aviesan
alliance nationale
pour les sciences de la vie et de la santé

Institut Thématique Multi-Organismes
Technologies pour la santé

TRAITER /INTERVENIR

Actualités du domaine

William Couet
U1070 - Poitiers

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

Ministère de l'Enseignement supérieur
de la Recherche et de l'Innovation

MINISTÈRE | STRATÉGIE | ENSEIGNEMENT SUPÉRIEUR | RECHERCHE | INNOVATIO

Accueil > Recherche > Domaines de la recherche > Biologie et santé

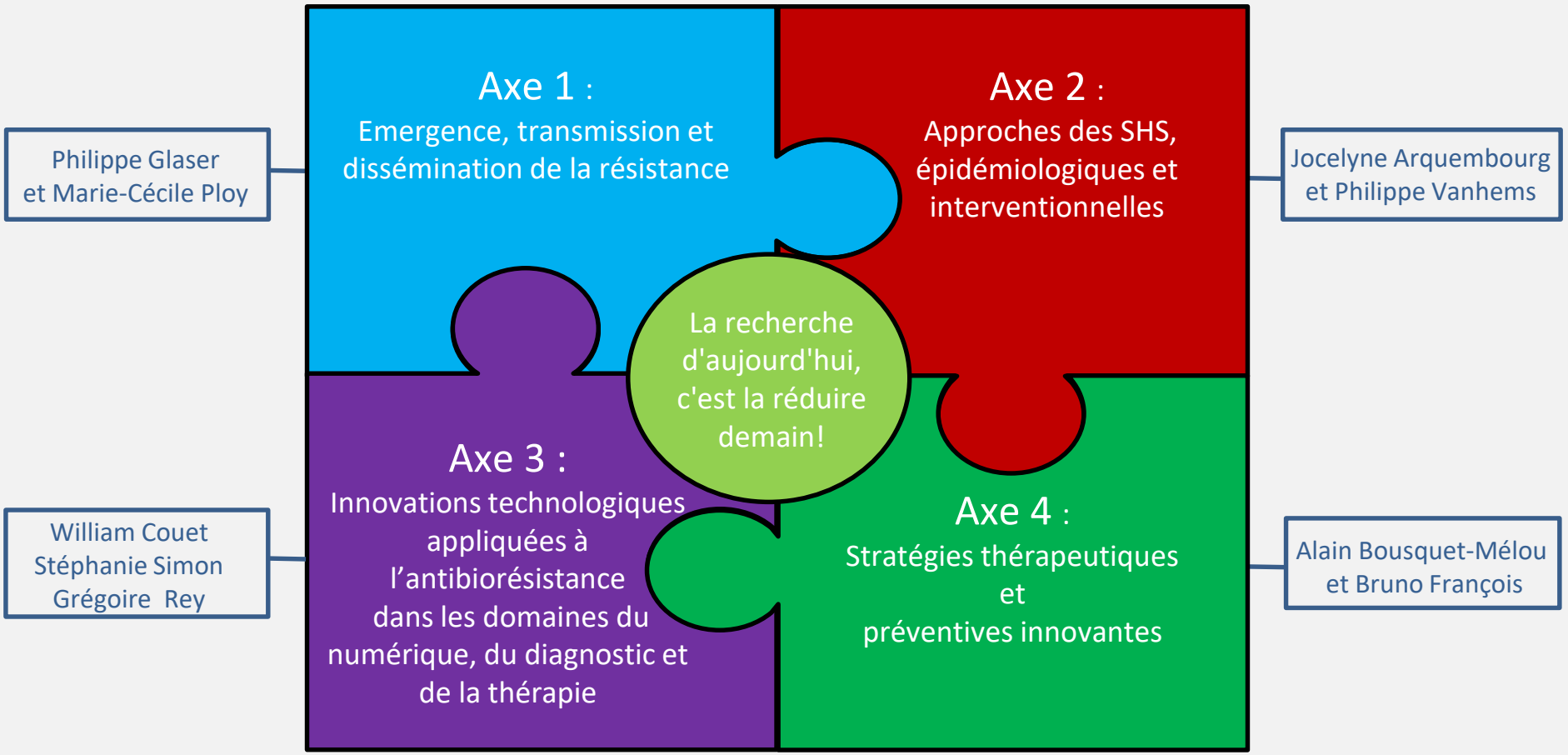
BIOLOGIE ET SANTÉ

Lancement d'un programme prioritaire de recherche de 40 millions d'euros pour lutter contre la résistance aux antibiotiques

Santé

Frédérique Vidal, ministre de l'Enseignement supérieur, de la Recherche et de l'Innovation, clôturera mercredi 14 novembre 2018 le colloque interministériel «Antibiorésistance : enjeux et besoins en recherche et innovation», qui réunit universités et organismes de recherche impliqués dans la lutte contre la résistance aux antibiotiques au ministère des Solidarités et de la Santé.

Programme Prioritaire de Recherche Antibiorésistance



DIAGNOSTIC

Différencier une infection virale d'une infection bactérienne

-développer des tests de diagnostic ciblant des biomarqueurs identifiés et validés

-participer à la validation de biomarqueurs

Identifier plus rapidement le pathogène impliqué

-Augmenter la sensibilité des tests existants

Identifier des biomarqueurs de résistances

- aider à l'identification ou la validation

Diagnostiquer plus rapidement les résistances

-Augmenter la sensibilité des tests existants :

