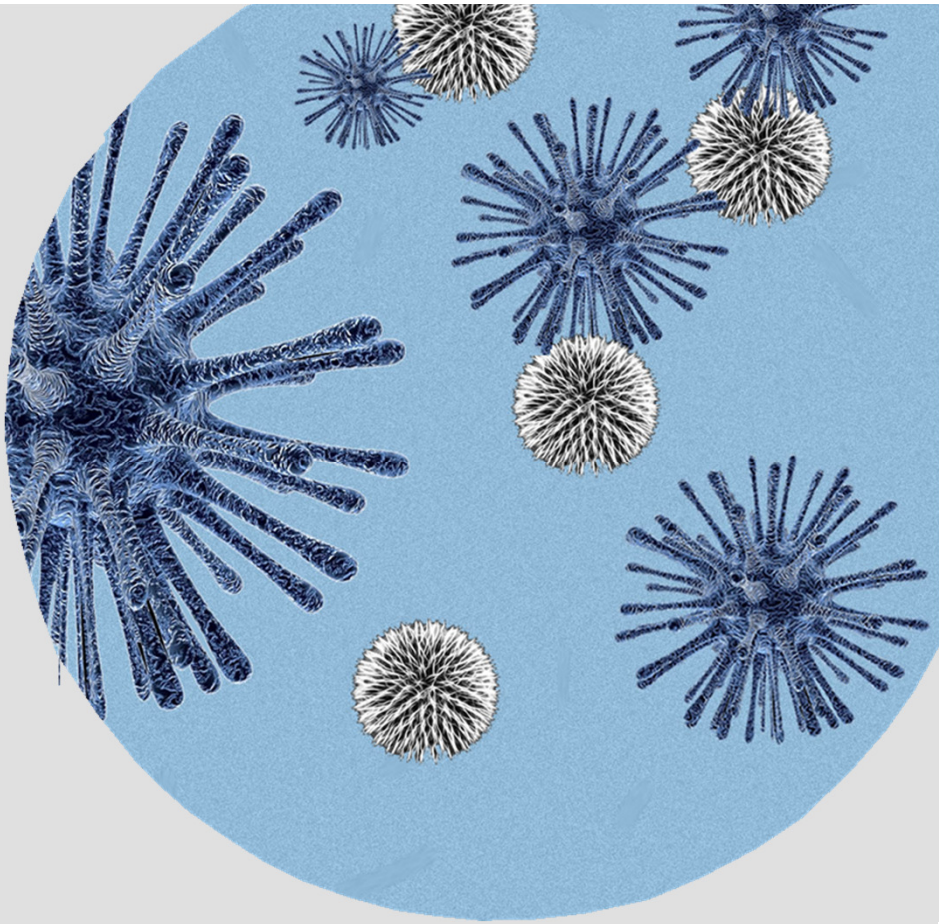
Anti-SUPERBUGS
Pre-Commercial Procurement



Beyond State of the Art

Barcelona, 15/12/2017

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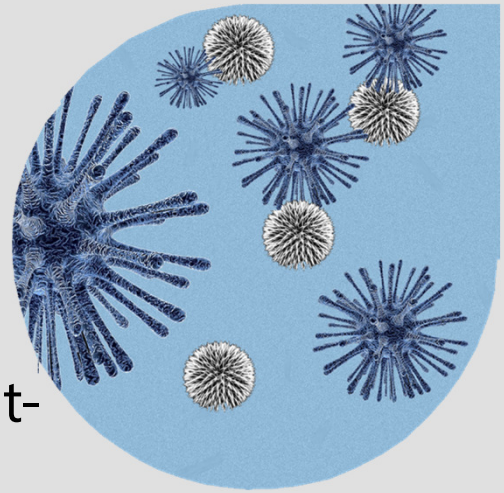
What should be Developed ?



