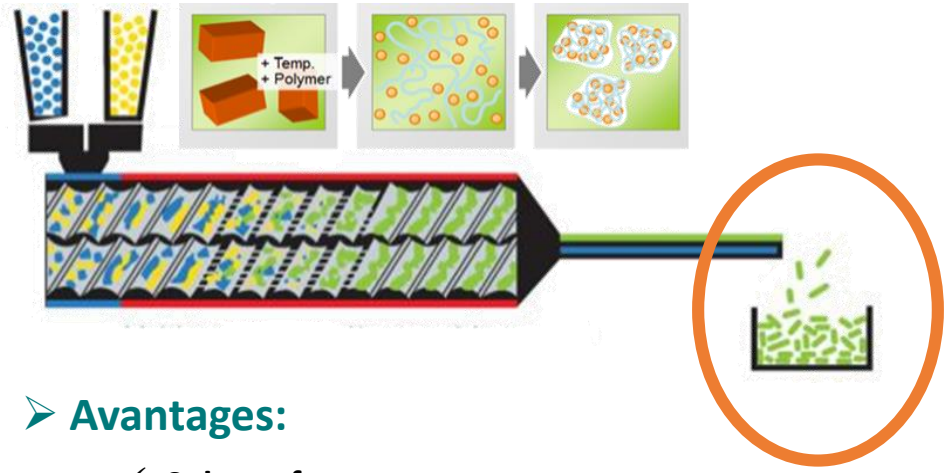
Thermoformating apparatus for continuous production of solid oral dosage forms

- Hot Melt Extrusion
- Fully integrated continuous process for the production of a medicine

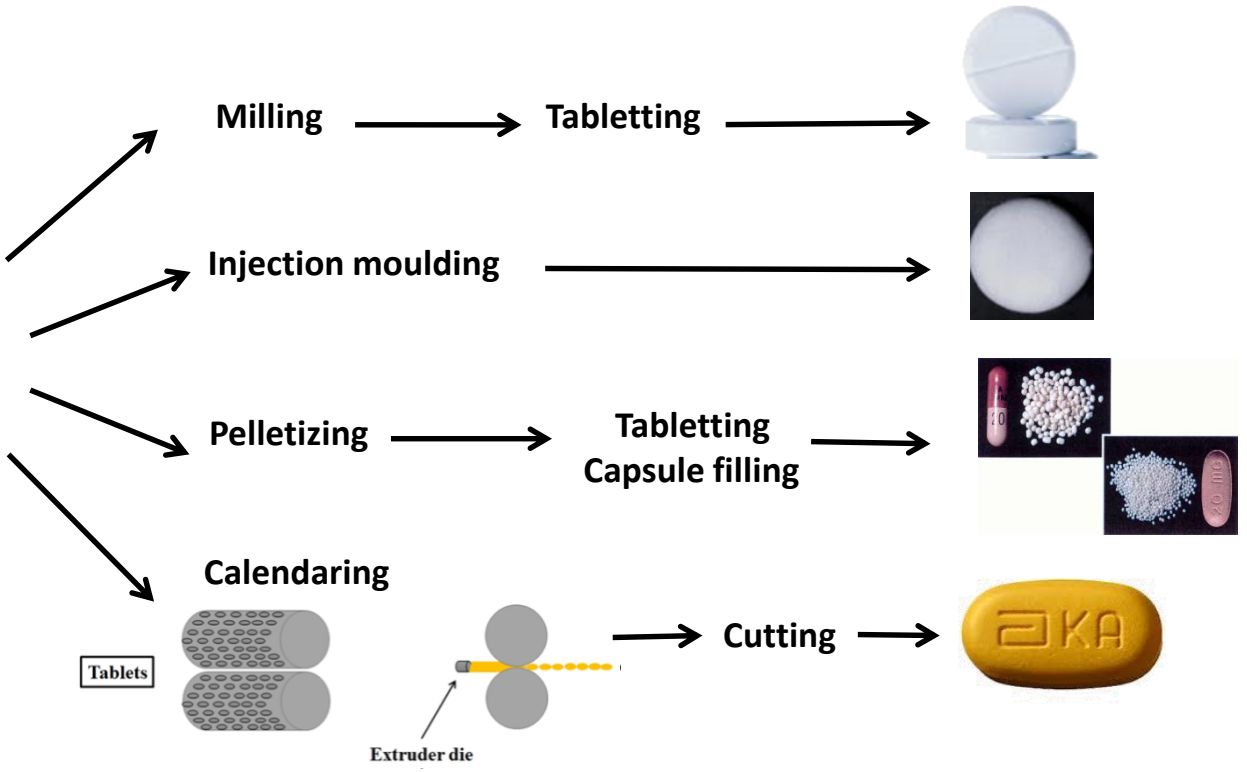
The LPTB's main objective is to design new pharmaceutical systems for controlled drug delivery and administration of drugs

Thermoformating apparatus for continuous production of solid oral dosage forms

- Hot Melt Extrusion for **continuous production** of drugs



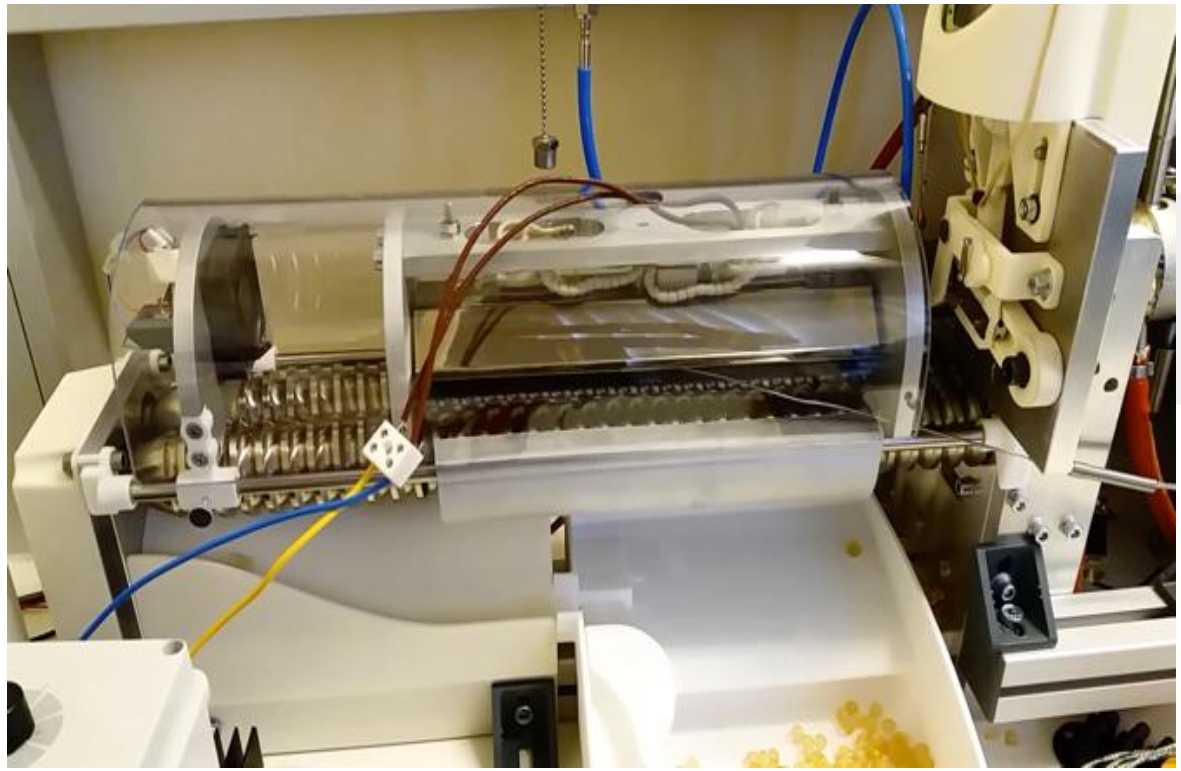
NOT CONTINUOUS processes



➢ **Avantages:**

- ✓ **Solvent free,**
- ✓ **Fast process,**
- ✓ **Cost effective,**
- ✓ **Low ecological foot print,**
- ✓ **Versatile process :**
- ✓ **Increased solubility/bioavailability of BCSII compounds (>50% of API)**
- ✓ **Continuous**

Thermoformating apparatus for continuous production of solid oral dosage forms



Prototype of thermoformating apparatus connected to commercially available extruder enabling production of stable and uniform solid oral dosage forms at a frequency of 1 form/second.

- Key advantages
  - Advantages of the hot melt extrusion process compared to a classical batch approach
  - Obtention of a **product with a constant quality and purity profile** in compliance with the European Pharmacopeia requirements

IP Status & Contact

- Intellectual Property :
  - Patent Application (Pending : PCT/EP2017/0744679) publication number **WO2018069057 (A1)**
  - BE1024283 (B1)

Contact Labo : *Prof. Brigitte Evrard*
Chef de Service
B.Evrard@uliege.be
+32 (0) 43 66 43 00

Contact KTO : *Helene Sabatel*
Technology Transfer Officer
h.sabatel@uliege.be
+32 (0) 43 49 85 29

The Namur Thrombosis and Hemostasis Center A gathering of experts from laboratory, clinical and regulatory field

Prof. Jonathan Douxfils

University of Namur
QUALIblood s.a.