Tests de Susceptibilité accélérés

Srugo et al, 2017 Pediatrics

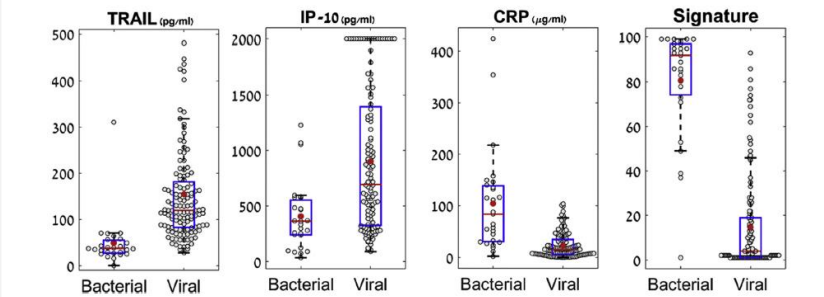
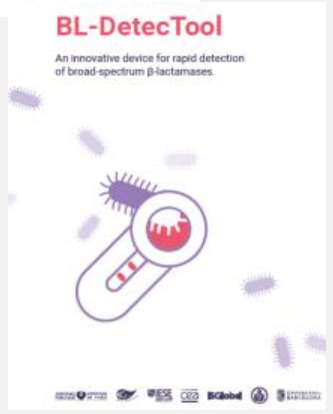
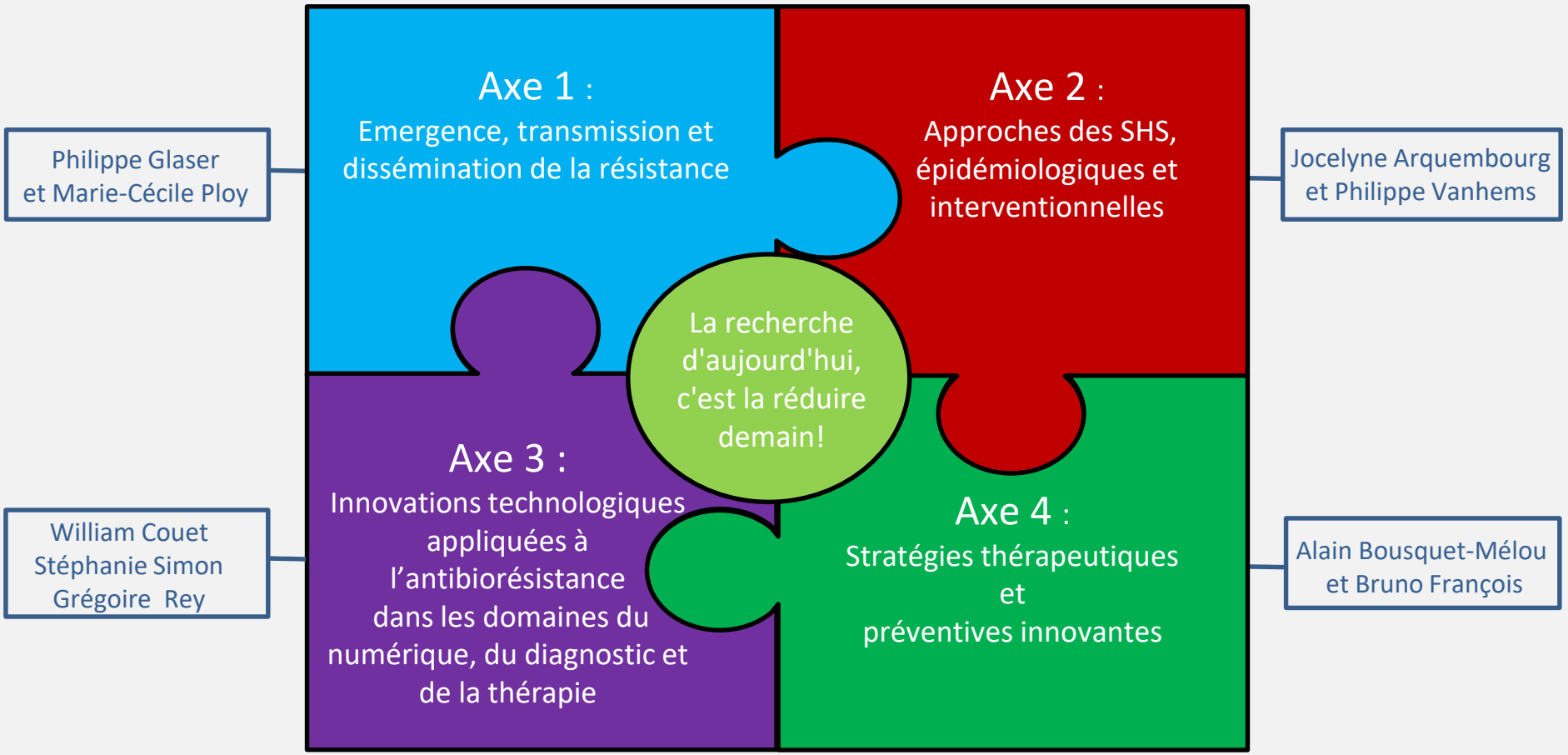


Figure 1 The host proteins TRAIL, IP-10 and CRP and combinatorial signature are differentially expressed in patients presenting with bacterial and viral infections. Box plots for TRAIL, IP-10, CRP, and host-signature measured over the microbiologically confirmed cohort (n = 155) are presented. Red line and circle correspond to group median and average respectively.



Programme Prioritaire de Recherche Antibiorésistance



Positionnement de l'ITMO Technologies pour la Santé ?

1- Recherche et Développement de Nouvelles Molécules

Discovery

Exemple N°1: Criblage de molécules adjuvantes (Inserm U1261 – Marseille / JM Bolla)

Contrat d'Interface Inserm-UDC — 2008

ANR E-BIO — 2009

Cifre Virbac — 2013

Valor-PACA — 2012

Maturation SATT — 2013

PreMat- SATT — 2016

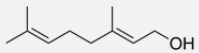
VLM — 2018

From natural products to chemistry… → from hits to leads…

Patent N° 1 deposited by UDC
N° EP 08 168691.7

Patent N° 2 co-deposited by UDC and AMU
PCT / EP2012 / 053113

Drug-Design:
- Modification of the isoprenyl domain
  - Geranyl
  - Farnesyl
- Addition of polyamines



Geraniol

Chemolibrary of **polyamino-isoprenyl** derivatives
80 compounds

Screening on **animal pathogens**
1 compound selected
Scale-up
Toxicity

Screening on ***Pseudomonas aeruginosa***
1 compound selected. PK/PD ongoing

Discovery

Exemple N°2: Nouvel antibiotique à partir d'une toxine bactérienne (Inserm U1230 – Rennes / B Felden)

De nouveaux antibiotiques mis au point par un laboratoire de l'Inserm et l'Université de Rennes 1

COMMUNIQUÉ | 09 JUIL. 2019 - 20H00 | PAR INSERM (SALLE DE PRESSE)
IMMUNOLOGIE, INFLAMMATION, INFECTIOLOGIE ET MICROBIOLOGIE

Des chercheurs de l'Inserm et de l'université de Rennes 1 ont récemment identifié une nouvelle toxine bactérienne et l'ont transformée en antibiotiques puissants et actifs contre différentes bactéries responsables d'infections humaines, tant à Gram positif que négatif.

