

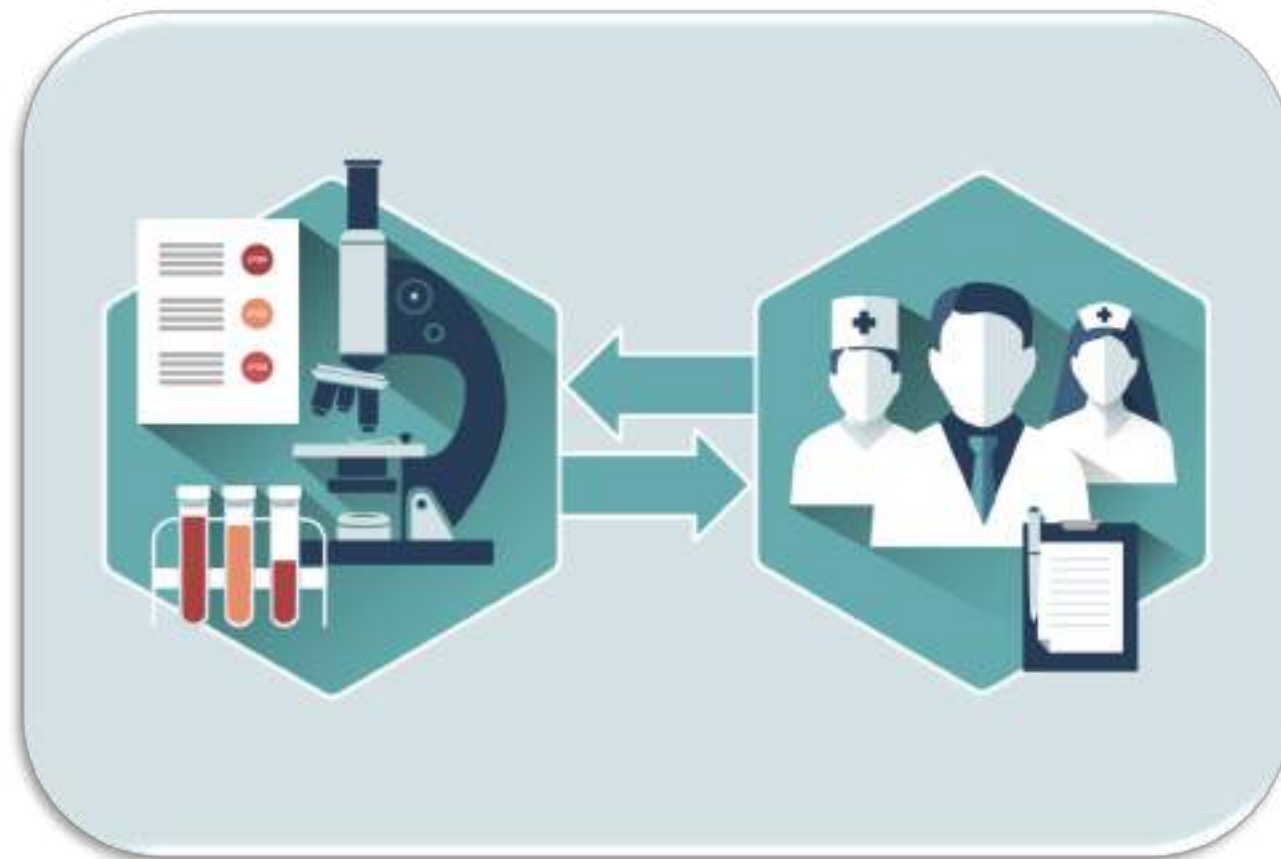


L'ANTIBIOFILMOGRAMMA: IL TRASFERIMENTO DEI RISULTATI DELLA RICERCA NELLA PRATICA CLINICA

Enea G. Di Domenico

TRANSLATIONAL RESEARCH: FROM BENCHSIDE TO BEDSIDE

*Translation of the achievements
of basic science into everyday
clinical practice*