CHU UCL NAMUR

NTHC Namur Thrombosis & Hemostasis Center

UNIVERSITÉ DE NAMUR

Headlines

- Gathering of expertise in thrombosis and hemostasis
- Basic and clinical research with a translational approach
- Synergy from the Department of Pharmacy of the UNamur and several clinical disciplines involved in the management of thrombotic diseases from the CHU UCL Namur

Potential contribution

- **4 main topics:**
  - Translational research
  - Public health
  - Basic research
  - Multicenter national studies with international societies and partners

Our mission

Improvement of public health by:

1. Improving diagnosis by providing new validated tools
2. Ensuring better implementation of treatments
3. Assessing risk minimization strategies for the best use of treatments
4. Providing special emphasis on some orphan diseases and unmet medical needs
5. Sharing knowledge with all stakeholders, especially patients and healthcare providers.

Our facilities and services

We provide:

- **all analytical services for blood investigations and hemocompatibility testing**
- **availability of plasma biobank from healthy and pathological subjects**

We offer:

- **tailor-made solutions, from the design of analytical protocols up to the development and validation of specific analytical methods**

Our facilities and services

- Through our expertise we have created an independent contract research organization (CRO) named **QUALIblood sa**.
- In this structure, we assist our clients from candidate selection, through non-clinical and clinical studies, to marketing authorization, using our state-of-the-art, product-dedicated expertise in blood analysis.
- We aim at sharing with our customer our expertise in research achievement and protocol design in order to reach their objectives.

QUALIblood
Your expert in blood testing

Thank you for your attention

We will be glad to welcome you in the heart of Wallonia

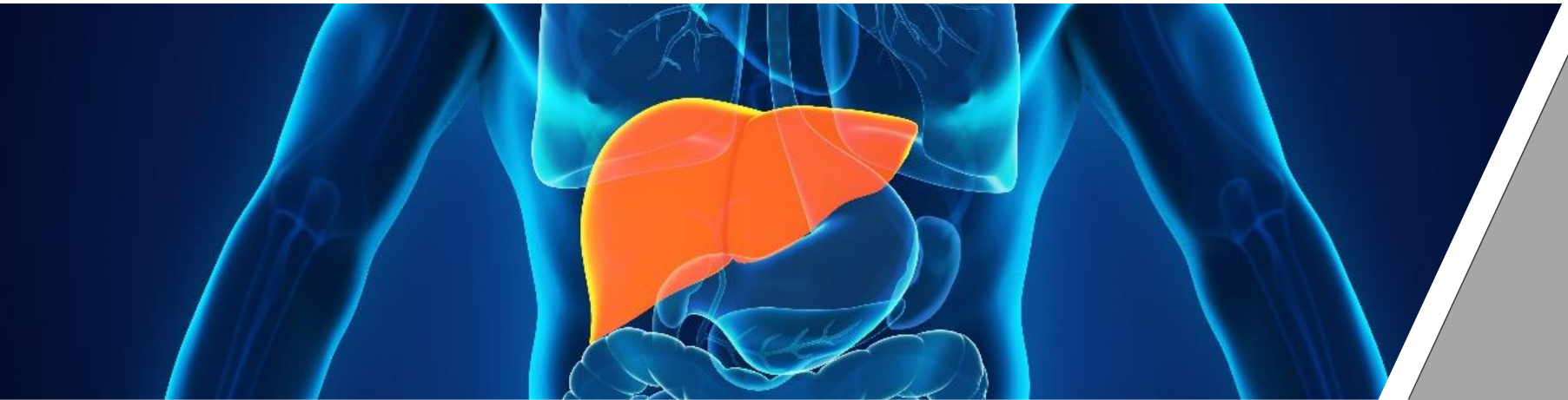
UNIVERSITÉ DE NAMUR

The *In Vitro* Toxicology and Dermato-cosmetology (IVTD) research group

Lab Head: Prof. Tamara Vanhaecke

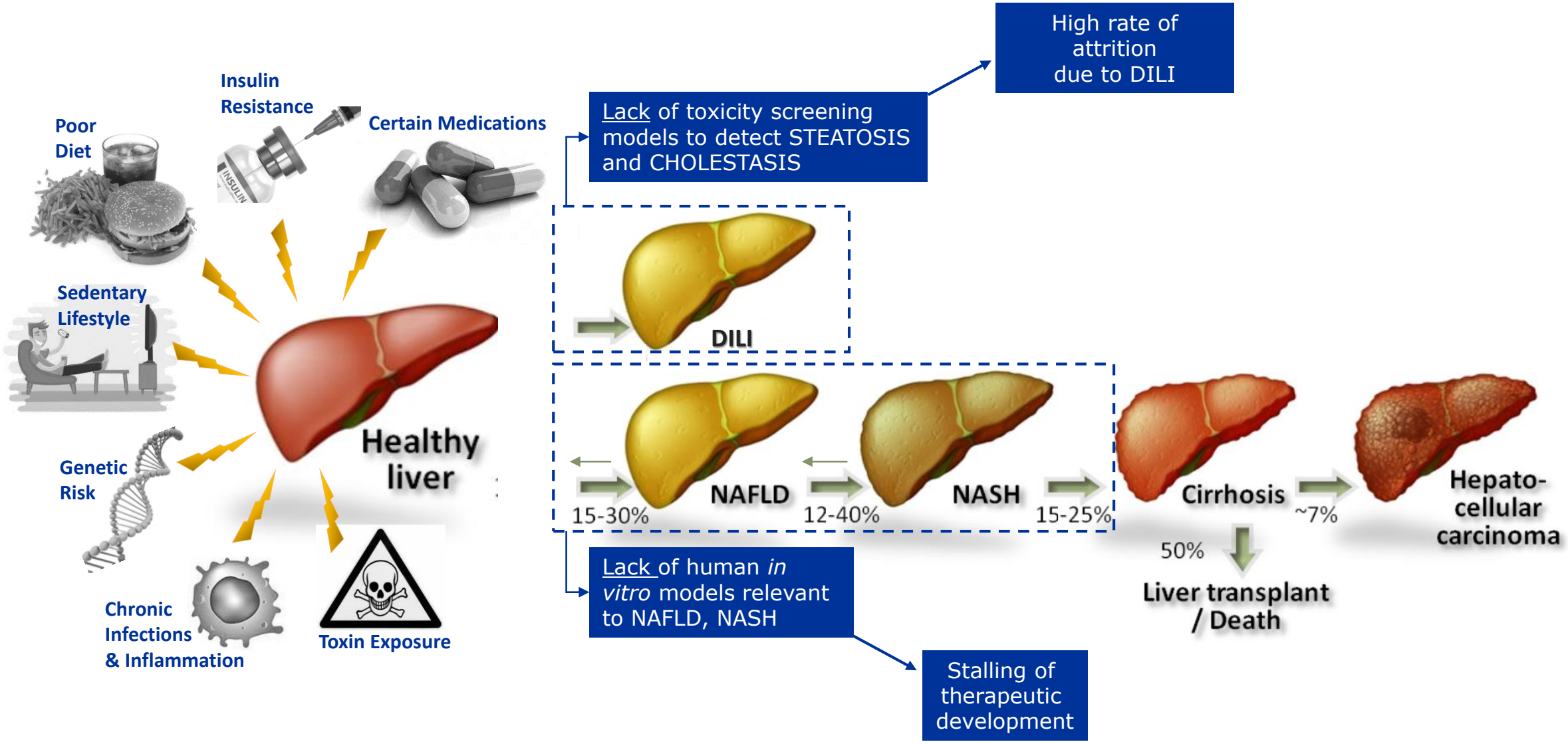
Business Developer: Dr Ruani Fernando

- **Developing robust and human-relevant liver-based *in vitro* models**
- **Identifying new drug targets and liver disease biomarkers**
- **Elucidating mechanisms that underlie liver diseases and toxicity**



VUB VRIJE UNIVERSITEIT BRUSSEL

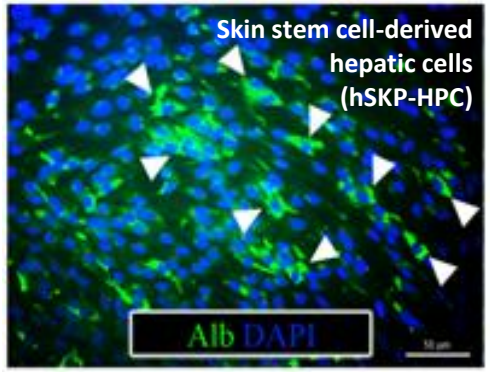
The Problem: Induced liver injury



Abbreviations: **DILI**, Drug Induced Liver Injury; **NAFLD**, Non-alcoholic fatty liver disease; **NASH**, Non-alcoholic steatohepatitis

Our Stem Cell Technology: hSKP-HPC

Patented hepatogenic differentiation protocol (EP 1824965, 2011)



	hSKP-HPC	Alternative hepatic cell models				
		Primary human hepatocytes	HepaRG®	HepG2	ESC derived hepatocyte -like cells	iPSC -derived hepatocyte -like cells
COMMERCIAL PARAMETERS						
Low cost to culture	*					
High-throughput compatibility	*					
Reproducibility	*					
Ethical considerations						
Accessibility						
Not reliant on liver tissue						
Cryopreservability	*					
Characterized multi-donor sources	*					
PERFORMANCE PARAMETERS						
Multipotent						
Metabolic competence	*					
Hepatic purity	*					
Non-tumour source						
Ease of culture	*					
Applicability for disease modelling	*					