Discovery

Exemple N°3: Adjuvants d'antituberculeux (Inserm U1177 – Lille / B Deprez)

Inserm
La science pour la santé
From science to health

Salle de Presse

FR | EN

SERVICE PRESSE | ACTUALITÉS | VIDÉOS | RESSOURCES / PUBLICATIONS

COMMUNIQUÉS ET DOSSIERS DE PRESSE

Accueil > Communiqués/Dossiers > Immunologie, inflammation, infectiologie et microbiologie
> Tuberculose et antibiorésistance : des chercheurs lillois inventent un nouveau prototype de médicament

Tuberculose et antibiorésistance : des chercheurs lillois inventent un nouveau prototype de médicament

COMMUNIQUÉ | 16 MARS 2017 - 19H06 | PAR INSERM (SALLE DE PRESSE)
IMMUNOLOGIE, INFLAMMATION, INFECTIOLOGIE ET MICROBIOLOGIE

Discovery

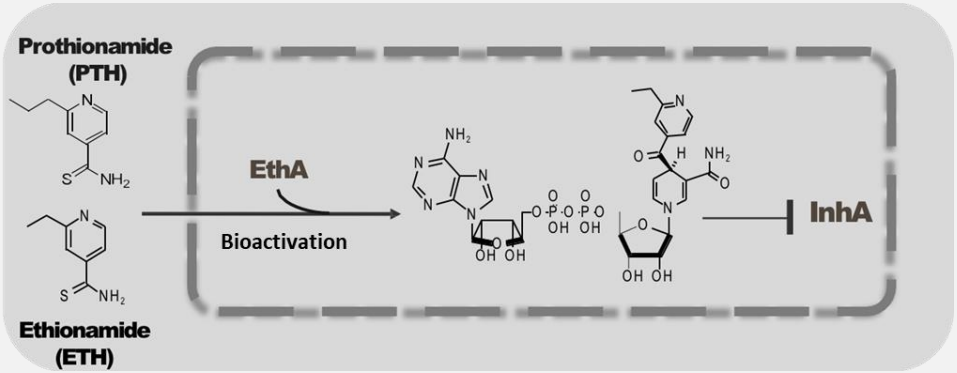
Nat Med. 2009 May;15(5):537-44. doi: 10.1038/nm.1950. Epub 2009 May 3.

Synthetic EthR inhibitors boost antituberculous activity of ethionamide.

Willand N[1], Dirié B, Carette X, Bifani P, Singhal A, Desroses M, Leroux F, Willery E, Mathys V, Déprez-Poulain R, Delcroix G, Frénois F, Aumercier M, Locht C, Villeret V, Déprez B, Baulard AR.

Author information

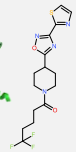
1 Institut National de la Santé et de la Recherche Médicale, Lille, France.



Discovery | **Optimization** | **Preclinical** | **Clinical trials**

TB Boost project starts on the *M. tuberculosis* transcriptional [illegible]: Ethionamide





Institut Pasteur de Lille

ETH zürich

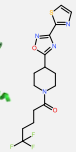
SATT NORD

- **14 publications / 8 patents**
  - **PNAS** 2008, **Nature Medicine** 2009, **Science** 2017

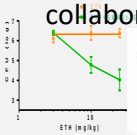
Inserm

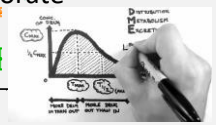
Discovery | **Optimization** | **Preclinical** | **Clinical trials**

TB Boost project starts on the *M. tuberculosis* transcriptional



BioVersys and ULille start to collaborate





GSK joins: collaboration agreement with BioVersys

Candidate declared

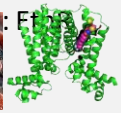
- **14 publications / 8 patents**
  - **PNAS** 2008, **Nature Medicine** 2009, **Science** 2017

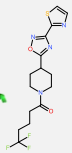
Inserm

En attendant les pôles Universitaires d'Innovation

Discovery

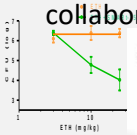
TB Boost project starts on the *M. tuberculosis* transcriptional

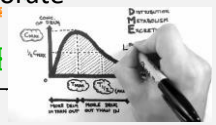




Optimization

BioVersys and ULille start to collaborate



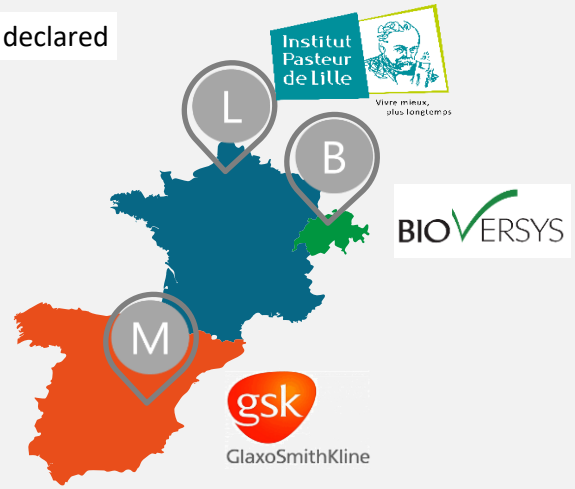


GSK joins: collaboration agreement with BioVersys

Preclinical

Clinical trials

Candidate declared



- **14 publications / 8 patents**
  - **PNAS** 2008, **Nature Medicine** 2009, **Science** 2017

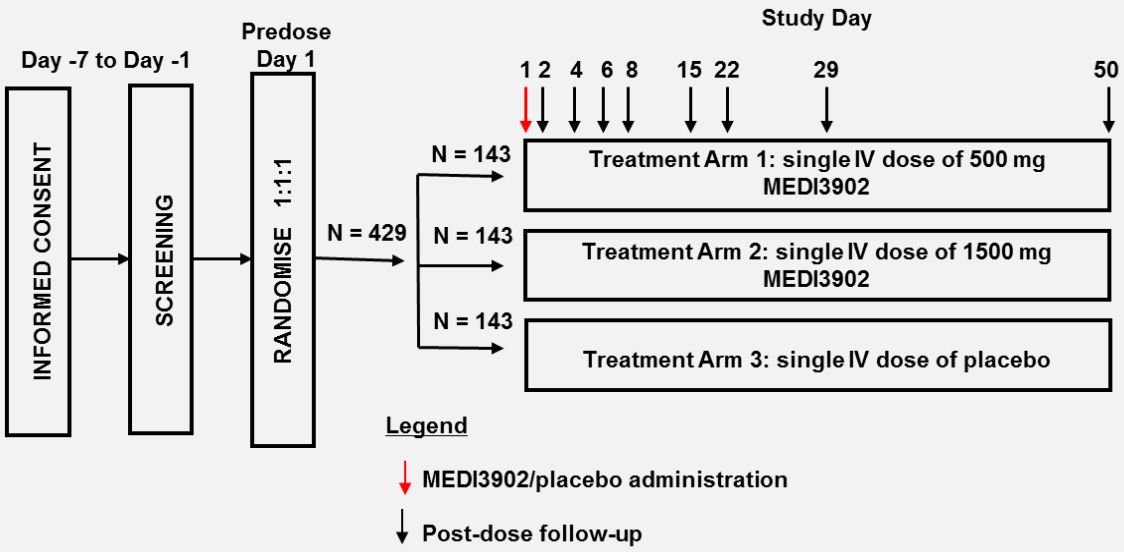
Inserm

CIC LIMOGES
CENTRE INVESTIGATION CLINIQUE

Clinical trials

EVADE

A Phase 2 Proof-of-concept Study to Evaluate the Efficacy and Safety of MEDI3902 in Mechanically Ventilated patients for the Prevention of Nosocomial Pneumonia Caused by *Pseudomonas aeruginosa*



Positionnement de l'ITMO Technologies pour la Santé ?