- **Early and rapid** detection of Multi-Drug-Resistant-Organisms
  - In patients
  - On health care workers/colonized individuals
  - The environment in health care facilities – mainly surfaces
- Major aims:
  - Improve patient care
  - Reduce spread of MDRO
- What organisms to detect?
  - Carbapenem resistant G^- bacteria = Highest on the list
  - ESBL producing G^- bacteria such as *Klebsiella pneumonia, Acinetobacter baumanii,* and *Escherichia coli*
  - ESBL producing G^+ bacteria such as *Clostridium difficili* or MRSA
- Possibility to complement with new analytes

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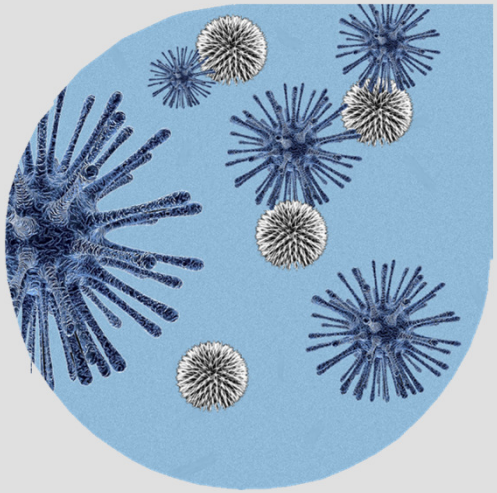
Methods in use today



- **Culture and isolation for identification**
  - Selective media
  - Biochemical analyzes; enzymes etc.
- **Culture in presence of antibiotics** to detect possible resistance to antibiotics that permits growth

- **Amplification/detection of signature genes** for the pathogen and possible resistance to antibiotics
  - PCR

Conclusions:

1) Excellent laboratory based methods exists
2) However, they require sampling and transport to laboratory followed by the analytical procedure

= time consuming and not suitable for continuous or frequent P.o.C. testing

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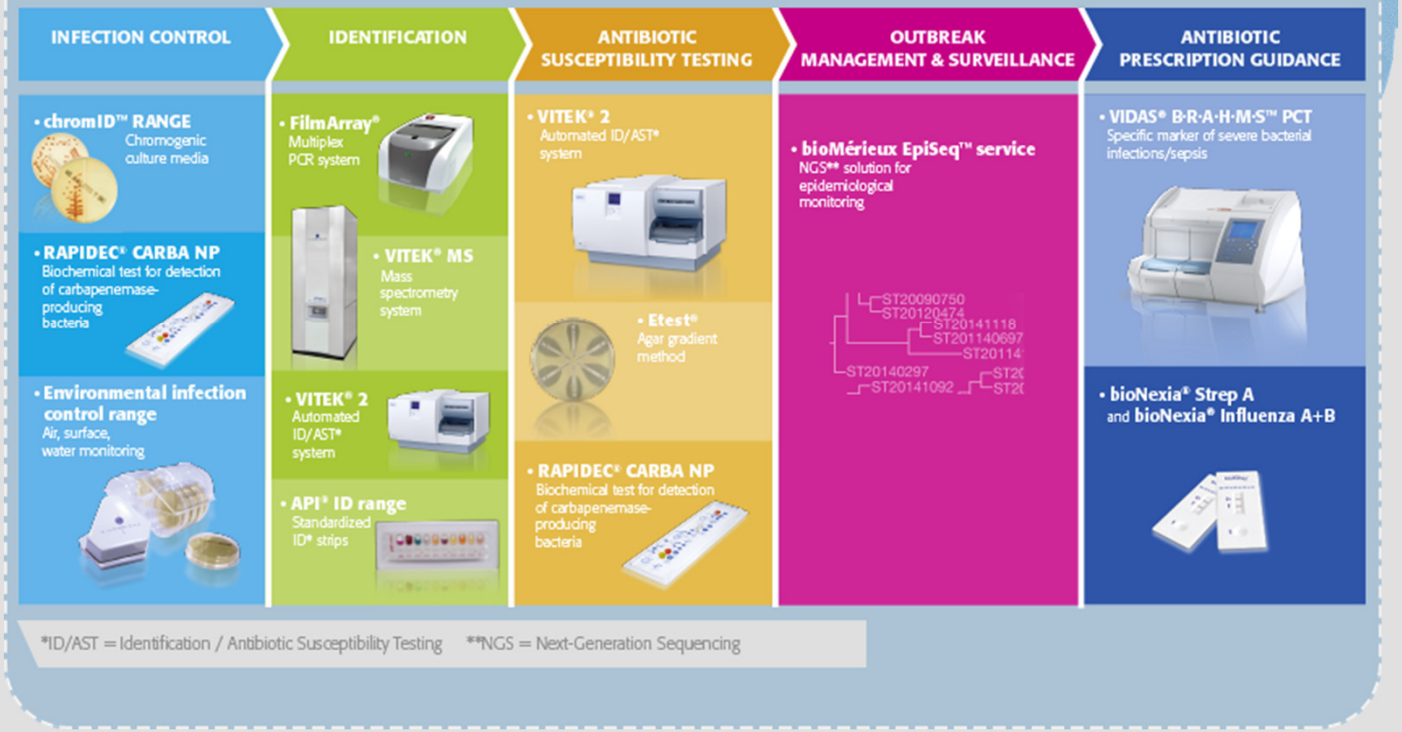
Example of systems



What is missing ?