THE ANTIBIOTIC RESISTANCE CRISIS



ANNOUNCEMENT

The rapid emergence of resistant bacteria is occurring worldwide



COSTS

Cost per patient range from \$18,588 to \$29,069



MORTALITY RATES

Mortality rates due to multidrug-resistant organisms are approximately 30%



ATTRIBUTABLE DEATHS

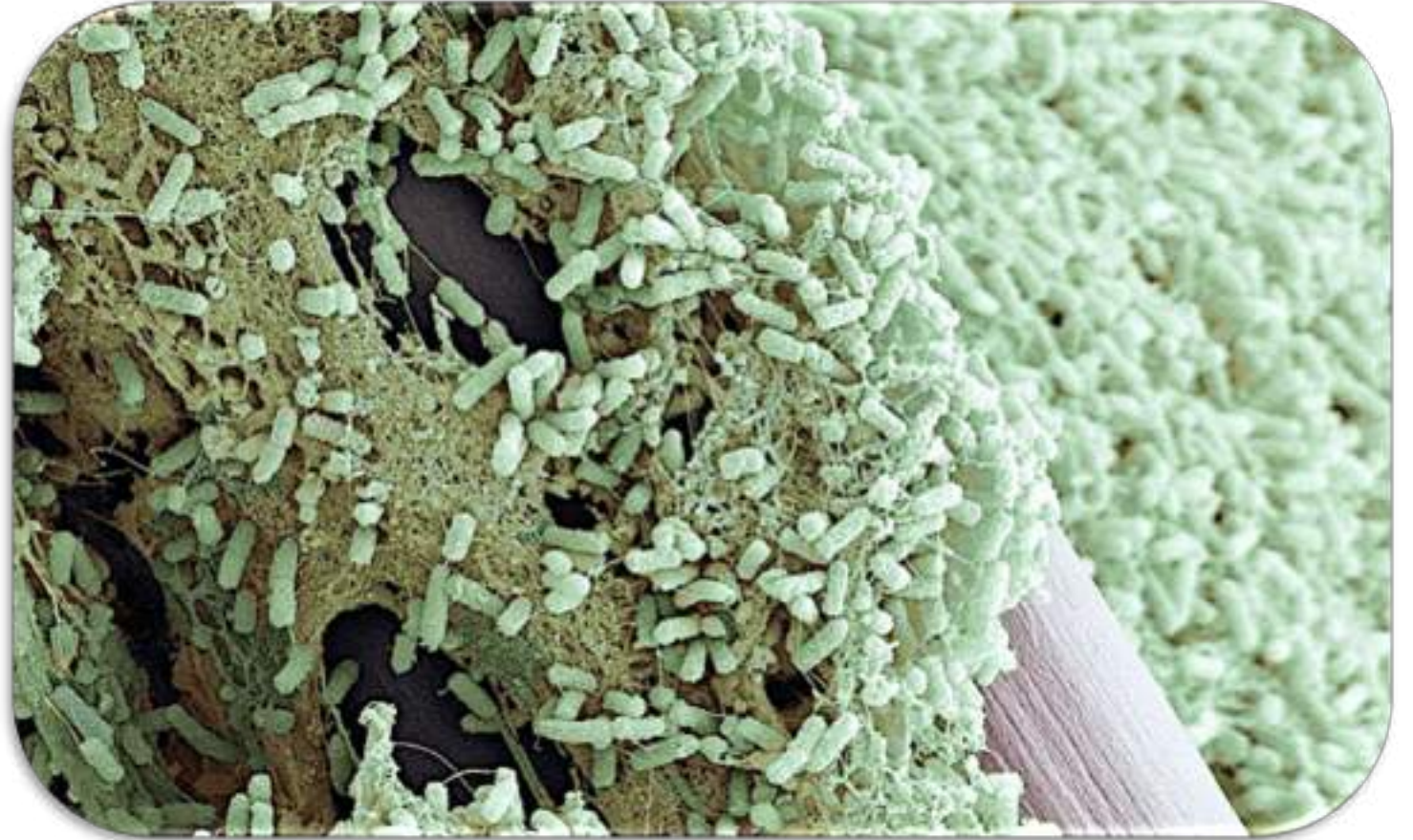
More than 700,000 people die each year due to MDR

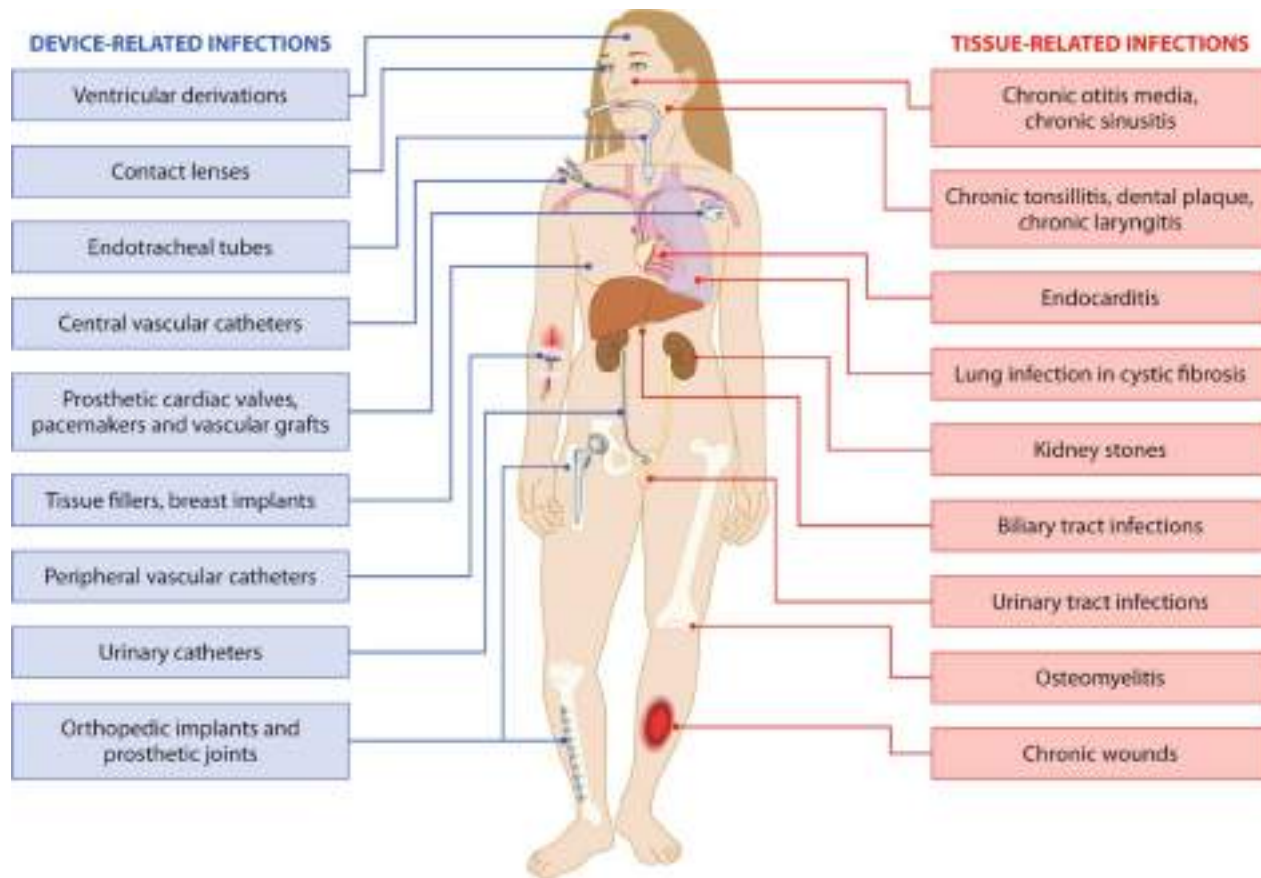


MICROBIAL BIOFILM

Biofilms pose a serious problem for public health because of the increased resistance to antibiotics