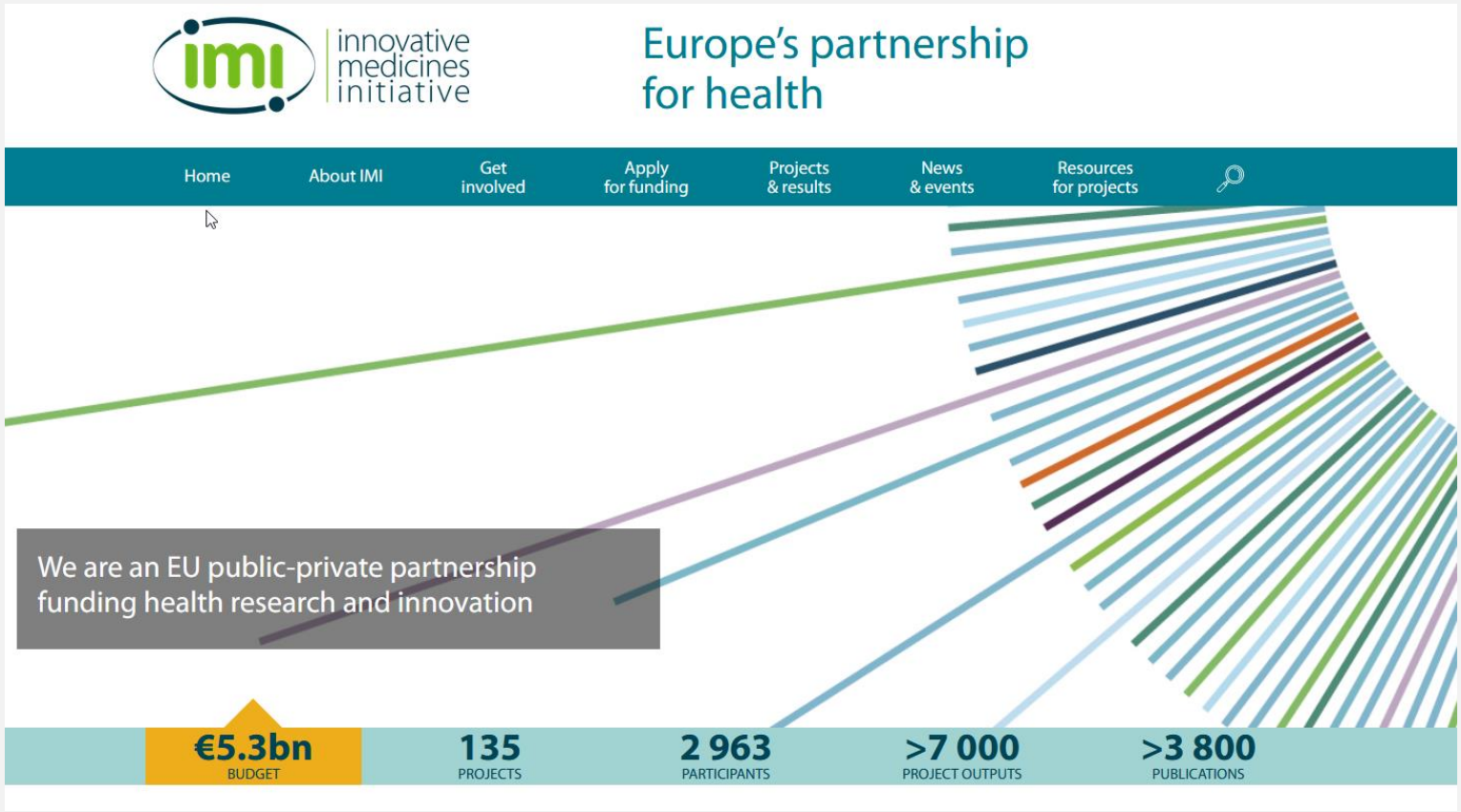
1- Recherche et Développement de Nouvelles Molécules

Positionnement de l'ITMO Technologies pour la Santé

2- Plan Antibiorésistance / Traiter ?

Que nous ont appris les précédents programmes ?