KEY - : optimal | : sub-optimal | : low | : very low | : not applicable (NA) | * : optimization ongoing

hSKP-HPC compare favourably with current gold standard hepatic

hSKP-HPC are a human-relevant, *in vitro* hepatic cell model applicable for:

HEPATOTOXICITY SCREENING

DILI prediction model
- Steatosis
- Phospholipidosis
- Acute Liver Failure

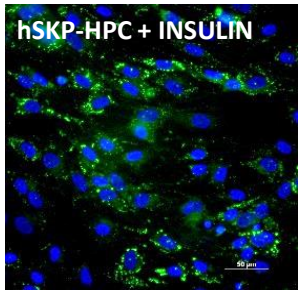
In vitro models of
Acute Liver Failure (ALF)
(Paracetamol exposure)

	hSKP-HPC	hHEP	HepaRG™	HepG2
Liver Failure (82 genes)	20%	11%	17%	-
Liver Proliferation (339 genes)	18%	9%	14%	2%
Liver Necrosis (583 genes)	11%	4%	9%	1%
Liver Damage (656 genes)	8%	6%	10%	1%

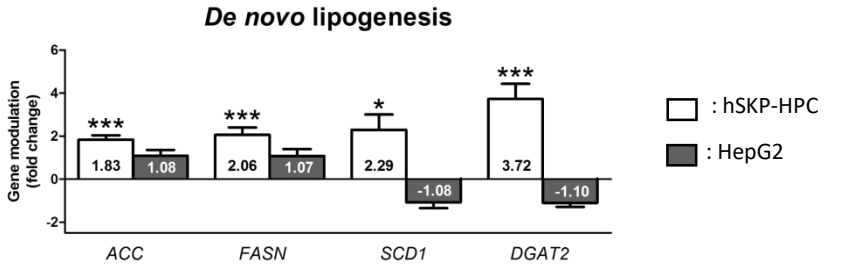
Pathway analysis of transcriptomics data

DE NOVO LIPOGENESIS (DNL) MODELLING

- Insulin & glucose driven DNL
- For non-alcoholic fatty liver disease (NAFLD) investigation & drug development

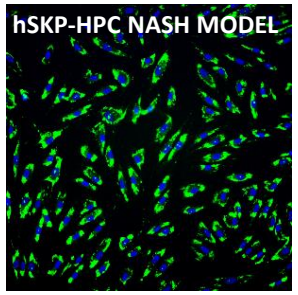


LipidTOX staining for neutral lipids (green) of hSKP-HPC (nuclei blue)

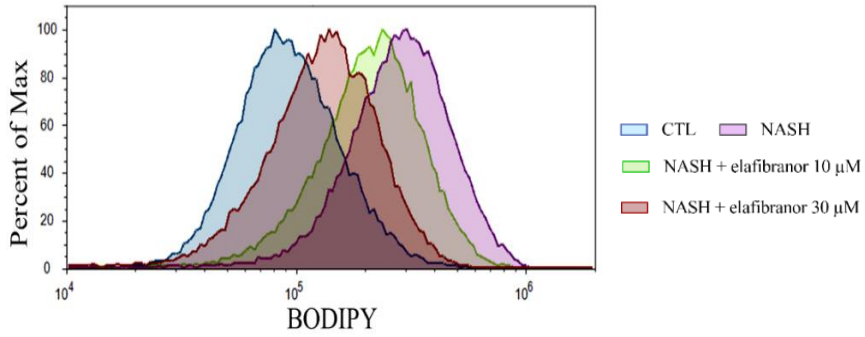


NASH MODELLING

- 'Multiple Hit' model
- Lipogenic & inflammatory triggers
- NASH specific endpoints
- For Anti-NASH drug discovery



BODIPY staining for neutral lipids (green) of hSKP-HPC (nuclei blue)



Pharmaceutical solid forms from screening to development

Prof. Tom Leyssens

Personal expertise

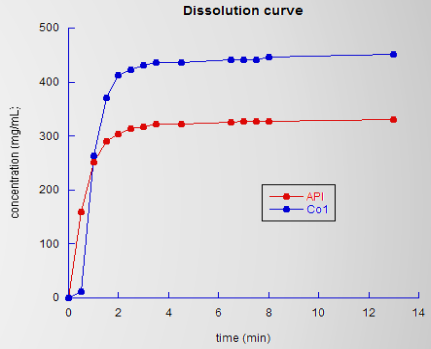
- **2007-2009 Automation Team Leader UCB**
  Crystallization process development
  Polymorphism, purity, PSD, …

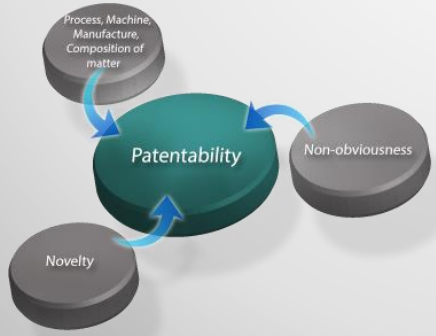
- **2009-… Professor UCL**
  Crystal engineering and crystallization

API solid form: why??

Processability

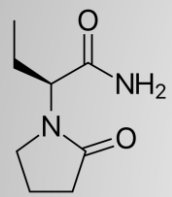
Solubility, dissolution, bioavailability



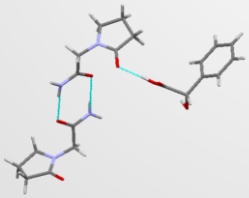


Patentability,
Drug repurposing,
Life cycle management

From screening to development



→ Polymorphs
→ Salts
→ Cocrystals



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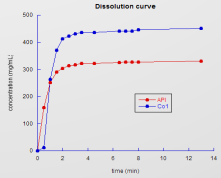


Success stories

Multiple contracts for **pharmaceutical** and agro-chemical **industries** (Belgium, US).

→ Polymorph screening (Patent)

→ Cocrystal screening and development (Patent)
- → Life cycle managament/drug repurposing

UCL and you

- Drug repurposing/ Life cycle management
- Solid state screening
- Analysis and property control of solid forms
- Crystallization development and optimization