An additional resistance mechanism that escapes conventional clinical analysis





BIOFILMS ARE PRESENT IN MORE THAN 80% OF ALL HUMAN INFECTIONS

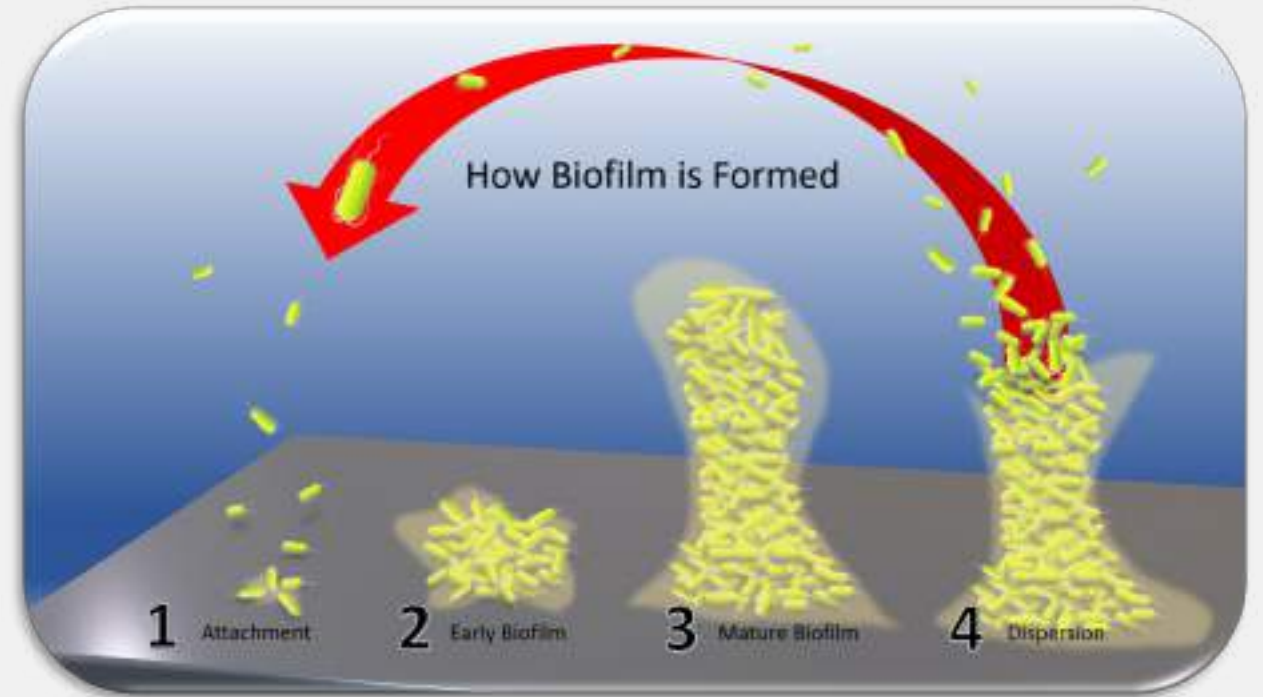
The total annual cost for biofilm infections in the USA is \$94 billion, with more than half a million deaths