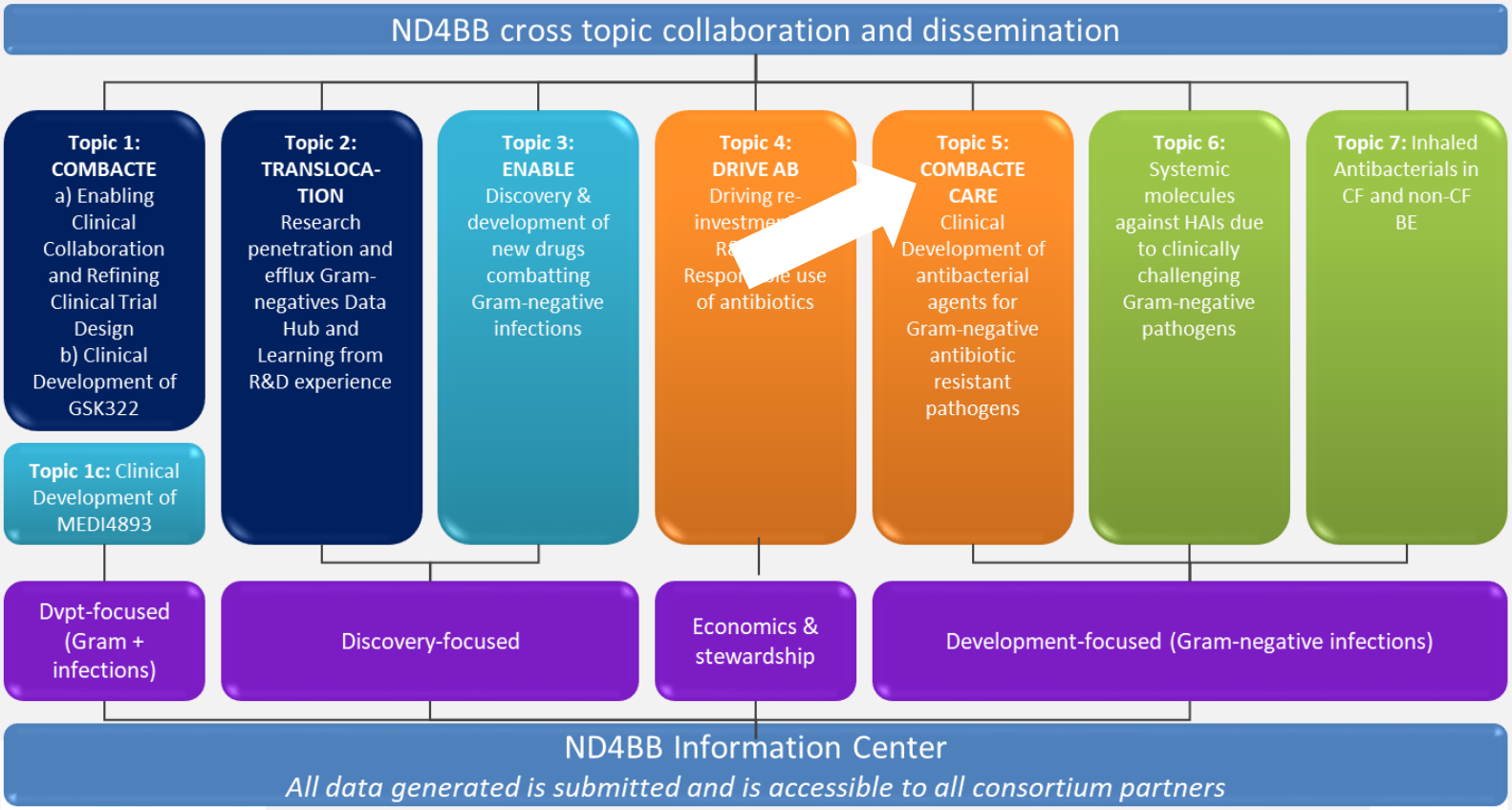
2-1: Les précédents programmes : IMI - Public/Privé



Innovative Medicines Initiative

The Anti-Microbial Resistance Programme: New Drugs For Bad Bugs (ND4BB)

Call 8
Call 9
Call 11



innovative medicines initiative

Europe's partnership for health

Home | About IMI | Get involved | Apply for funding | Projects & results | News & events | Resources for projects

Home | Projects & results | Project Factsheets | COMBACTE-CARE

COMBACTE-CARE

Combatting Bacterial Resistance in Europe - Carbapenem Resistance

Ongoing | IMI1 | Antimicrobial resistance, Infectious diseases, ND4BB, Clinical trial design, Conducting clinical trials

ND4BB COMBACTE CARE

Summary

Infections caused by bacteria known as 'carbapenem-resistant enterobacteriaceae' (CRE) are resistant to most available antibiotics and are so difficult to treat they are considered to be one of the most dangerous drug-resistant bacteria in the world. Worryingly, cases of CRE infections are on the rise in Europe and globally. The COMBACTE-CARE project aims to shed new light on the best ways to understand and treat CRE infections. It will also run clinical trials of a novel antibiotic combination product designed to tackle a sub-type of CRE infections for which there are limited or no treatment options.

Achievements & News

COMBACTE-CARE completes recruitment for major antimicrobial resistance study

January 2019

COMBACTE-CARE has recruited 2 266 patients to its EURECA study on infections that are resistant to antibiotics called carbapenems, which are considered to be among the most

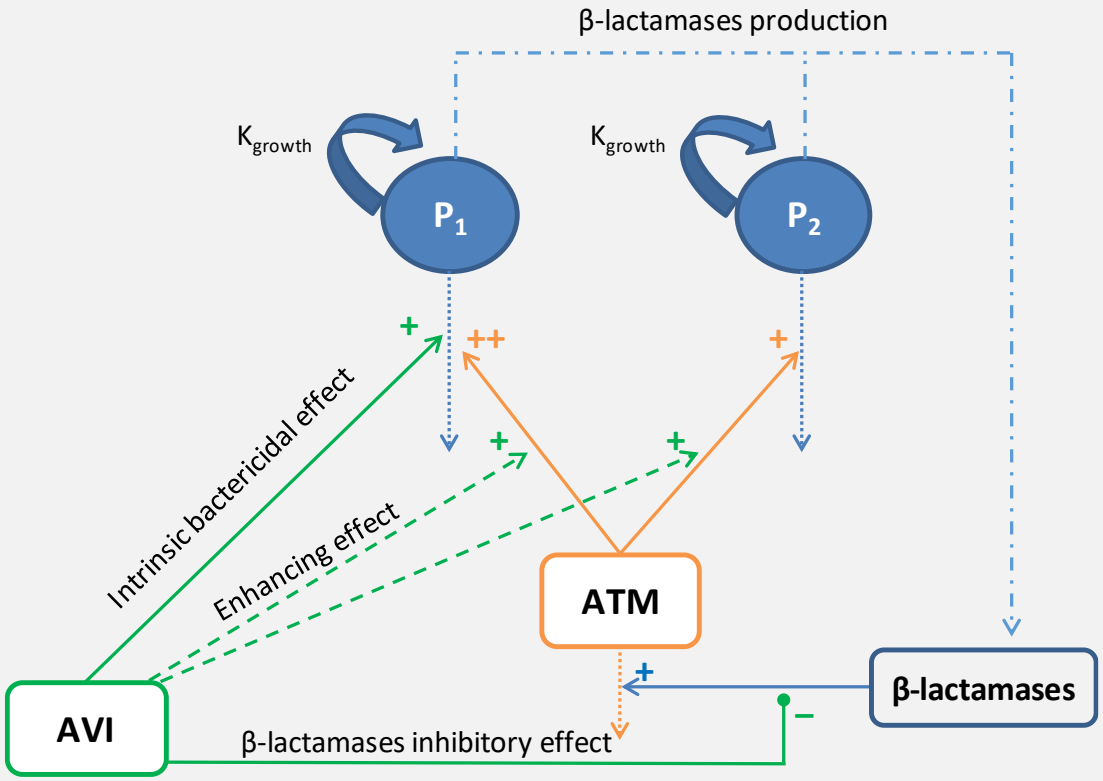
FACTS & FIGURES

Start Date	01/03/2015
End Date	28/02/2020
Call	IMI1 - Call 9
Grant agreement number	115620

