

# TAE Trainees Day 2018



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## DEGREES

2017	Habilitation thesis (Privatdozent)
2015	Medical Board certified Medical Microbiology specialist
2011	Doctoral thesis (Dr. med.)
2009	Medical Board certified Clinical Pharmacology specialist
2002	MD

## POSITIONS

Since 11/2009	Institute of Medical Microbiology, University Hospital Münster, Germany
2008-2009	Institute of Clinical Pharmacology, University Hospital Dresden, Germany
2006-2008	CRS Clinical Research Services, Mönchengladbach, Germany
2005-2006	Department of Internal Medicine, Hospital Landshut-Achdorf, Landshut, Germany
2002-2004	Department of Internal Medicine, Smolensk district hospital, Russia

**“A straight path is not always the shortest ...”**



# MALDI-TOF MS from shortly incubated solid medium cultures

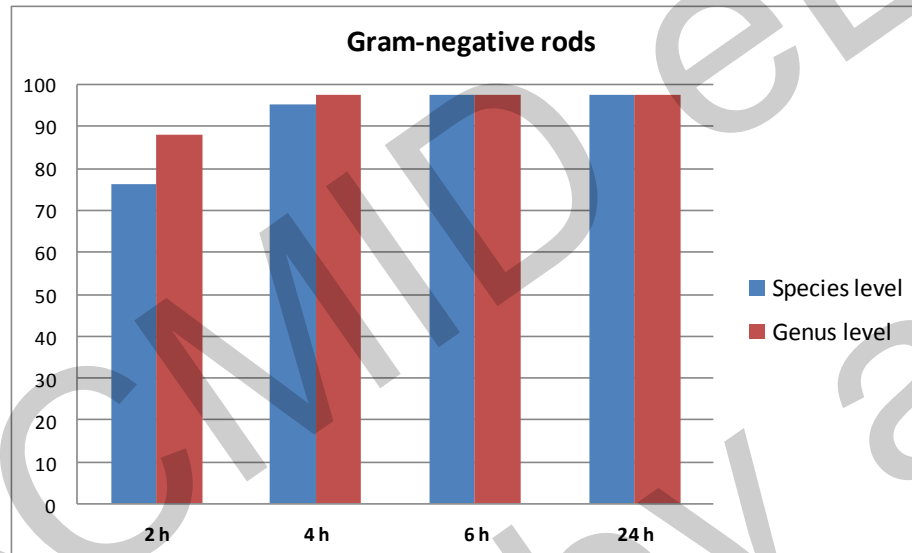


2 h

4 h

6 h

24 h



Gram-negative rods

Average incubation time to ID:

Species level (score  $\geq 2.0$ )

**2.0 h**

Genus level (score  $\geq 1.7 - < 2.0$ )