www.uclouvain.be/leyssens-group
f.goossens@sopartec.com

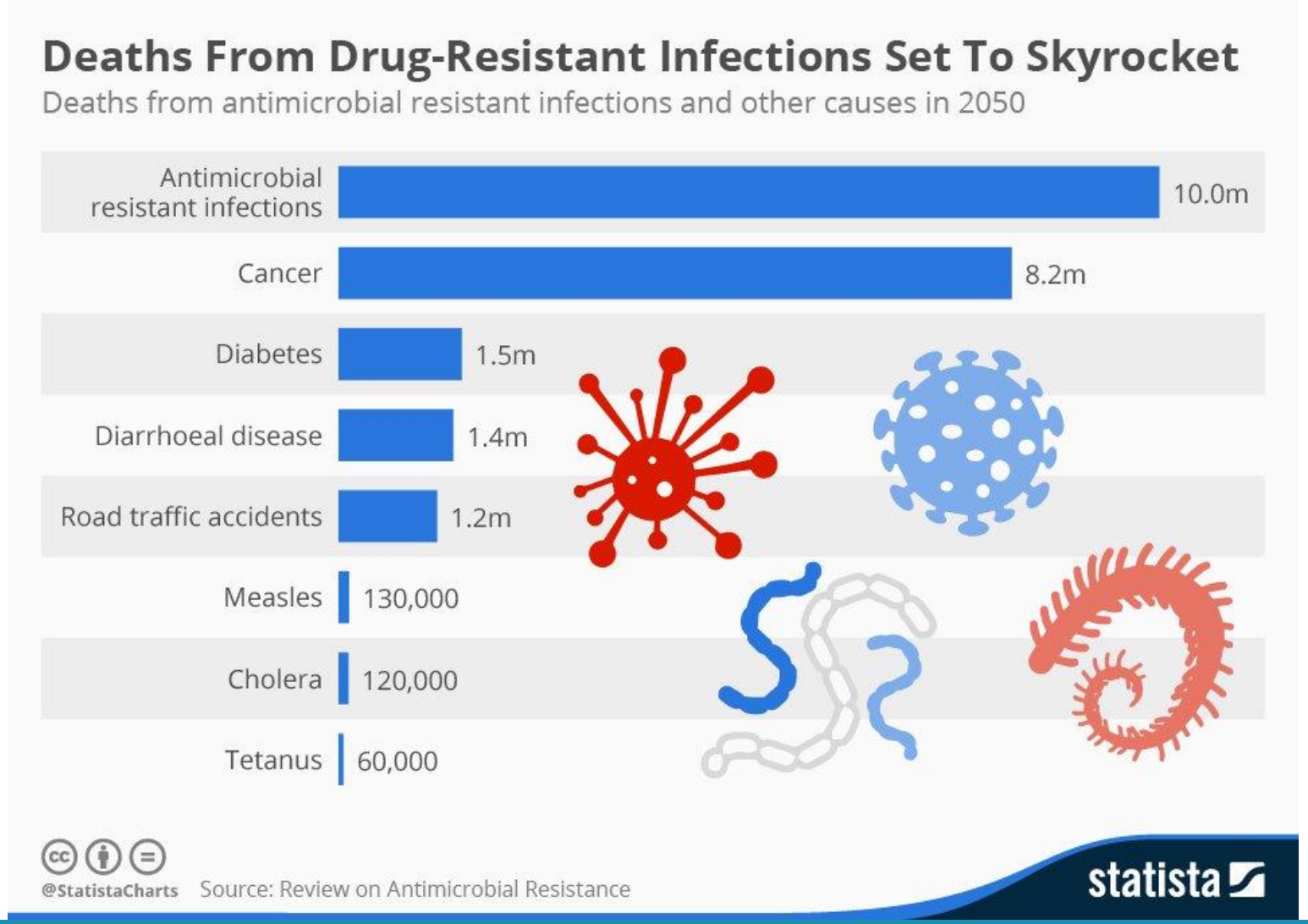
KU LEUVEN

Antibiotic Mode of Action

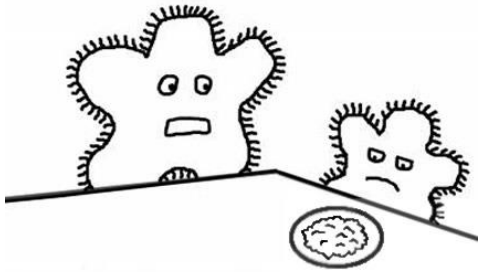
Dr. Bart Landuyt

Functional Genomics & Proteomics

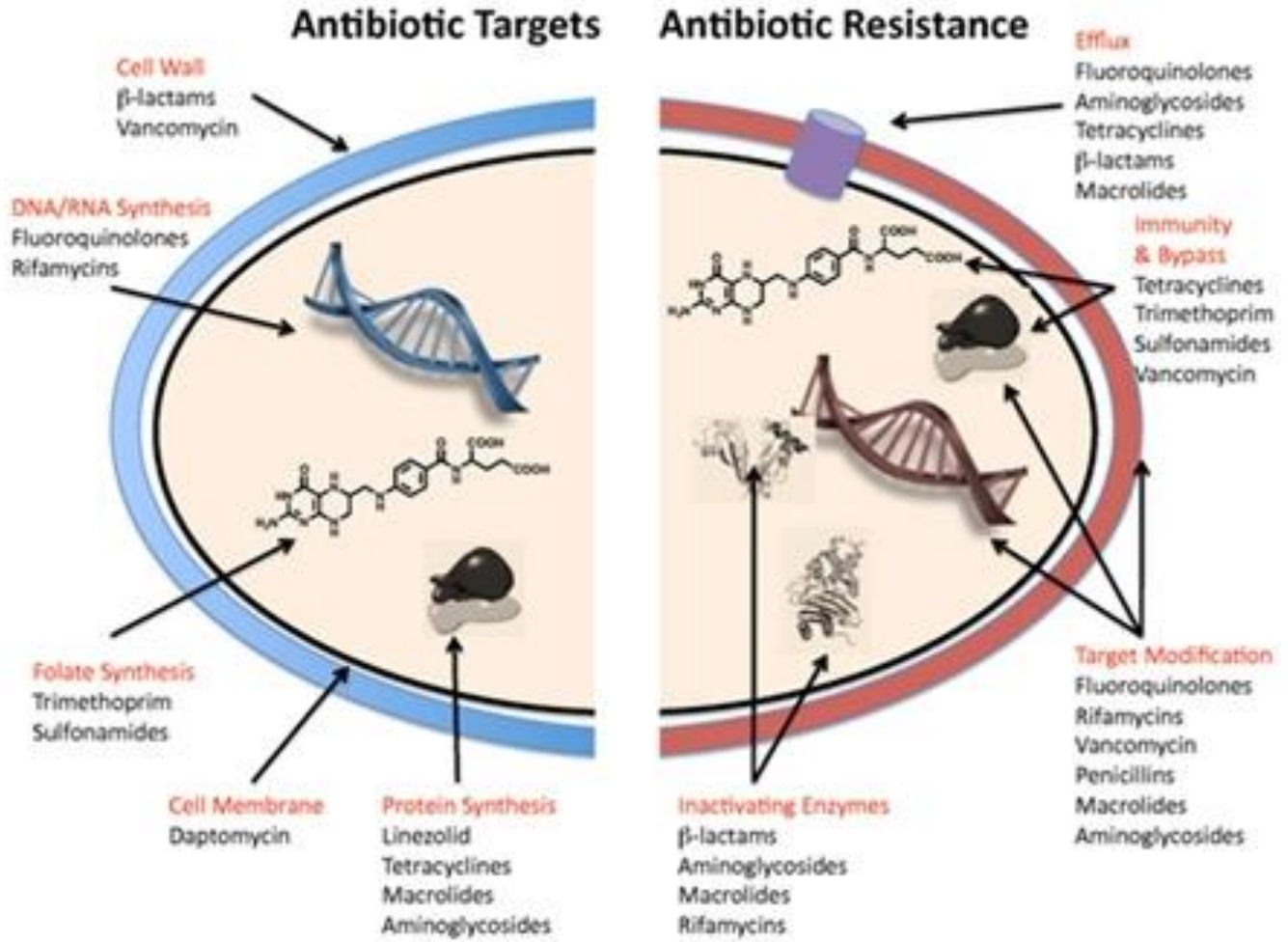
Antiobiotic resistance



Antibiotic resistance



"But Timmy, you have to eat your antibiotics or you'll never become a big strong bacteria."



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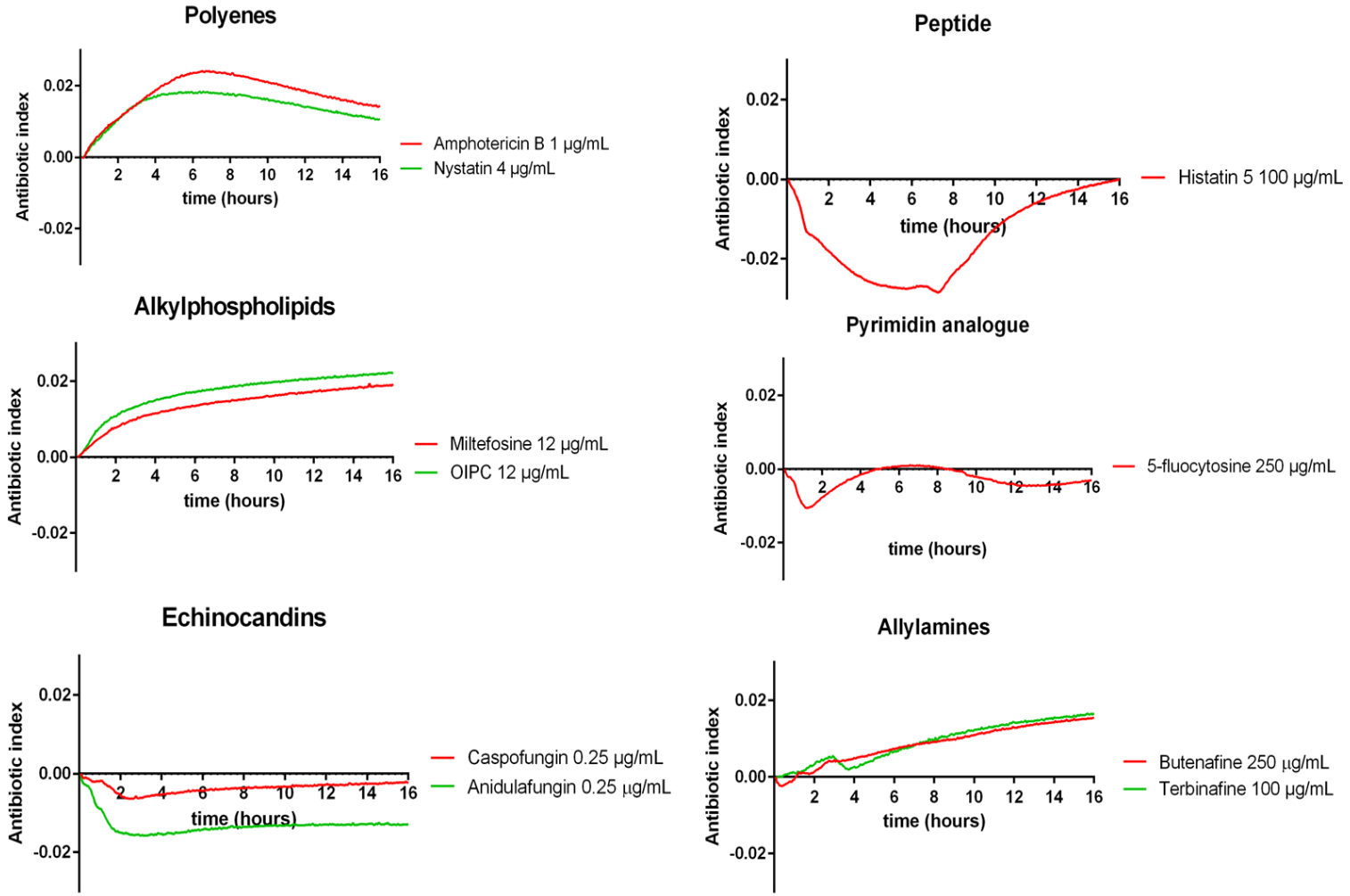
Antibiotic index antifungals