Type of Action:
RIA (Research and Innovation Action)

Contributions	**€**
IMI Funding	23 871 500
EFPIA in kind	59 833 500
Other	1 408 336
Total Cost	85 113 336

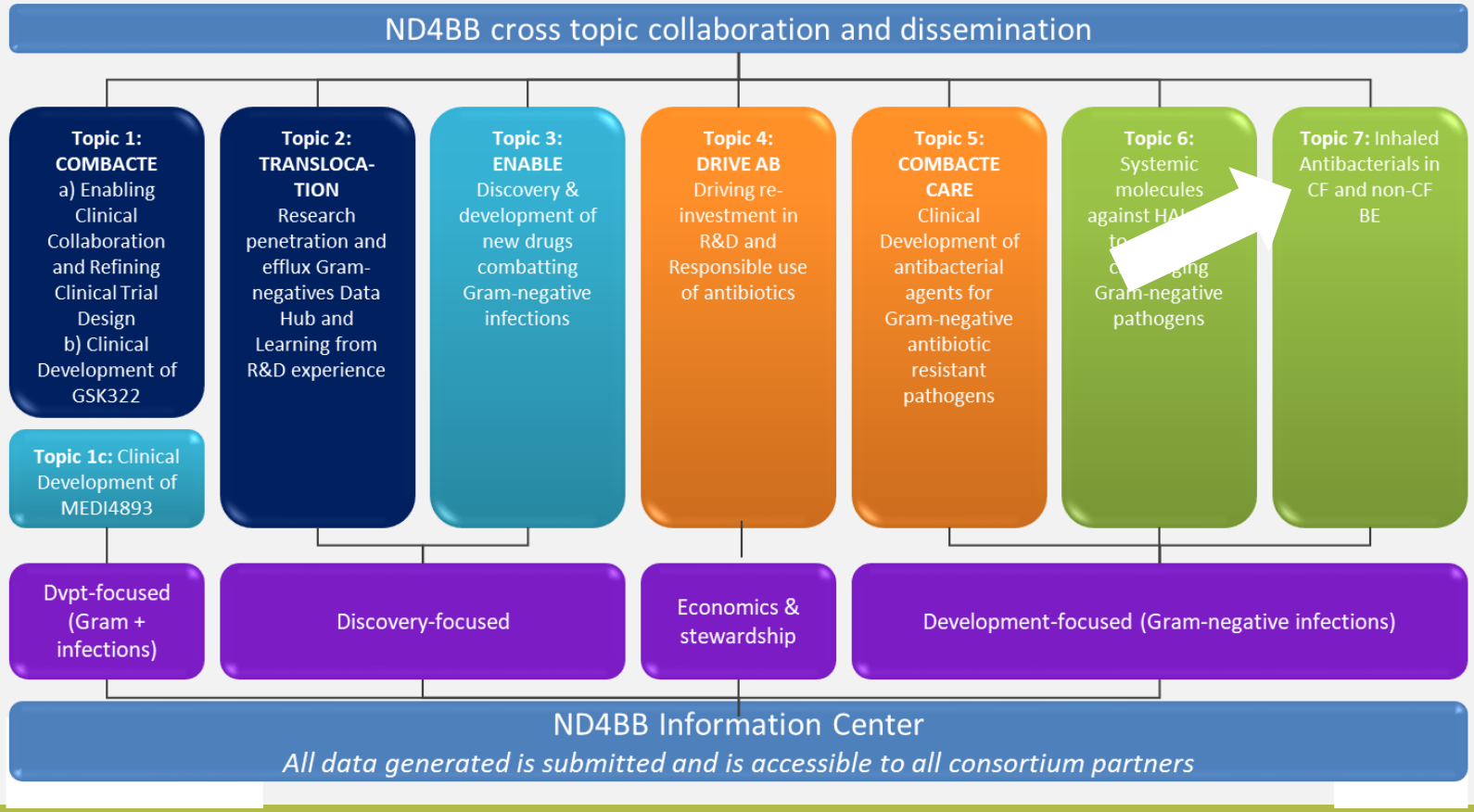
PK-PD modeling of aztreonam / avibactam combination



(Chauzy et al., CPT Pharmacometrics Syst Pharmacol. 2019)

Innovative Medicines Initiative

The Anti-Microbial Resistance Programme: New Drugs For Bad Bugs (ND4BB)



innovative medicines initiative

Europe's partnership for health

Home | About IMI | Get involved | Apply for funding | Projects & results | News & events | Resources for projects

Home | Apply for funding | Closed calls | IMI2 - Call 16

IMI2 - Call 16

IMI2 – Call 16 was launched on 18 July 2018 with the following topics:

- Progress new assets (one pre-new molecular entity (preNME) and one first-time-in-human (FTIH) start) for tuberculosis (TB) that act synergistically with bedaquiline, cytochrome bc or cytochrome bd inhibitors
- Progress novel assets (one FTIH start) for non-tubercular mycobacteria (NTM) that may act synergistically with bedaquiline and cytochrome bc drugs
- Discover and progress novel assets with new mechanisms of action (one preNME for TB and one preNME for NTM) and biomarkers for TB and NTM infection
- Determination of gepotidacin levels in tonsils and prostatic tissue
- Infection site targeting, antibiotic encapsulated in nanoparticles for treating extracellular bacterial infections
- Functional Ethionamide boosters: a novel combination for tuberculosis therapy
- Intravenous treatments of serious infections (urinary tract infections (UTI), intra-abdominal infections (IAI) & hospital-acquired pneumonia/ventilator associated pneumonia (HAP/VAP)) caused by Gram(-) bacteria (Enterobacteriaceae +/- Pseudomonas and/or Acinetobacter)

AB-Direct
Antibiotic Distribution & Recovery
IMI AMR Accelerator

innovative medicines initiative

Europe's partnership for health

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GNA NOW
IMI AMR ACCELERATOR

2-2: Les précédents programmes « 100% Public »

SEVENTH FRAMEWORK PROGRAMME

Innovative Nanoformulation of Antimicrobial Peptides To Treat Bacterial Infectious Diseases

(U 1066 – Angers)