**1.7 h**

Idelevich *et al*, CMI 2014

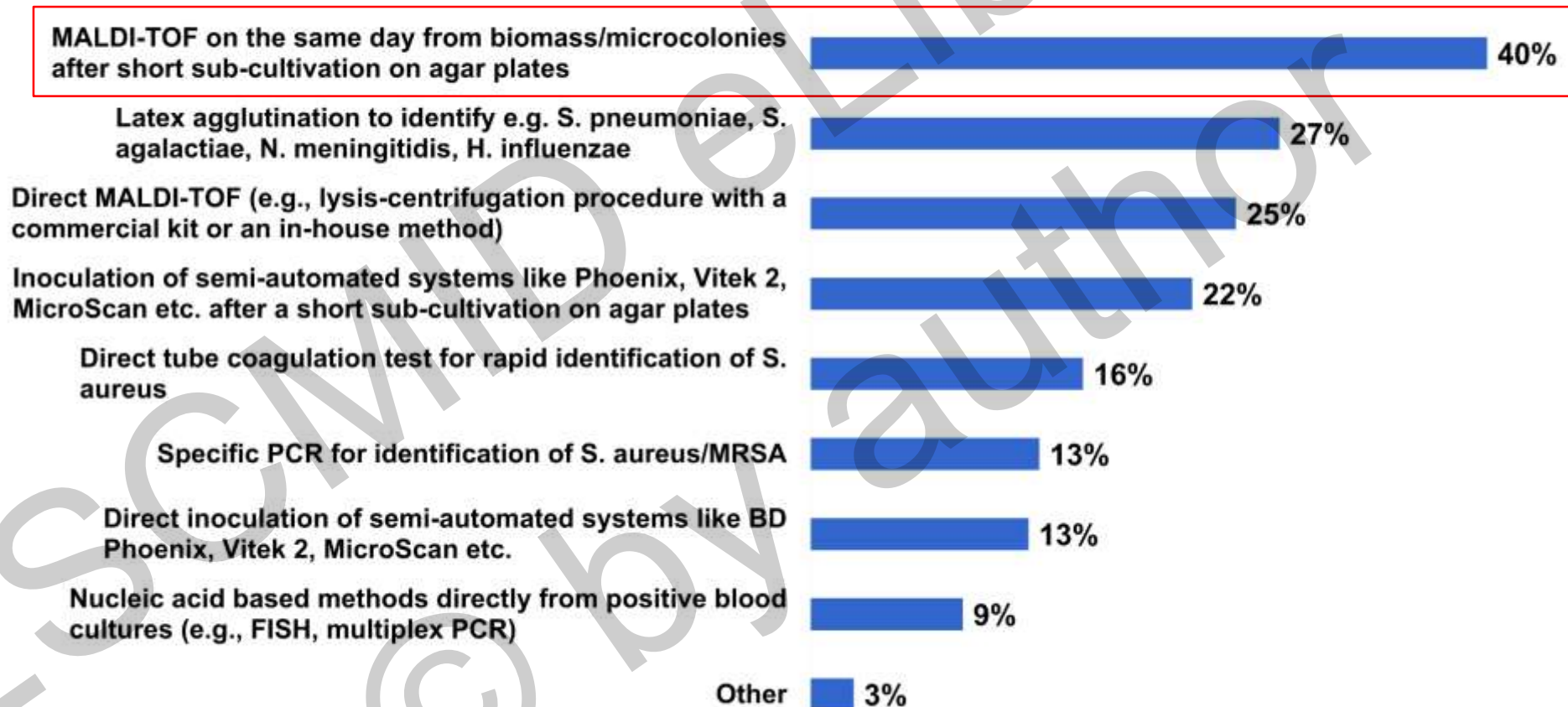
**“Simplicity is the ultimate sophistication”**  
**Leonardo da Vinci**



# Microbiological diagnostics of *BLOOD*stream infections in Europe – an ESGBIS survey Y (BLOODY)

Preliminary results: **157** labs from **26** countries

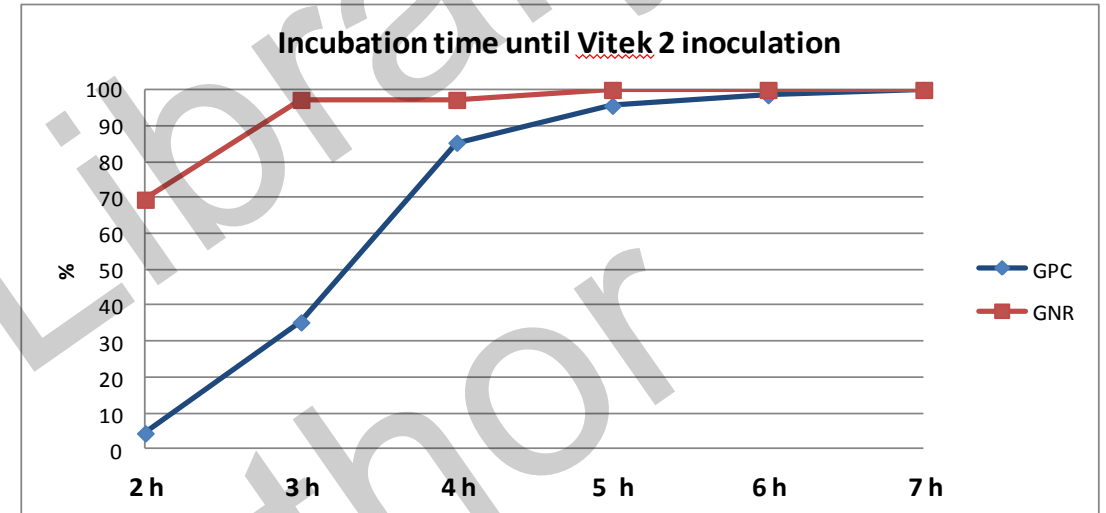
## Rapid identification technologies used after the blood culture bottle became positive



# Antimicrobial susceptibility testing (AST) from shortly incubated solid medium cultures

## Time to Vitek 2 inoculation and AST result for Gram-positive cocci

AST from shortly incubated cultures		Control cultures
Time until Vitek 2 inoculation	<b>3.8 h</b>	24 h
Duration Vitek 2 AST	9.8 h	9.8 h
Time until Vitek 2 result	13.6 h	33.8 h