- Early warning - Point of Care
- Minimal (or no) work load on health care worker
- Speed – Real time detection is the final goal
- Continuous/frequent sampling
- Connectivity to healthcare data handling system (HL7)

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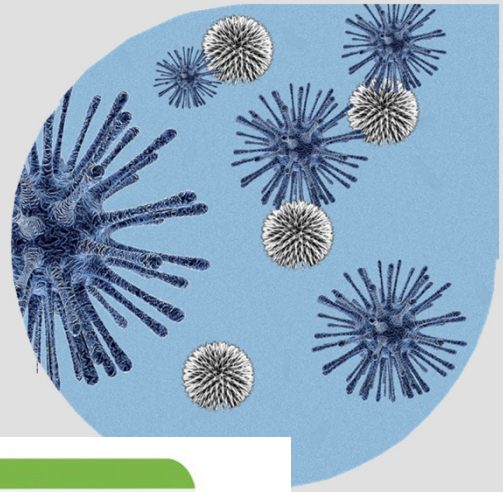
Examples of quick tests



- MRSA from colony in 5 min

- Legionnaires disease in 15 min from urine

- Clostridium difficile in 30 min

- **These are examples of existing products. However, they require:**
  - Various degree of sample handling/ culture
  - Manual work
  - Manual registration in patient data handling system
  - No automatic alarm

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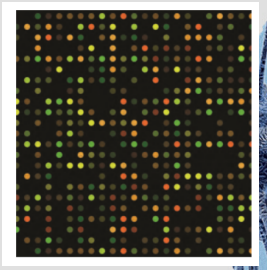
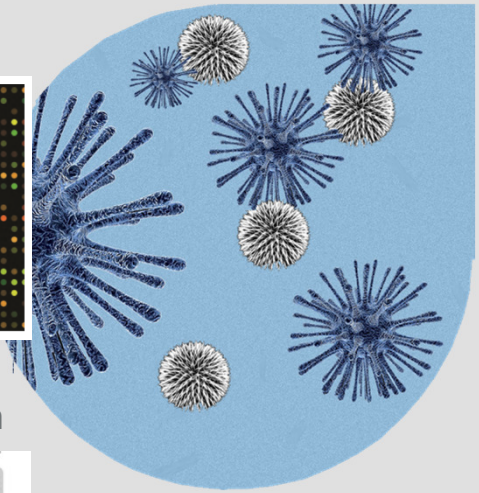
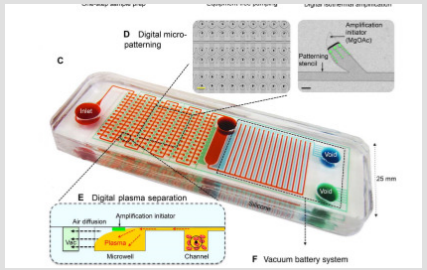
Examples of new developments

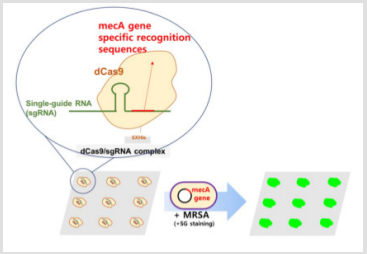




- **Detect "everything" - bugs and resistance**
  - **Whole genome sequencing** of tbc for resistance profiling (Lancet 2015)
  - LLMDA - identify 6000 targets within 24 hrs – based on DNA based hybridization array (2013)
- **Detect specific infectious agents**
  - **ISDA** (Isothermal strand displacement amplification) 20 min (2015)
  - RPA (Isothermal recombinase polymerase amplification + integrated sample prep on chip (Science Adv. 2017)



- Detection of MRSA using a **CRISPR-mediated DNA FISH** method in 30 min (Biosensors and Bioelectronics 2017)



In general:

- "New" DNA based methods e.g. isothermal amplification facilitates design of equipment for Point of Care
- Sample preparation is a challenge for Point of Care devices
- Continuous, or frequent, measurements still not here