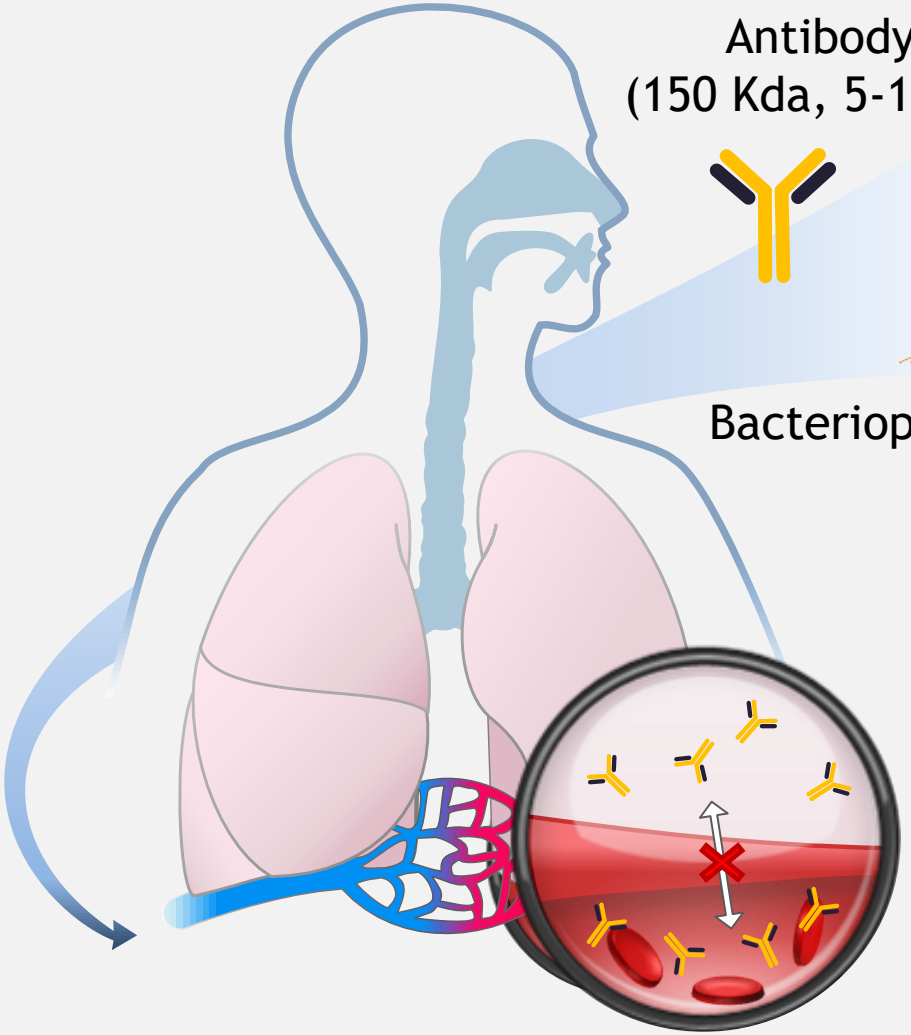
université angers

U1066 MiNt
MICRO & NANOMÉDECINES BIOMIMÉTIQUES

FORMAMP

CHU ANGERS
CENTRE HOSPITALIER UNIVERSITAIRE

FP7 Collaborative Project
Grant agreement n° 604182
NMP 2013.12-2



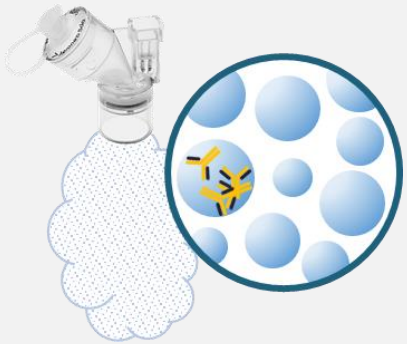
Antibody
(150 Kda, 5-10 nm)

Bacteriophage (50-100 nm)

MAbImprove
LabEx Tours Montpellier

U 1100 - Tours

depends on the device & formulation



2-1: Les précédents programmes « 100% Public »

SEVENTH FRAMEWORK PROGRAMME

FP7 Cooperation Work Prog… …ealth-2011

HEALTH.2011.2.3.1-1 Investigator-driven … off-patent antibiotics. FP7-HEALTH-2011-two-stage. Research sh… …ming optimal treatment regimens (including drug choice, combinations … of therapy, PK/PD, individualisation) of off-patent antimicrobial agent… …difficult-to-treat infections caused by multi-drug resistant bacterial patho… …maximise clinical benefit and minimise selection for resistance. Research… …participation is highly encouraged and this will be

Repositionnement

AIDA

Preserving old antibiotics for the future

assessment of clinical efficacy by a pharmacokinetic/pharmacodynamic approach to optimize effectiveness and reduce resistance for off-patent antibiotics

2-1: Les précédents programmes « Public »

jpiamr
Joint Programming Initiative on Antimicrobial Resistance

SECOND CALL FOR TRANSNATIONAL RESEARCH PROJECTS WITHIN THE JOINT PROGRAMME INITIATIVE ANTIMICROBIAL RESISTANCE

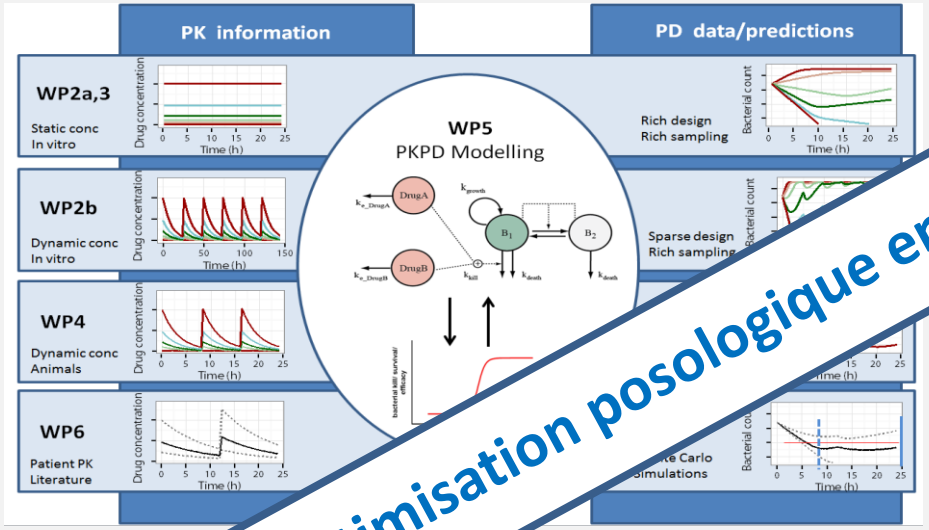


Fig. 2 Illustrate… …ing, prediction and validation after intial …reening

Optimisation posologique en vie réelle

JPI… - Transnational call for proposals on Antimicrobial Resistance

Developing combinations of CO-ACTIVE antimicrobials and non-antimicrobials – CO-ACTION

2-1: Les précédents programmes « Public »

Prévenir les résistances
pour préserver les nouveaux antibiotiques
Interdisciplinarité pharmaco – microbio (omic)

Investigations of the emergence, d… …dance using epidemiology, modelling, mi…

CO-PROTECT will i… …ional recognition, to investigate c… …beta-lactamase inhibitors with other l… …vorable combination regimens preventi… …ice of multi-drug resistant (MDR) Gram-negative b…

CO-PROTECT …y on innovative semi-mechanistic PK/PD modeling approaches, integrating sequencing and metabolomics approaches that will be applied to further research investigating combination therapies.