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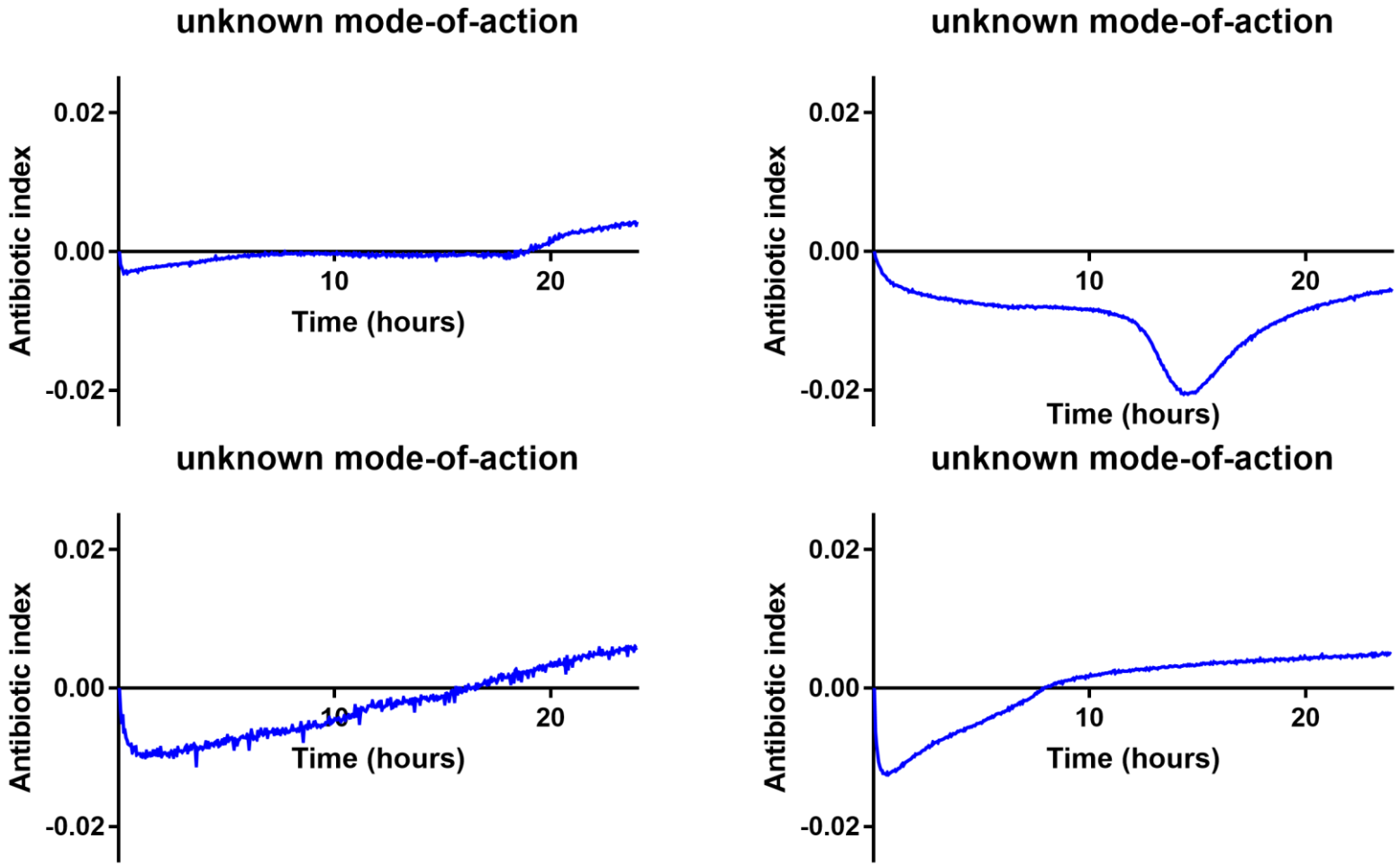
De-replication hits anti-fungals



Contact

bart.landuyt@kuleuven.be

Functional Genomics & Proteomics

Naamsestraat 59

3000 Leuven

KU LEUVEN

Molecular Medicine @KU Leuven

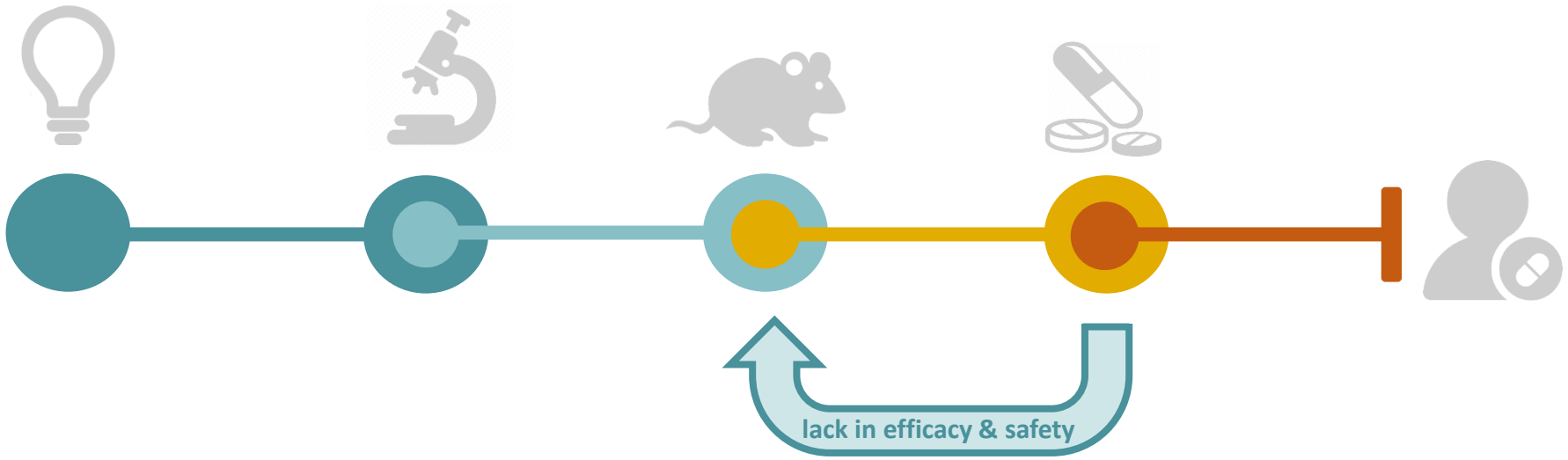
Organoids as alternative models of human disease

frauke.christ@kuleuven.be
marianne.carlon@kuleuven.be

Laboratory for molecular virology and drug discovery

KU LEUVEN

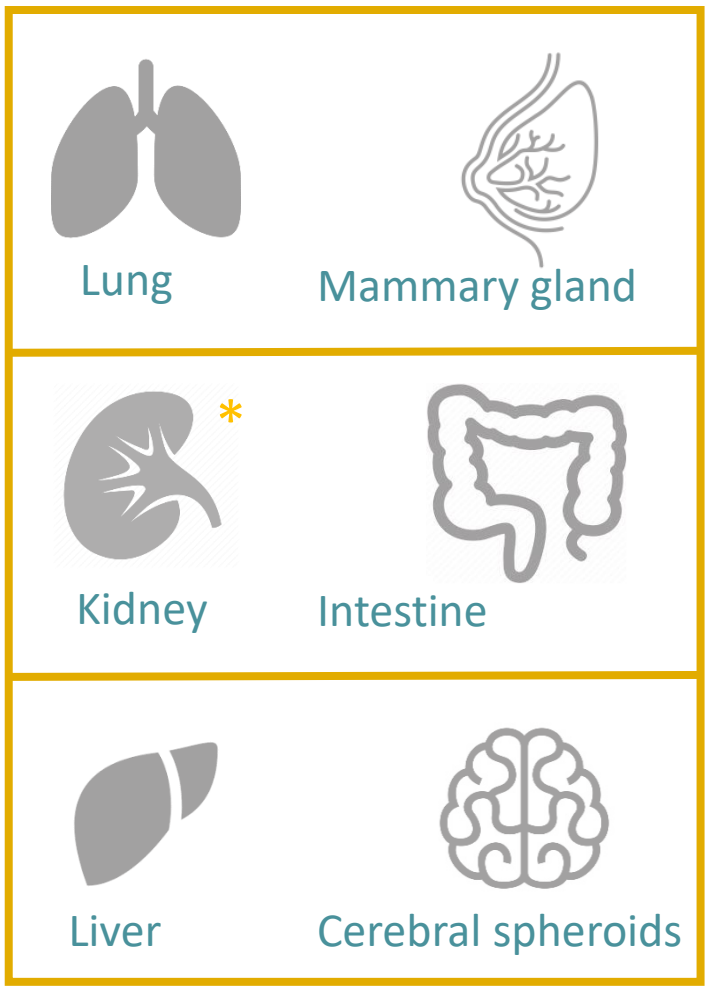
Humanizing the drug discovery pipeline

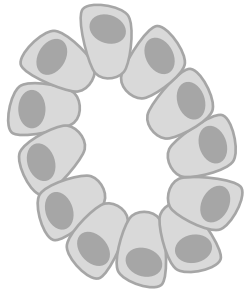


Animal models recapitulate diseases genetically but (can) fail to demonstrate the human phenotype leading to poor translation from preclinical to clinical development