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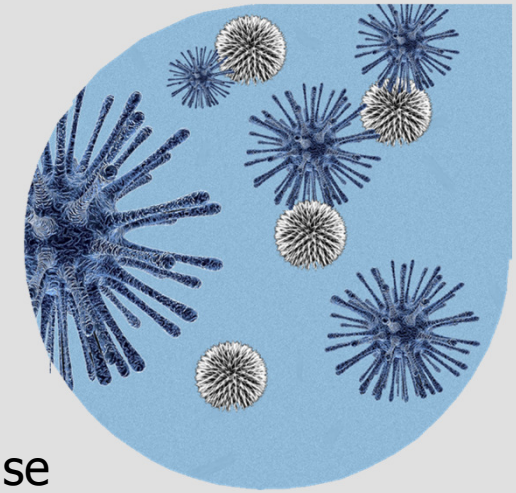
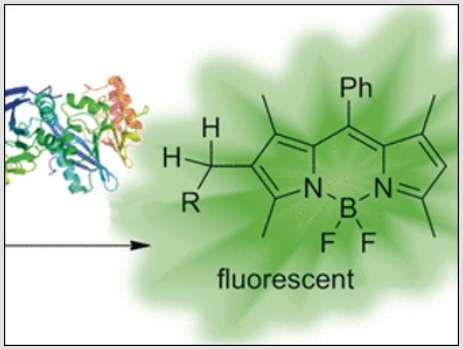
Non-nucleic acid based methods



- Antibiotic resistance
  - Detection of ESBL by detecting hydrolysis of β-lactamase
  Within 90 min (EMBL are looking for partner/licensee)
  - HPLC/MS

  - Light-up probes
  - Modified Carbapenem turn fluorescent upon cleavage by β-lactamase



- In summary:
  - New, or modified old methods, making analyses faster/simpler
  - However, sample preparation and/or cultivation often required
  - Many publications from universities – still far from the market
  - Autonomous and continuous / high frequency measurements not available

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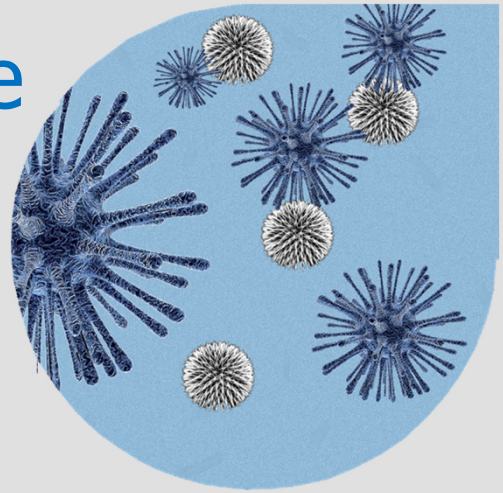
How to get beyond state of the art ?



1. Point of Care located detection of MDRO
   - Patients, HCW, and colonized individuals
2. Local detection of MDRO on surfaces in health care settings

- Common demands:
  - Fast and continuous / high frequency detection of MDRO
  - Easily applied!
    - Minimal labor input
    - No handling of dangerous substances
    - Possibilities for integration with patient data handling system (HL7) or local alarms
  - Cost efficient
    - Cost comparable to presently used routines (e.g. PCR for patients, or ATP for surfaces)
  - Sensitivity/specificity as good as clinical bacteriology lab

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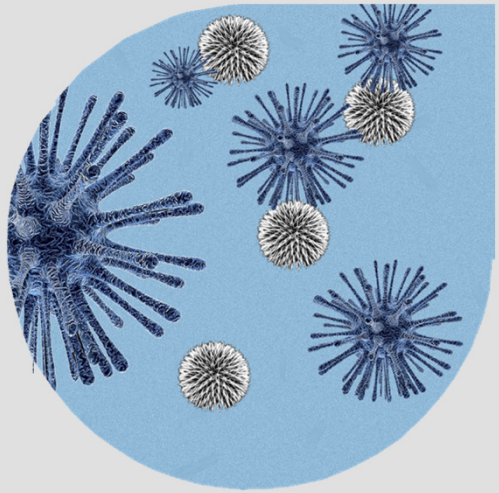

Thank you

- Dag Ilver
- Dag.ilver@ri.se
- http://www.antisuperbugs.eu

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