Pharmacologie au service de la médecine de précision

Università di Pavia

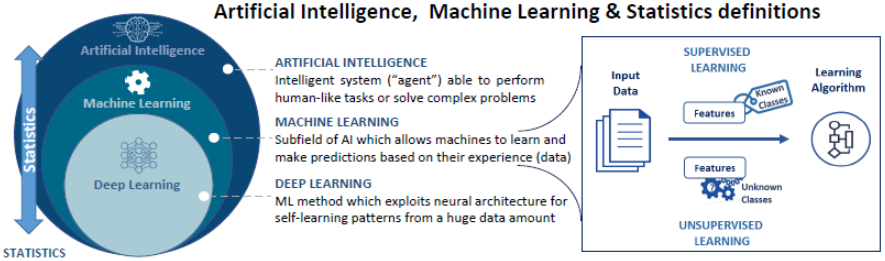
Artificial intelligence and machine learning: just a hype or a new opportunity for pharmacometrics?

R. Bartolucci, S. Grandoni, N. Melillo, G. Nicora, E. Sauta, E. M. Tosca, P. Magni
Department of Electrical, Computer and Biomedical Engineering, University of Pavia, via Ferrata 5, Pavia, I-27100, Italy

BMS bioinformatics mathematical modeling and synthetic biology

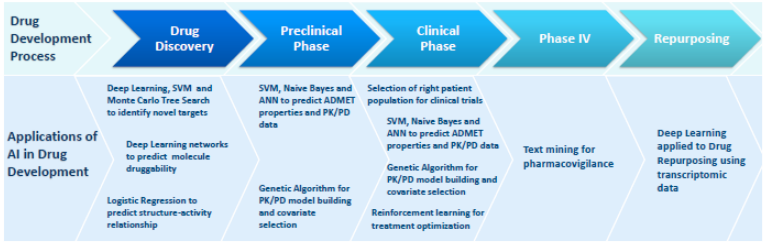
BACKGROUND:

Artificial Intelligence, Machine Learning & Statistics definitions



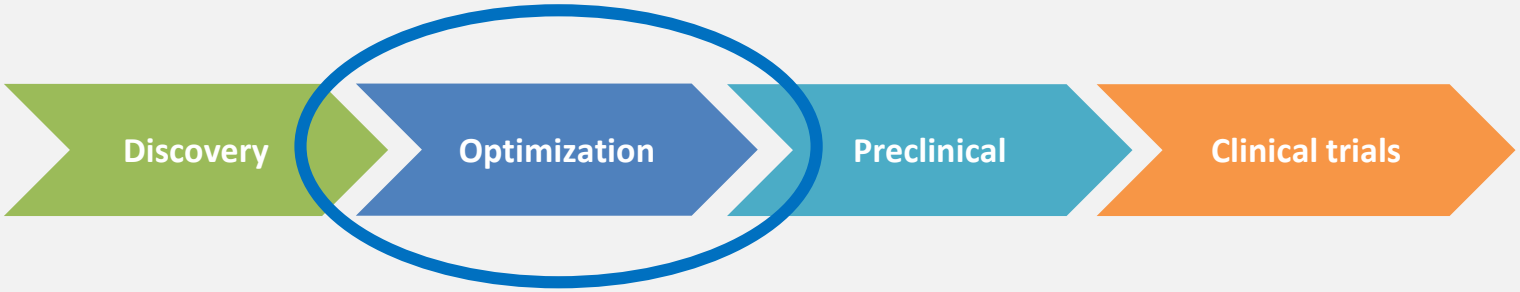
STATISTICS
Statistical data modeling can be exploited and integrated by ML techniques

AI/ML in drug discovery and development



Positionnement de l'ITMO Technologies pour la Santé ?

1- Recherche et Développement de Nouvelles Molécules

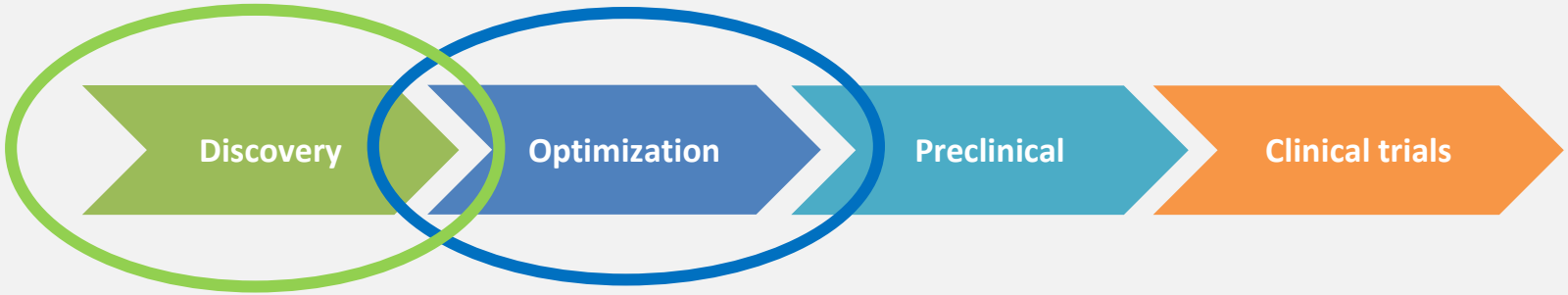


OUI mais surtout en post-AMM

CONCLUSION

L'ITMO TS a sa place dans le plan Antibio-R

- sur l'aspect traitement (médecine de précision / interfaces)



- sur d'autres aspects (diagnostic …)

Remerciements

- Stéphanie Simon — CEA Saclay
- Nathalie Manaud — CEA Saclay
- Elias Fattal — CNRS Paris Sud
- Patrick Saulnier — U1066 Angers
- Nathalie Heuzé-Vourc'h — U1100 Tours
- Benoît Deprez — U1177 Lille
- Brice Felden — U1230 Rennes
- Pierre Marquet — U1248 Limoges
- Jean Michel Bolla — U1261 Marseille
- Bruno François — CIC 1435 Limoges

CIC 1435 (Limoges): Axe Infectiologie