ANTIBIOTIC PROFILING ON BIOFILM-GROWING BACTERIA

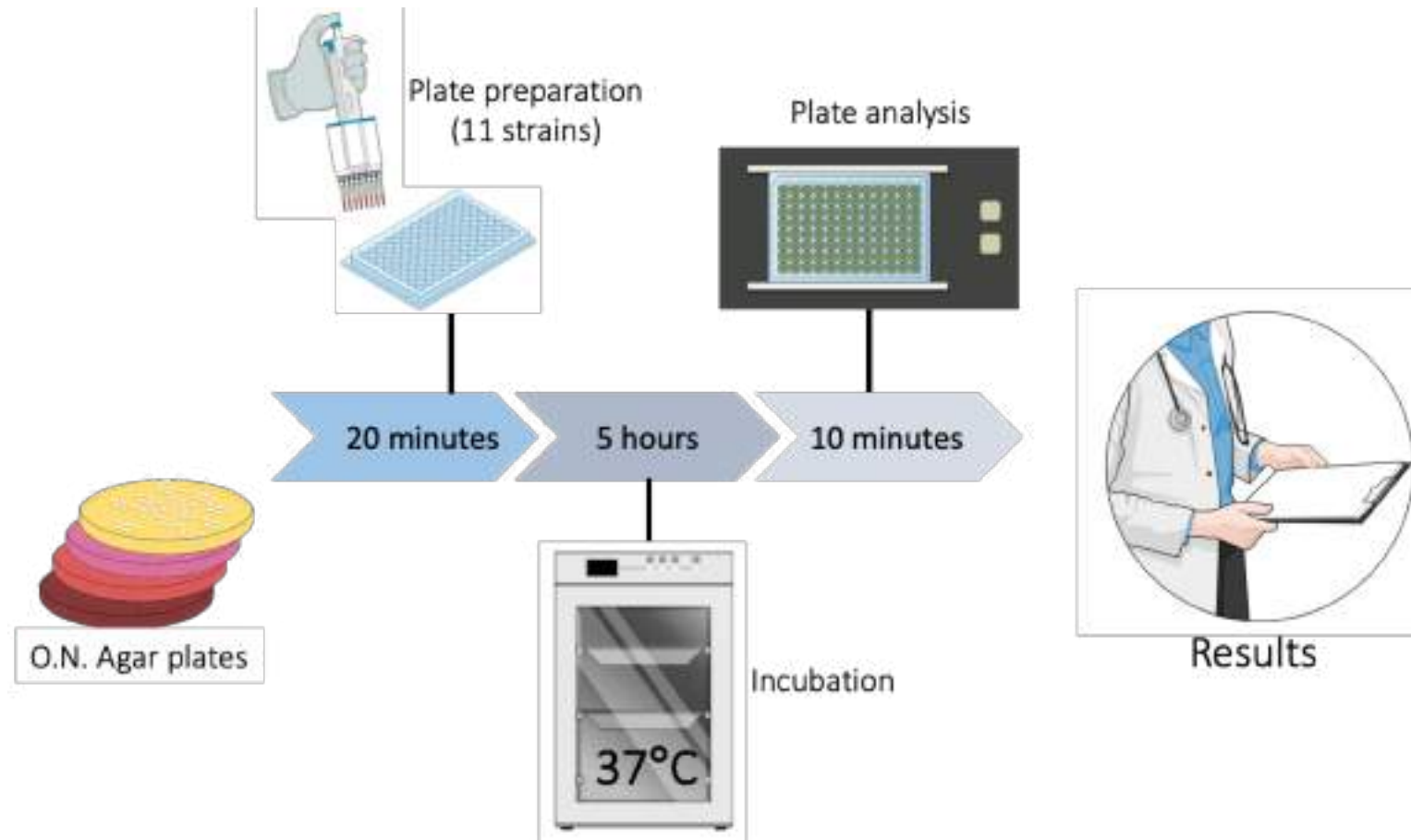


AN UNMET CLINICAL NEED

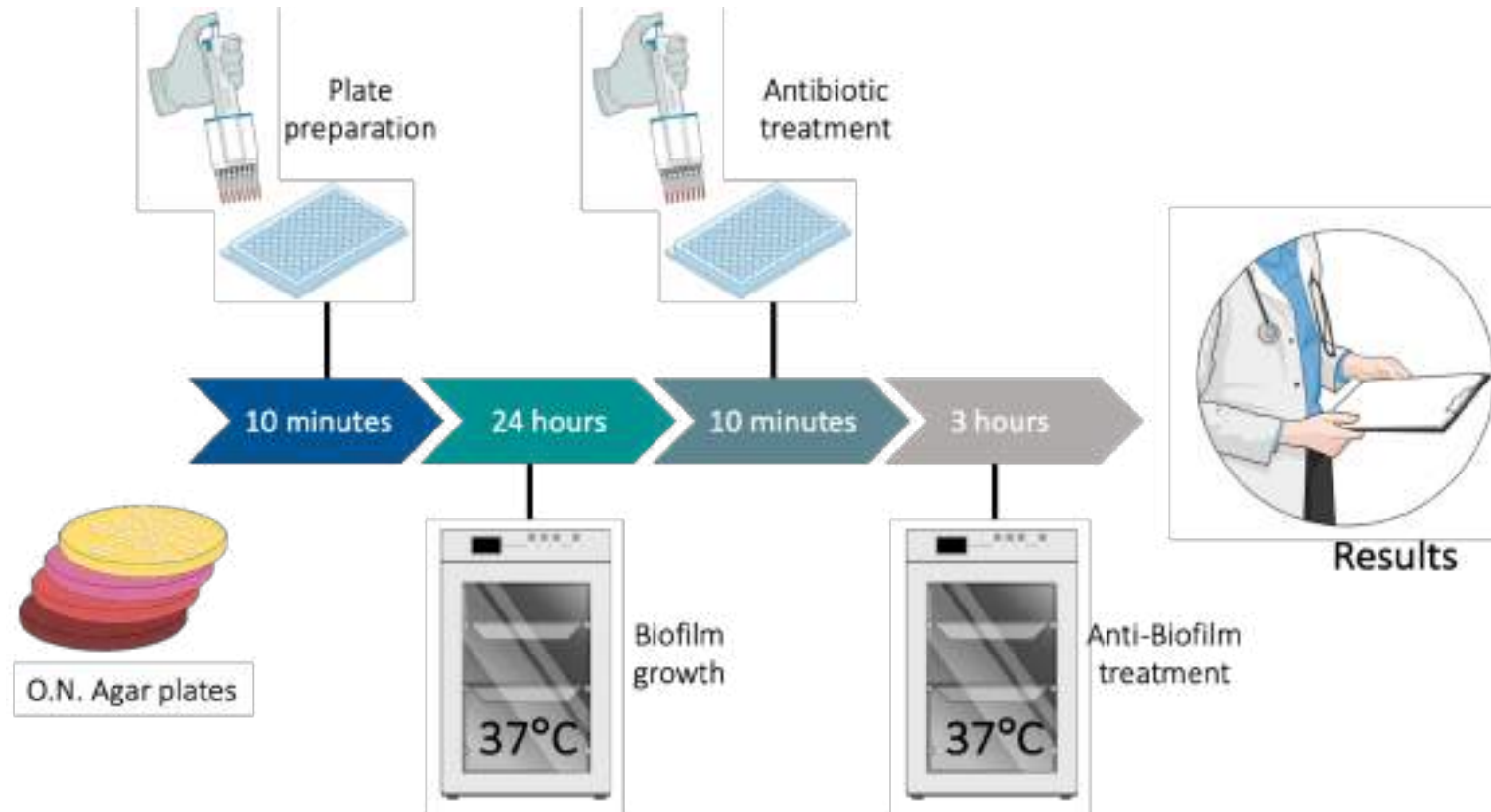
Antibiograms are performed on planktonic cells and do not take into account biofilm-production



clinical BIOFILM RING TEST[®] (cBRT)



ANTIBIOFILMOGRAMMA (BIOFILM SUSCEPTIBILITY TEST - BST)



WHY

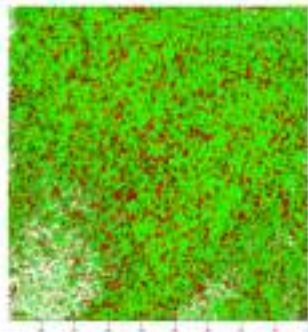
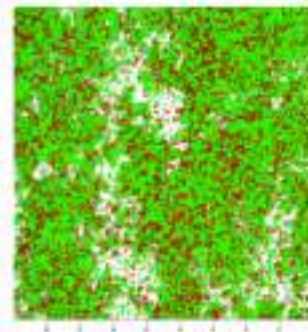
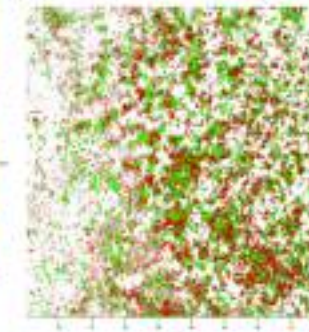