Laboratory for
molecular virology
and drug discovery

Organoids in human disease





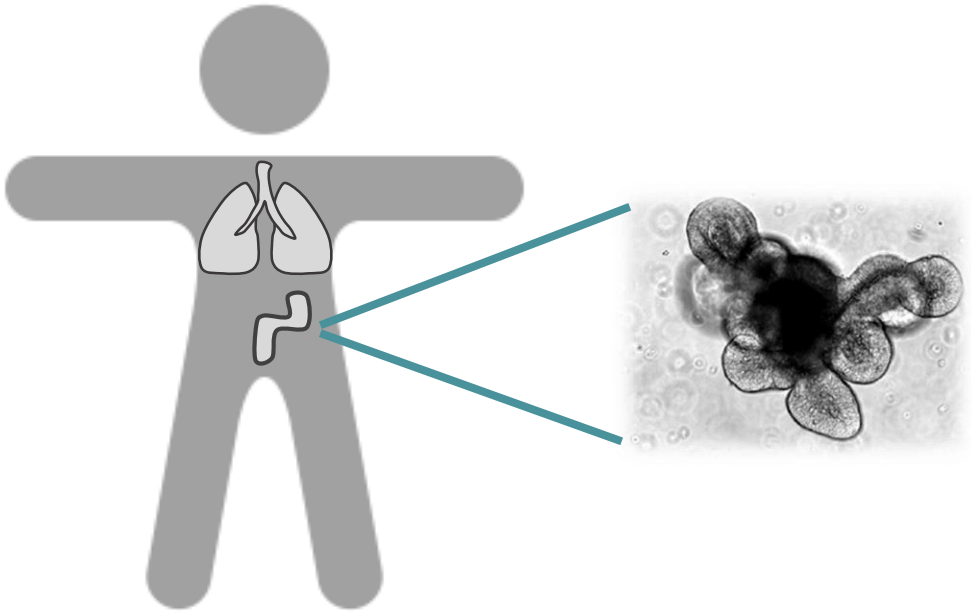
Model systems for:

- Target validation
- Drug ‘screening’ and repurposing
- Personalized medicine (prediction of therapeutic benefit)

*Prof. Rik Gijsbers

Laboratory for
molecular virology
and drug discovery

Organoids @ KUL



Application gut organoids

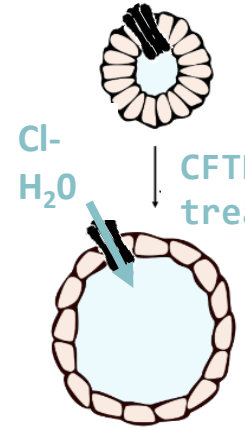
- Inflammatory bowel disease (MD PhD Marc Ferrante)
- Cystic Fibrosis (MD PhD Christiane De Boeck, PhD Marianne Carlon)
- Colon cancer

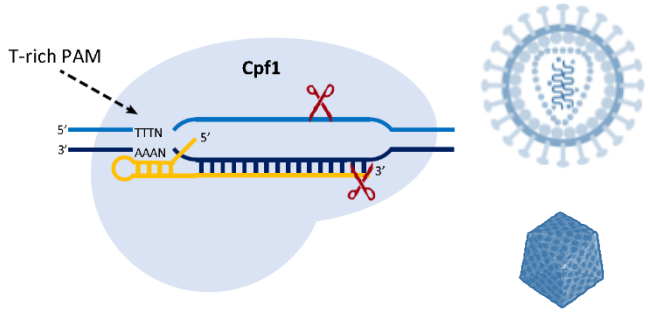
Inflammatory bowl disease	Cystic fibrosis
>200 patient samples	>300 patient samples
microbiota studies & inflammation	Repurposing & drug discovery & gene therapy
disease driving mechanisms	disease driving mechanisms

Laboratory for
molecular virology
and drug discovery

Organoid technology@KUL (CF)

Organoid swelling



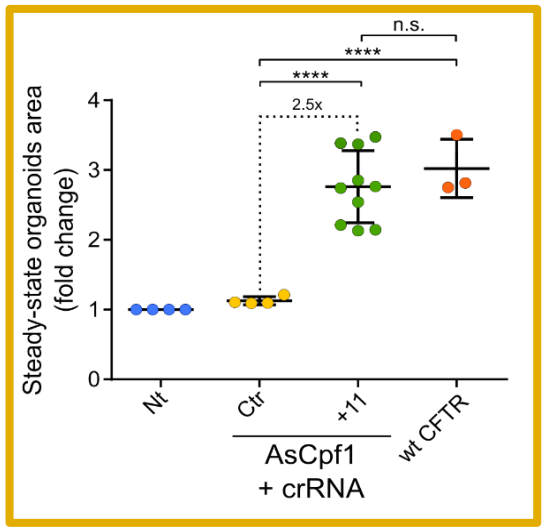


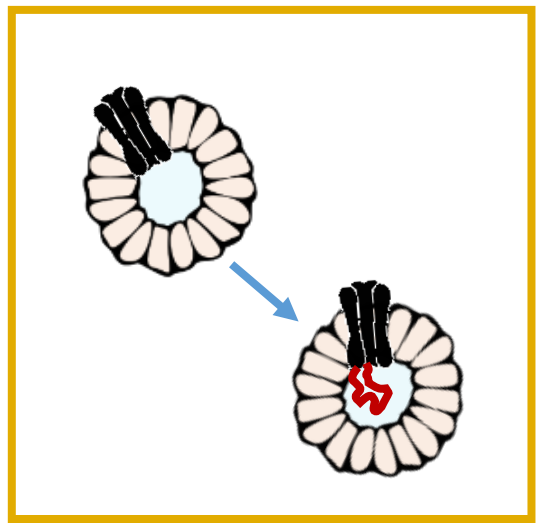
Correction of splicing mutations (gene editing)

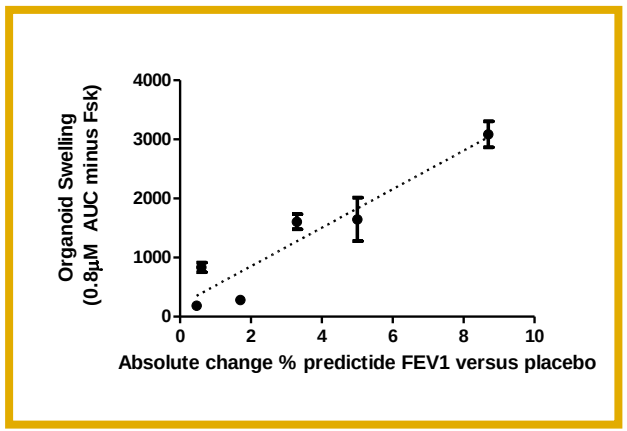
Endogenous tagging in organoids for assay develoment

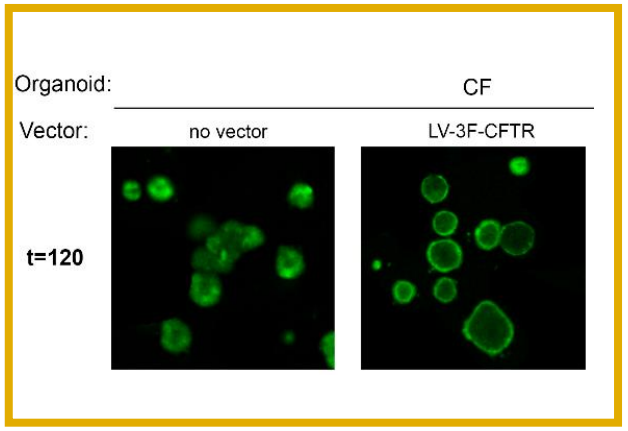
Drug screening

Gene therapy

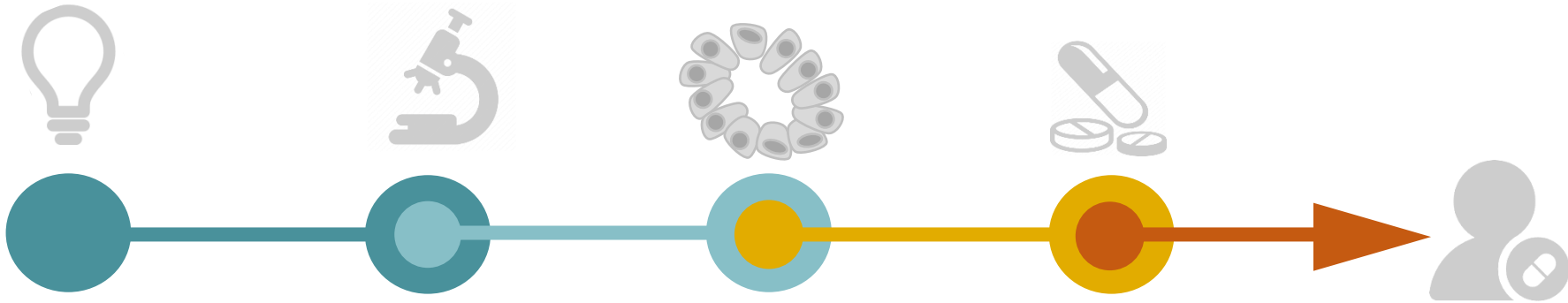








Vidovic*, Carlon* et al., AJRCCM, 2016
Maule et al., Nat Commun. 2019 (final revision)



frauke.christ@kuleuven.be

marianne.carlon@kuleuven.be

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Immune biomarkers for diagnosis and therapy response in rheumatoid arthritis

An Voets, PhD – business developer Uhasselt - BIOMED

BIOMED
BIOMEDISCH
ONDERZOEKSINSTITUUT

UHASSELT

RHEUMATOID ARTHRITIS (RA)