## Time to Vitek 2 inoculation and AST result for Gram-negative rods

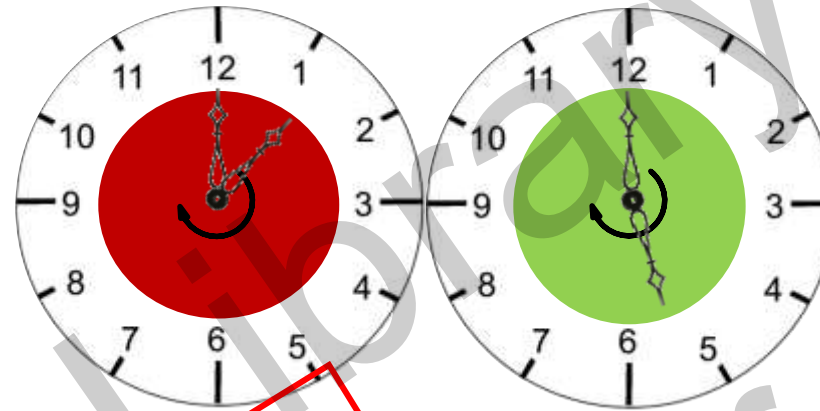
AST from shortly incubated cultures		Control cultures
Time until Vitek 2 inoculation	<b>2.4 h</b>	24 h
Duration Vitek 2 AST	8.8 h	9.0 h
Time until Vitek 2 result	11.2 h	33.0 h

## VME, ME, mE, Categorical agreement

	Gram-positive cocci, n=68	Gram-negative rods, n=36
No. isolate-antibiotic combinations	1,163	609
Very major errors (VME)	1.6 %	0.0 %
Major errors (ME)	0.3 %	0.5 %
Minor errors (mE)	0.1%	0.8%
<b>Categorical agreement (CA)</b>	<b>99.2%</b>	<b>99.2%</b>

## DNA-based identification from whole blood

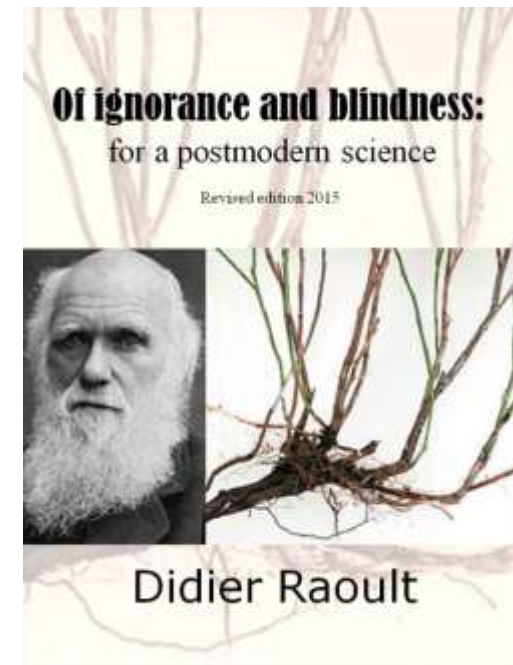
Time until therapy modification  
 SeptiFast group **21.4 h**  
 Control group **47.5 h**  
 ( $p < 0.05$ )