IT

MATTERS



TOLERANCE TO ANTIBIOTICS IS DIRECTLY RELATED TO THE LEVEL OF BIOFILM

Antibiotics	<i>S. aureus</i> (High)				<i>S. aureus</i> (Moderate)				<i>S. aureus</i> (Weak)			
	MIC (mg/L)	BMIC (mg/L)	MIC (mg/L)	BMIC (mg/L)	MIC (mg/L)	BMIC (mg/L)	MIC (mg/L)	BMIC (mg/L)	MIC (mg/L)	BMIC (mg/L)	MIC (mg/L)	BMIC (mg/L)
Clindamycin	0.5	>1	0.25	0.5	0.25	0.5	0.25	0.125	0.5	0.25	0.125	0.5
Daptomycin	0.5	1	1	>4	1	>4	0.5	1	0.5	1	0.5	1
Erythromycin	≤0.25	>4	0.5	1	0.5	1	0.5	≤1	0.5	≤1	0.5	≤1
Fusidic Acid	≤0.5	>1	≤0.5	≤125	≤0.5	≤125	≤0.5	≤0.125	≤0.5	≤0.125	≤0.5	≤0.125
Gentamicin	≤0.5	>4	≤0.5	>4	≤0.5	>4	≤0.5	0.125	≤0.5	0.125	≤0.5	0.125
Levofloxacin	0.25	>4	0.25	2	0.25	2	≤0.12	0.12	≤0.12	0.12	≤0.12	0.12
Oxacillin	≤0.25	≤0.25	0.5	1	0.5	1	0.5	0.5	0.5	0.5	0.5	0.5
Rifampicin	≤0.03	1	≤0.03	0.125	≤0.03	0.125	≤0.03	0.0625	≤0.03	0.0625	≤0.03	0.0625
Teicoplanin	≤0.5	2	≤0.5	1	≤0.5	1	≤0.5	0.25	≤0.5	0.25	≤0.5	0.25
Tigecyclin	≤0.12	>0.5	≤0.12	>0.5	≤0.12	>0.5	≤0.12	≤0.0625	≤0.12	≤0.0625	≤0.12	≤0.0625
TMP/SMX	≤10	>4	≤10	>4	≤10	>4	≤10	>4	≤10	>4	≤10	>4
Vancomycin	1	>4	1	>4	1	>4	1	1	1	1	1	1

Resistance (%)	8%	83%	0%	67%	0%	8%
						
	HIGH	HIGH	MODERATE	MODERATE	WEAK	WEAK

MIC: Minimum Inhibitory Concentration
 BMIC: Biofilm Minimal Inhibitory Concentration

“Translation of the achievements of basic science...”

BIOFILM-ASSOCIATED SURGICAL SITE INFECTIONS

78-Year-old woman with oral cancer

Tracheostomy over the second tracheal ring

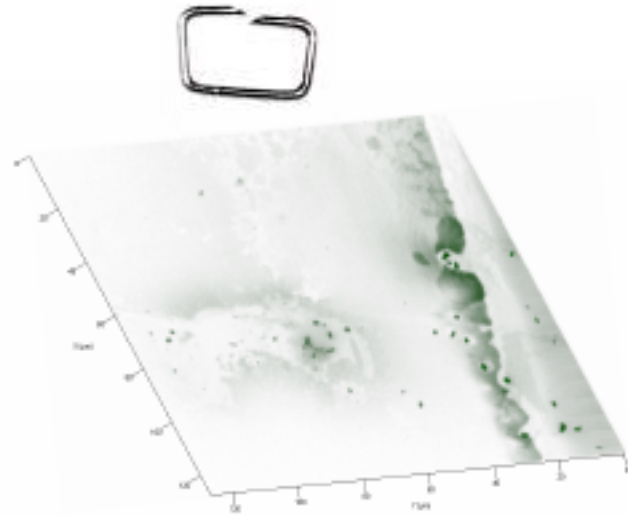
Pectoralis major flap for reconstructive head and neck surgery

Surgical site infection by: *Staphylococcus aureus*
Pseudomonas aeruginosa

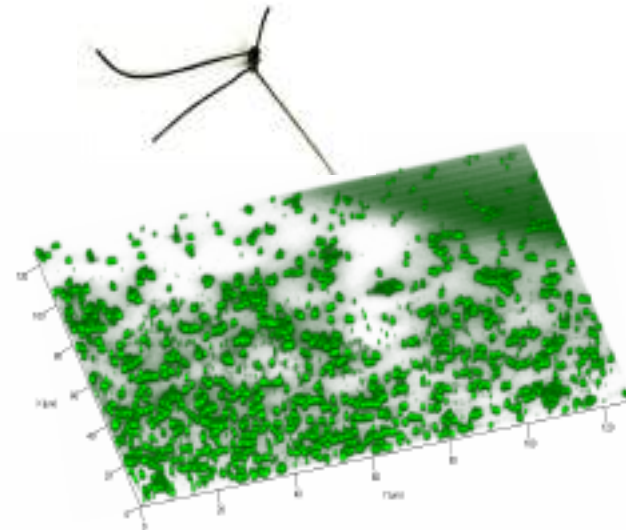


BIOFILM ON SUTURE

STAINLESS STEEL



NYLON



CO-INFECTION BY *S. aureus* AND *P. aeruginosa*



I.D.: XXX Sig. XXX	Sesso F	MICROBIOLOGIA
Data di Nascita: XXX	Età: 78 Anni	PROVENIENZA: OTORINO
		Materiale: TAMPONE ULCERA