RA = common autoimmune disease, characterized by chronic inflammation of synovial joints, often resulting in joint destruction

RA diagnosis:

- 1 out of 3 patients negative blood test for current diagnostic biomarkers (RF and ACPA)
- Early diagnosis results in better outcome (less joint damage and disability)

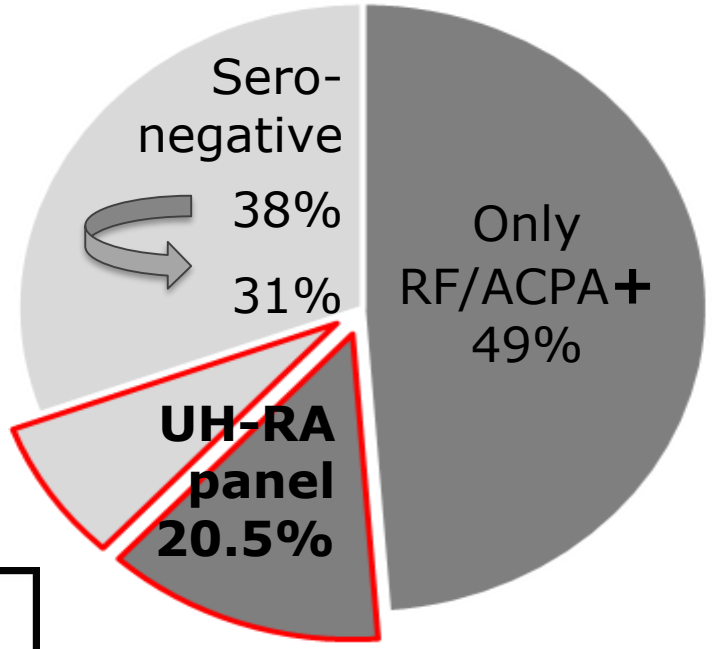
Additional unmet need:

Biomarkers that predict or rapidly identify treatment response

COMPELLING RESULTS

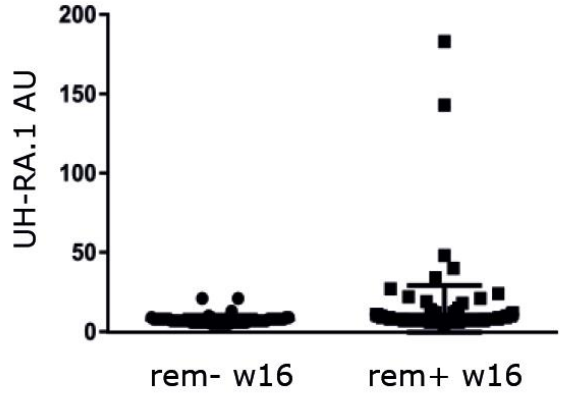
2 plasma biomarkers for diagnosis, prognosis and therapy response

Diagnostic potential
Combined with RF & ACPA the UH-RA panel could reduce the serological gap from 38 to 31%



Prognostic and theranostic potential
Anti-UH-RA.21 antibody levels
- associated with inflammation and erosions
- decrease in titers in patients on DMARD

Baseline anti-UH-RA.1 antibody levels associated with remission at week 16 (Mann Whitney p value 0.0011):



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KEY FEATURES

ADVANTAGES

- Diagnostic potential validated in 3 independent cohorts (n = 1114)
- High-throughput peptide ELISA assay available
- Diagnose earlier – treat sooner
- Ability to monitor treatment efficacy

MARKET POTENTIAL

- 1% of the population affected by RA
- 128 billion USD annual expenses in medical care
- 5-10 new cases per 10,000 adults can be diagnosed better using our biomarkers
- Companion diagnostics

OPPORTUNITY

- Patents that are available for licensing:
  EP2307451B1
  US9683031B2
- Open for collaboration on monitoring treatment efficacy

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Contact: An Voets, an.voets@uhasselt.be - +32 11 269323

Blood Flow Simulating Device

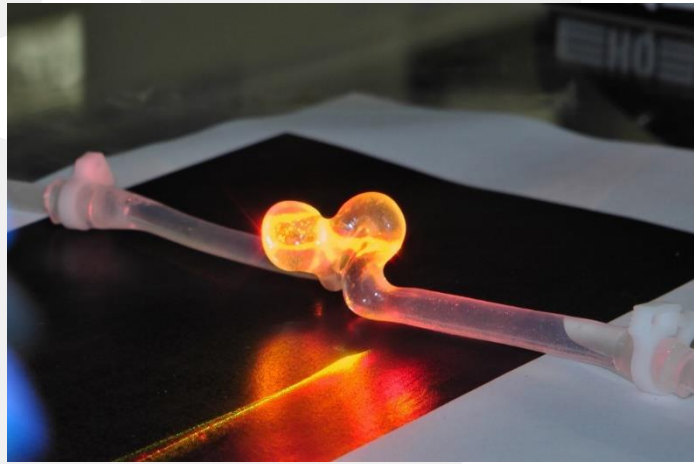
In vitro testbed, Blood flow simulator, Artificial cardiovascular technology, Cardiovascular medical devices

- Laboratory
  - UMONS, Fluids-Machines Department
  - ULB, Experimental Medicine Laboratory
- Team expertise
  - Numerical simulation of biological fluids
  - Study of cardio-vascular diseases mechanisms, e.g. atheroscleroris

Blood Flow Simulating Device

- State of the art
  - **Cardiovascular diseases** among the top causes of mortality and morbidity in the world
  - After detection of an unruptured aneurysm, **physicians have to rely entirely in their experience** and reported cases to evaluate the chances of the aneurysm to rupture and what type of therapeutic approach to choose.
  - **Should surgery be undertaken?**
  - **Should a vascular prosthesis be placed?**

- Technology description
  - **In-vitro device** reproducing cardiovascular hemodynamic conditions
  - **Specific shapes of aneurysm** (based in a patient's real case) can be modelized in silicon and placed into the device.
  - **TRL 6** : a functional prototype system is being tested in a simulated environment.



Blood Flow Simulating Device

- Key advantages
  - Control any real in vivo pulsatile flow rate
  - Not invasive for the patient
  - Compatible to sterile conditions
  - Possibility to use whole blood
  - Fully automatic and easy to use controls

- Commercial Interest
  - **Support in aneurysm surgery decision-making** by analyzing in-vitro a silicon model of the patient's aneurysm, placed in realistic pulsatile conditions.
  - **Testing of vascular prostheses** in a realistic pulsatile in-vitro environment. This may help designers and producers of vascular prostheses design and test their products before having to run tests in animal subjects.
  - **Training device for surgeons** in the placement of vascular prostheses in a simulated in-vivo conditions.

IP Status & Contact

- Intellectual Property :
  - **European patent granted** (EP2779144) and validated in FR, BE, UK, GE and CH.
  - Title: device for simulating blood flow.
  - Priority date: March 12th 2013

Prof. Grégory Coussement (UMONS, Fluids-Machines Department), Head of Department
Gregory.COUSSEMENT@umons.ac.be

Prof. Karim Zouaoui-Boudjeltia
(ULB, Experimental Medicine Laboratory), Head of Department
karim.zouaoui.boudjeltia@ulb.ac.be

Contact KTO : *Dr. Marlène Genlain*
Scientific advisor Life Sciences

Marlene.GENLAIN@umons.ac.be
+32 65 374 778

OASIS

Omnibus Animalibus Studia Sanitatis

narilis

Namur Research Institute for Life Sciences

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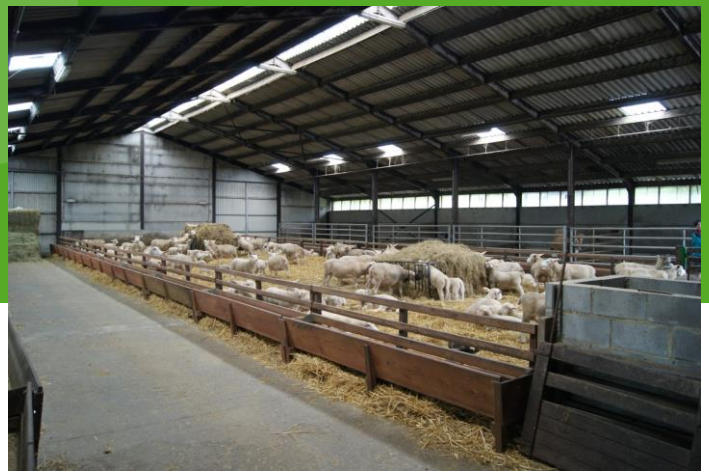
Ovine Model



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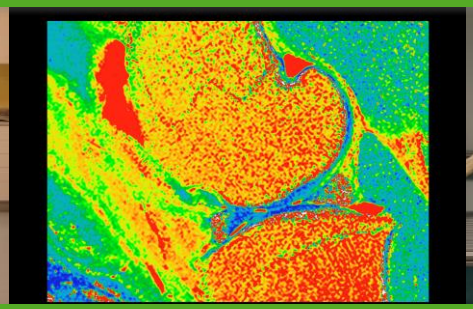