**Time to arrival 13.8 h**      **Test 5.3 h**

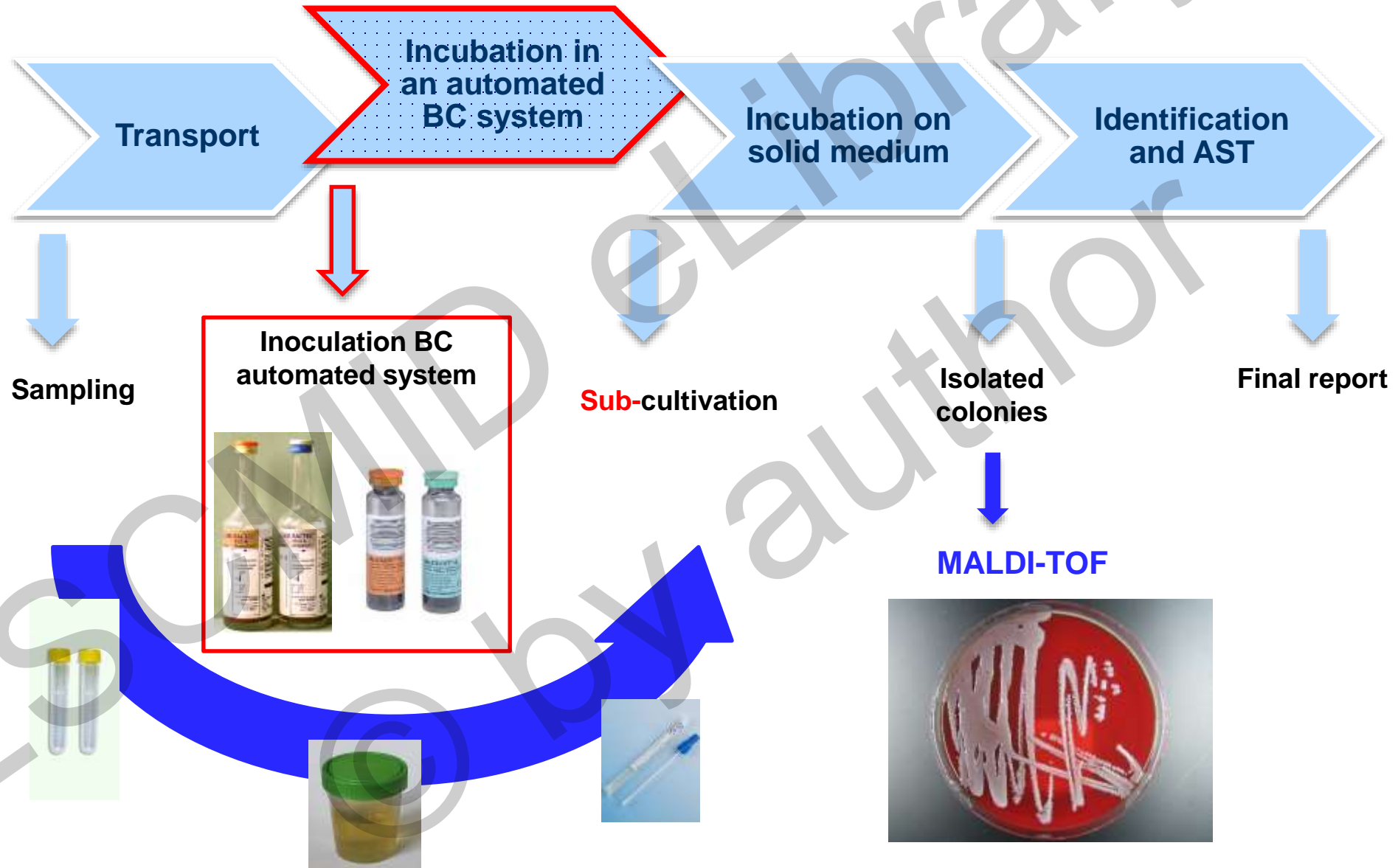
Median (IQR) laboratory transport time for three tertiary-care hospitals by time of sampling.

	Karolinska University Hospital, Huddinge		Stockholm South General Hospital		Södertälje Hospital	
	No. of samples	Median (IQR)	No. of samples	Median (IQR)	No. of samples	Median (IQR)
Weekdays	274	4 (2-13)	250	8 (3-13)	133	14 (4-18)
Weekends	102	10 (2-15)	98	11 (6-15)	52	17.5 (11-21)
8-16	167	2 (1-3)	117	3 (2-5)	90	18 (4-21)
16-24	154	13 (10-15)	159	13 (11-15)	70	16 (13-17)
24-8	61	6 (4-7)	72	6 (4-8)	25	7 (4-9)



**Microbiologistics!**

“Research is to see what everybody else has seen, and to think what nobody else has thought”  
Albert Szent-Gyorgyi



## Direct blood culturing on solid medium

Organism	Concentration, cfu/ml	Time to MALDI-TOF MS identification after direct blood culture method, h	Time to BACTEC positivity signal, h
		High confidence (score $\geq 2.0$ )	
<i>E. coli</i>	100	7	9.5
	10	7	10.0
	1	8	11.0
<i>P. aeruginosa</i>	100	11	13.5
	10	11	15.5
	1	12	17.2
<i>S. aureus</i>	100	8	10.7
	10	8	12.7
	1	10	14.0
<i>S. epidermidis</i>	100	14	13.9
	10	15	16.1
	1	15	17.8
<i>E. faecalis</i>	100	9	10.7
	10	9	11.9
	1	10	13.0
<i>S. pneumoniae</i>	100	9	10.2
	10	9	11.5
	1	12	12.4
<i>H. influenzae</i>	100	11	16.3
	10	11	18.6
	1	11	20.0



## Direct blood culturing on solid medium

**„Whoever wishes to read the future  
must leaf through the past“**

**André Malraux**

### Technical improvement

- ✓ **Contamination-free operation**
- ✓ **Easier blood processing**
- ✓ **Utilization of transportation and storage times**
- ✓ **Compatibility with “intelligent” incubators:**
  - early automatic growth detection by imaging technology
  - automatic transfer of microcolonies to the identification and AST systems.