STRAIN:	<i>Staphylococcus aureus</i>				<i>Pseudomonas aeruginosa</i>					
RESULT:	Moderate biofilm producer				High biofilm producer					
	Antimicrobials	MIC (mg/L)	INT	BMIC (mg/L)	INT	Antimicrobials	MIC (mg/L)	INT	BMIC (mg/L)	INT
	Benzilpenicillin	> 0.5	R	> 8	R	Amikacin	≤ 2	S	≤ 2	S
	Clindamycin	≤ 0.25	S	> 2	R	Cefepime	≤ 1	S	> 32	R
	Daptomycin	≤ 0.50	S	4	R	Ceftazidime	4	S	32	R
	Erythromycin	> 2	R	4	R	Ciprofloxacin	≤ 0.25	S	> 2	R
	Fusidic Acid	≤ 0,5	S	≤ 1	S	Gentamicin	≤ 1	S	1	S
	Gentamicin	≤ 1	S	1	S	Imipenem	2	I	> 16	R
	Linezolid	2	S	1	S	Meropenem	1	S	> 16	R
	Oxacillin	> 2	R	> 2	R	PIT	8	S	> 128	R
	Rifampicin	-	-	≤ 0.06	S					
	Teicoplanin	≤ 0,5	S	4	R					
	Tigecycline	0.25	S	0.25	S					
	TMP/SMX	≤ 10	S	≤ 10	S					
	Vancomycin	≤ 0,5	S	2	S					

Piperacillin/Tazobactam (PIT)
 TMP/SMX = Trimethoprim/Sulfamethoxazole



EUCAST Clinical breakpoints - bacteria (v 9.0)

D=0



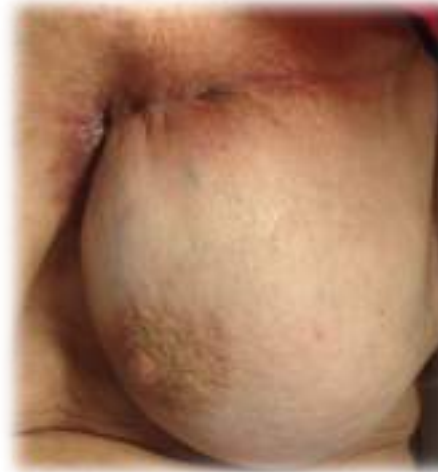
D=7



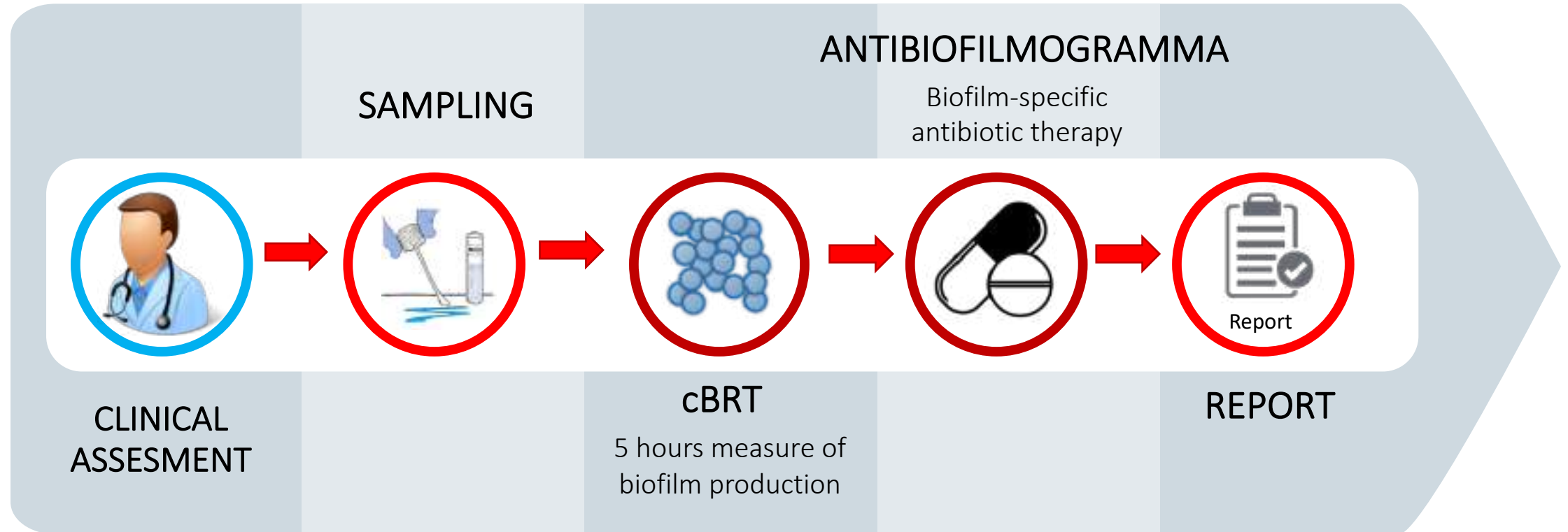
D=14



D=21



DEVELOPMENT OF INNOVATIVE STRATEGIES FOR THE TREATMENT OF BIOFILM INFECTIONS



VALIDATION STUDIES

frontiers in Neurology

The Emerging Role of Microbial Biofilm in Lyme Neuroborreliosis

Enza Gioia Di Domenico^{1,2}, Barla Cavallò¹, Valentinia Bonfigliani¹, Giovanna D'Agostini¹, Martina Pontone¹, Elisabetta Trenti¹, Maria Teresa Gallo¹, Grazia Prignano¹, Fulvia Pingitore¹, Luigi Tassi¹ and Fabrizio Escoli¹

frontiers in Microbiology

Development of an *in vitro* Assay, Based on the BioFilm Ring Test[®], for Rapid Profiling of Biofilm-Growing Bacteria

Enza G. Di Domenico^{1,2}, Luigi Tassi¹, Christian Procesi¹, Florentina Accatoni¹, Isabella Spaduti¹, Grazia Prignano¹, Maria T. Gallo¹, Fulvia Pingitore¹, Valentinia Bonfigliani¹, Thierry Bernard¹ and Fabrizio Escoli¹

SCIENTIFIC REPORTS

Inflammatory cytokines and biofilm production sustain *Staphylococcus aureus* outgrowth and persistence: a pivotal interplay in the pathogenesis of Atopic Dermatitis

E. G. Di Domenico^{1,2}, I. Cavallò¹, V. Bonfigliani¹, G. Prignano¹, I. Spaduti¹, A. Gattone¹, E. Trenti¹, L. Tassi¹, F. Pingitore¹, B. Caporaso¹ & F. Escoli¹