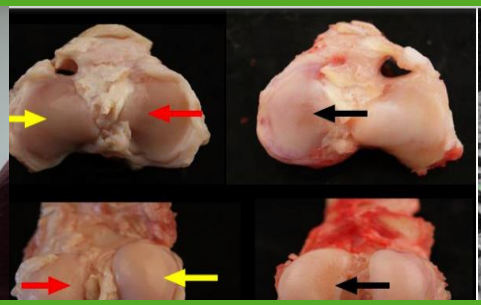
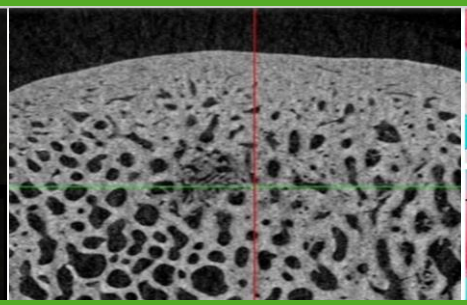


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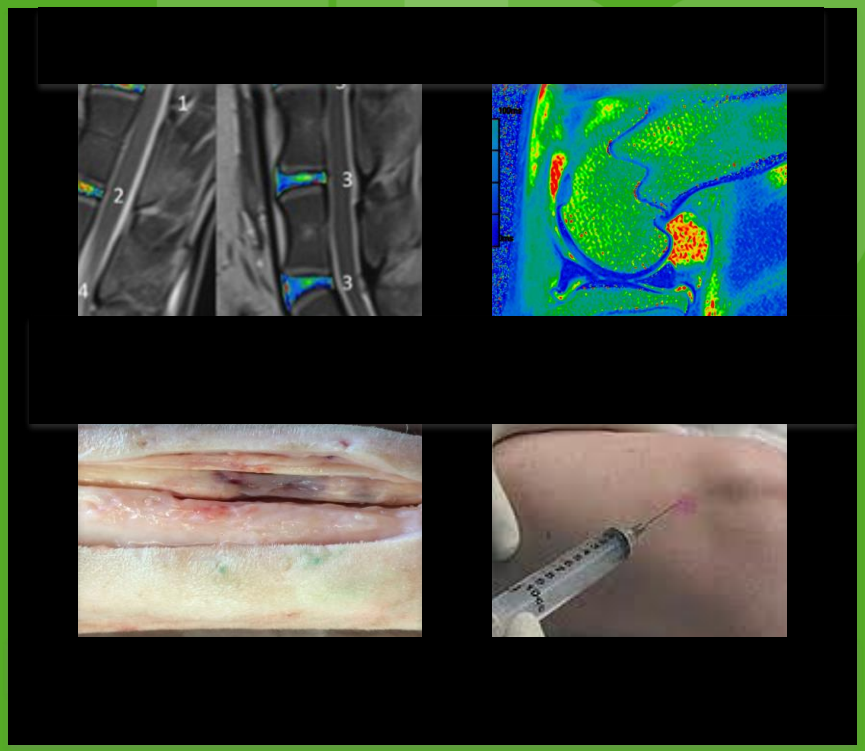
Examples of research questions

- A new model of osteoarthritis (OA) assessed by compositionnal imaging
- A model for intervertebral disc disease
- A model for novel tendon repair strategy
- New viscosupplement for OA
- Dental pulp stem cells for OA and tendonitis
- New scaffolds and umbilical cord stem cells for cartilage repair
- Stem cell therapy in an ovine model of critical bone defect
- Effects of triamcinolone hexacetonide on articular cartilage
- …



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VRIJE UNIVERSITEIT BRUSSEL

µFlow Cell
BiR&D
19/03/2019

ir. Filip Legein, Valorization Manager

µFlow Cell

Diabetes Research Center (DRC)
Prof. Karine Hellemans
5 Researchers
GMP Cleanroom
Animalarium
→ CenTR

Bioengineering Sciences (DBIT)
Prof. Wim De Malsche
15 Researchers
ERC Starting Grant
Microfabrication Platform

µFlow Cell

Design Microfluidic Solutions

Fabricate Microfluidic Devices

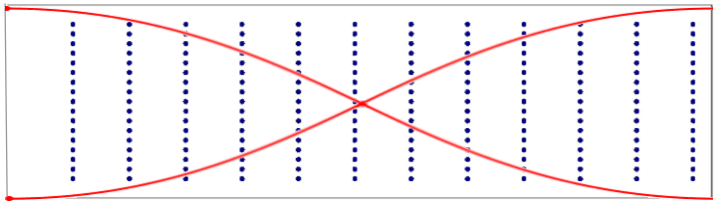
Engineer Functional Microparticles

Fundamental Research + Instruments

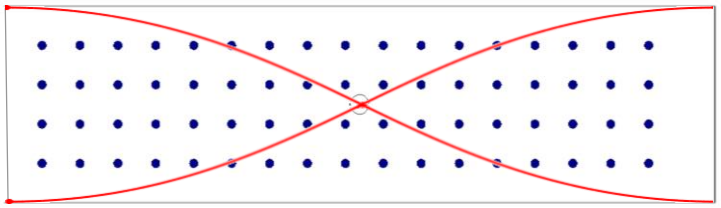
RL	TRL 1-2	TRL 3-4	TRL 5-7
1	Vortex flows/mixing	Vortex flows/mixing	
2	Particle/droplet/cell manipulation	Particle/droplet/cell manipulation	
3	Tuning surface functionalities	Tuning surface functionalities	
4		3D imaging	3D imaging
5		Advanced flow tools for precipitation	Advanced flow tools for precipitation

- New technological concepts
- Novel instruments to study these concepts

- Polystyrene particles = 0,5 µm

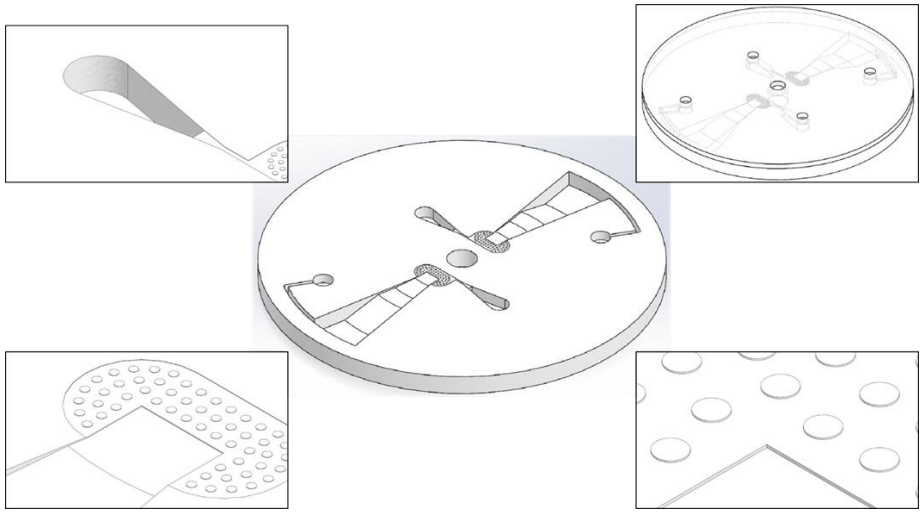


- Polystyrene particles = 5,0 µm



Advanced Fabrication + Devices

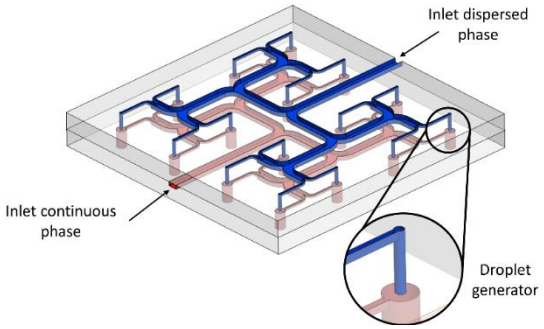
RL	TRL 1-2	TRL 3-4	TRL 5-7
6	Advanced fabrication processes	Advanced fabrication processes	Advanced fabrication processes
7	Advanced separations	Advanced separations	Advanced separations
8		Handling biological matrices	Handling biological matrices
9		3D emulsifier	3D emulsifier

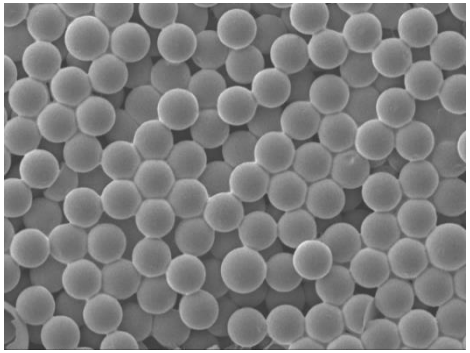


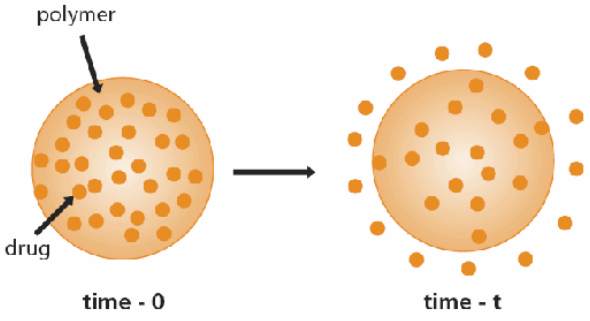
- In-house micro-fabrication platform
- Design, modelling and fabrication of novel devices

Functional Microparticles

RL	TRL 1-2	TRL 3-4	TRL 5-7
10		Drug-loaded microparticles	Drug-loaded microparticles







- Bottom-up engineering of particle and fabrication strategy
- In vitro and in vivo validation
- GMP manufacturing