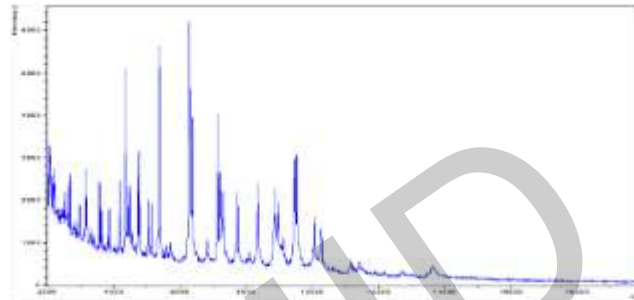
# Rapid detection of antibiotic resistance by MALDI-TOF MS using a novel direct-on-target microdroplet growth assay (DOT-MGA)



A. Prior to incubation

B. In the „humidity chamber“

C. Medium removal after incubation

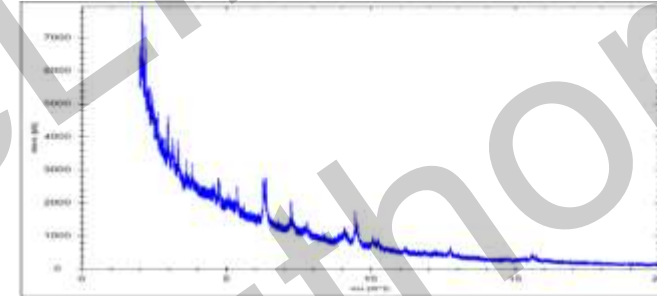


**A. Meropenem-resistant strain**  
MALDI Biotyper result: *Klebsiella pneumoniae*

MALDI Biotyper result:  
**Expected species identification**  
(score  $\geq 1.7$ )



**Antibiotic-resistant strain**



**B. Meropenem-susceptible strain**  
MALDI Biotyper result: No identification

MALDI Biotyper result:  
**No identification**  
(score  $< 1.7$ )

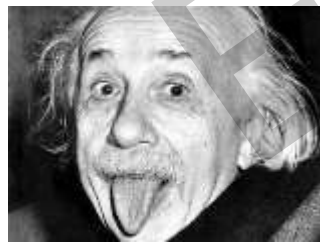


**Antibiotic-susceptible strain**

Idelevich *et al*, CMI 2017

“Everything should be made as simple as possible, but no simpler”

Albert Einstein



# Rapid detection of **carbapenem resistance** by MALDI-TOF MS using a novel direct-on-target microdroplet growth assay (DOT-MGA)

## *Klebsiella pneumoniae*

Incubation time	Microdroplet total volume														
	2 $\mu$ l			4 $\mu$ l			6 $\mu$ l			8 $\mu$ l			10 $\mu$ l		
	Valid	Sensitivity	Specificity	Valid	Sensitivity	Specificity	Valid	Sensitivity	Specificity	Valid	Sensitivity	Specificity	Valid	Sensitivity	Specificity
3 hours	45.8%	50%	100%	70.8%	50%	100%	87.5%	90%	100%	87.5%	90%	90.9%	79.2%	87.5%	90.9%
4 hours	100%	58.3%	100%	100%	66.7%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
18 hours	83.3%	91.7%	100%	95.8%	100%	100%	100%	100%	100%	95.8%	100%	100%	87.5%	100%	100%

- Easy-to-perform
- Rapid
- Mechanism-independent (universal)
- Capability for automation (High-throughput feasible)
- Expandable to further applications

## Transparency declaration

Co-inventor of patents on microbiological diagnostics

**“I have been impressed with the urgency of doing.  
Knowing is not enough; we must apply.  
Being willing is not enough; we must do.”**

**Leonardo da Vinci**



Karsten Becker

Damayanti  
Kaiser

Alexandra  
Busch

Carlos  
Correa-Martinez

Luise  
Stork

Ilka Nix  
Annkatrin Bibo  
Michaela Schreiner  
Barbara Grünastel  
Katrin Blaschke