BMC Microbiology

Microbial biofilm correlates with an increased antibiotic tolerance and poor therapeutic outcome in infective endocarditis

Enza Gioia Di Domenico^{1,2}, Sara Giordano Riccardi¹, Barla Cavallò¹, Giovanna D'Agostini¹, Florentina Trenti¹, Giovanni Caporaso¹, Riccardo Falaschi¹, Cristina Pagani¹, Francesca Romani¹, Daria De Mico¹, Monica Schiavini¹, Daniela Sotgiu¹, Carlo Antonio¹, Giuliano Rappelli¹, Rita Barbara Di Chiara¹, Luigi Tassi¹, Daniela Novati¹, Giorgia Cardelli¹, Maria Teresa Gallo¹, Maria Rita Giromardi¹ and Fabrizio Escoli¹

International Journal of Molecular Sciences

Biofilm is a Major Virulence Determinant in Bacterial Colonization of Chronic Skin Ulcers Independently from the Multidrug Resistant Phenotype

Enza Gioia Di Domenico^{1,2}, Barla Cavallò¹, Grazia Prignano¹, Maria Teresa Gallo¹, Matteo Vespignani¹, Barla Cavallò¹, Isabella Spaduti¹, Martina Pontone¹, Valentinia Bonfigliani¹, Laura Cibi¹, Alessandra De Santis¹, Fabiola Di Salvo¹, Fulvia Pingitore¹, Daria Lorenza La Ferla¹, Luigi Tassi¹ and Fabrizio Escoli¹

FEMS Microbiology Letters

The clinical Biofilm Ring Test: a promising tool for the clinical assessment of biofilm-producing *Candida* species

Enza Gioia Di Domenico^{1,2}, Barla Cavallò¹, Martina Pontone¹, Luigi Tassi¹ and Fabrizio Escoli¹

International Journal of Molecular Sciences

Biofilm Producing *Salmonella* Typhi: Chronic Colonization and Development of Gallbladder Cancer

Enza Gioia Di Domenico^{1,2}, Barla Cavallò¹, Martina Pontone¹, Luigi Tassi¹ and Fabrizio Escoli¹

Antonie van Leeuwenhoek

***Raistonia mannitolilytica* infections in an oncologic day ward: description of a cluster among high-risk patients**

Giulia Lucarelli^{1,2}, Enza Gioia Di Domenico¹, Luigi Tassi¹, Domenico Ricci¹, Grazia Prignano¹, Maria Pontone¹, Lucrezia Pingitore¹, Valentinia Trenti¹, Thomas Pontone¹, Aurora Garcia-Aranda¹, Annalisa Santoro¹ and Isabella Spaduti¹

International Journal of Pharmaceutics

Nanosized ion pair complex of tobramycin forming microparticles for the treatment of *Pseudomonas aeruginosa* infections in cystic fibrosis

Carla Sadei¹, Enza Gioia Di Domenico¹, Barbara Pozio¹, Davide De Rocco¹, Roberto Santucci¹, Florentina Accatoni¹, Gerardo Giannone¹, Giovanna Cardelli¹

MAGNETIC RESONANCE IN MEDICINE

A Novel Approach Based on Low-Field NMR for the Detection of the Pathological Components of Sputum in Cystic Fibrosis Patients

Michela Abassi¹, Florentina Accatoni¹, Enza Gioia Di Domenico¹, Massimo Macellà¹, Alessandro Vignone¹, Marco Garbellotti¹, Susie Di Gioia¹, Massimo Grossi¹, Barbara Diga¹, Gabriele Grossi¹ and Marco Grossi¹

Springer

Positively charged biopolymeric nanoparticles for the inhibition of *Pseudomonas aeruginosa* biofilms

Luca Chiosso¹, Enza Gioia Di Domenico¹, Florentina Accatoni¹, Clelia Palazzi¹

microorganisms

***Staphylococcus aureus* and the cutaneous microbiota biofilms in the pathogenesis of atopic dermatitis**

Enza Gioia Di Domenico¹, Barla Cavallò¹, Bruno Caporaso¹, Florentina Accatoni¹, Fulvia Pingitore¹, Aldo Marzani¹, Fabrizio Escoli¹

BMC Infectious Diseases

Characterization of the virulence of *Pseudomonas aeruginosa* strains causing ventilator-associated pneumonia

Beatrice Rossi^{1,2}, Luca Ferrando-Rodríguez¹, Enza Gioia Di Domenico¹, Marzia Marzi¹, Irene Ferrarini¹, Sara Morici^{1,2,3,4}, Marcela de Patis¹, Francisca Muñoz^{1,2,3,4} and Maria Gomez^{1,2}

frontiers in Microbiology

Escaping the phagocytic oxidative burst: role of SODB in the survival of *Pseudomonas aeruginosa* within macrophages

Luca Cavaliotti¹, Elena Gattone¹, Francesco Renato Lufy¹, Enza Gioia Di Domenico¹, Paolo Del Porto and Florentina Accatoni¹

Journal of Clinical Medicine

Silver Sulfadiazine Eradicates Antibiotic-Tolerant *Staphylococcus aureus* and *Pseudomonas aeruginosa* Biofilms in Patients with Infected Diabetic Foot Ulcers

Enza Gioia Di Domenico^{1,2}, Barbara De Angelis^{1,2}, Barla Cavallò¹, Francesca Ricci¹, Felicia Orlandi^{1,2}, Margherita Fossarello-Lopez Merello Di Nardo¹, Chiara Di Sapa¹, Felicia Gattone^{1,2}, Maria Giovanna Toldi¹, Agnese Orlandi^{1,2}, Giovanna D'Agostini¹, Elisabetta Trenti¹, Daria De Mico¹, Giorgia Cardelli¹, Annalisa Santoro¹, Teresina Rosalinduzzi¹, Grazia Prignano¹, Fulvia Pingitore¹, Daria Lorenza La Ferla¹, Luigi Tassi¹, Nadia Cavallò¹ and Fabrizio Escoli¹

frontiers in Cellular and Infection Microbiology

Biofilm Production as a Risk Factor and Predictor of Mortality for Carbapenem-Resistant *Klebsiella pneumoniae* in oncological patients

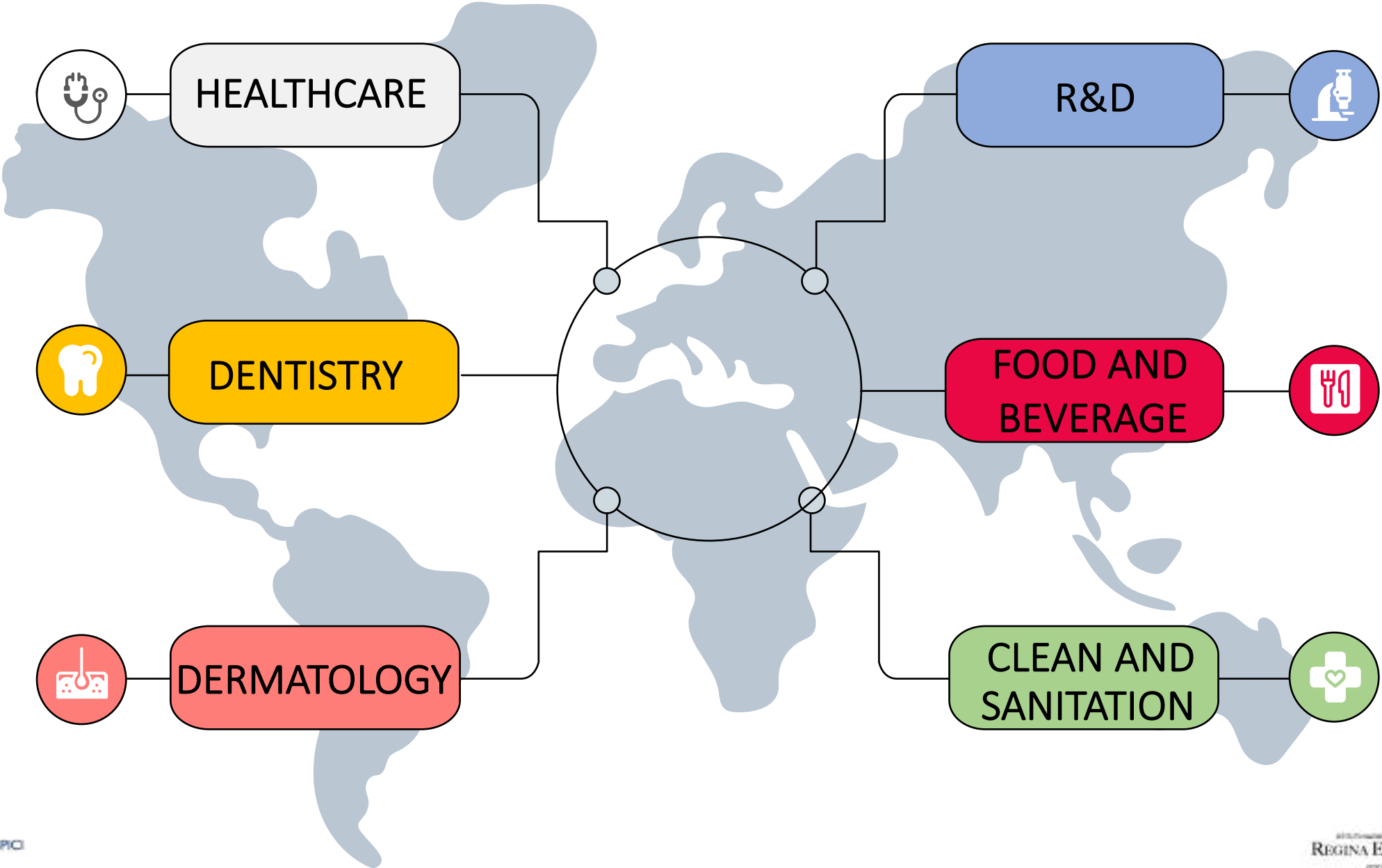
Enza Gioia Di Domenico¹, Barla Cavallò¹, Francesca Ricci¹, Grazia Prignano¹, Isabella Spaduti¹, Francesco Marchetti¹, Fulvia Pingitore¹, Carmelina Procesi¹, Lavinia Paganelli¹, Luigi Tassi¹, Andrea Margonelli¹, Assunta De Luca¹, Fabrizio Escoli¹

Biofilm Production by Carbapenem-Resistant *Klebsiella pneumoniae* significantly increases the risk of death in oncological patients

Enea Gino Di Domenico^{1†}, Ilaria Cavallo², Francesca Sivori², Francesco Marchesi³, Grazia Prignano², Fulvia Pimpinelli², Isabella Sperduti⁴, Lorella Pelagalli⁵, Fabiola Di Salvo⁶, Ilaria Celesti⁶, Silvia Paluzzi², Carmelina Pronesti⁷, Fiorentina Ascenzioni⁸, Luigi Toma⁹, Assunta De Luca¹⁰, Andrea Mengarelli² and Fabrizio Ensoli²

“...the presence of strong biofilm-producing Carbapenem-resistant K. pneumoniae (CRKP) significantly increases the risk of death in oncological patients. Thus, the assessment of biofilm production may provide a key element in supporting the clinical management of high-risk oncological patients with CRKP infection.”

FIELDS OF APPLICATION



CONCLUSIONS

01

The strength of biofilm production is a key risk factor affecting the efficacy of antimicrobial therapy

02

The assessment of biofilm combined with antibiotic profiling may help direct the therapeutic intervention and improve the clinical outcome

03

BST represents a promising tool to predict the clinical outcome of antibiotic therapy



IRE  **ISG**
ISTITUTO NAZIONALE TUMORI ISTITUTO DERMATOLOGICO
REGINA ELENA **SAN GALLICANO**

ISTITUTI DI RICOVERO E CURA A CARATTERE SCIENTIFICO

Microbiology and Virology
San Gallicano Institute

I.F.O. Istituti Fisioterapici Ospitalieri

THANKS!

Do you have any questions?

enea.didomenico@ifo.gov.it