

AMSTERDAM


COPENHAGEN

UNIVERSITY OF COPENHAGEN

Faculty of Health and Medical Sciences

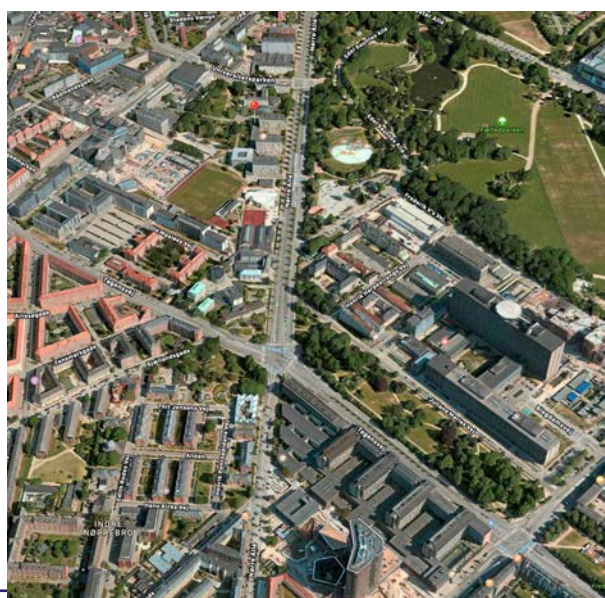
School of Pharmaceutical Sciences
Dept. of Pharmacy & Dept. of Drug Design and Pharmacology

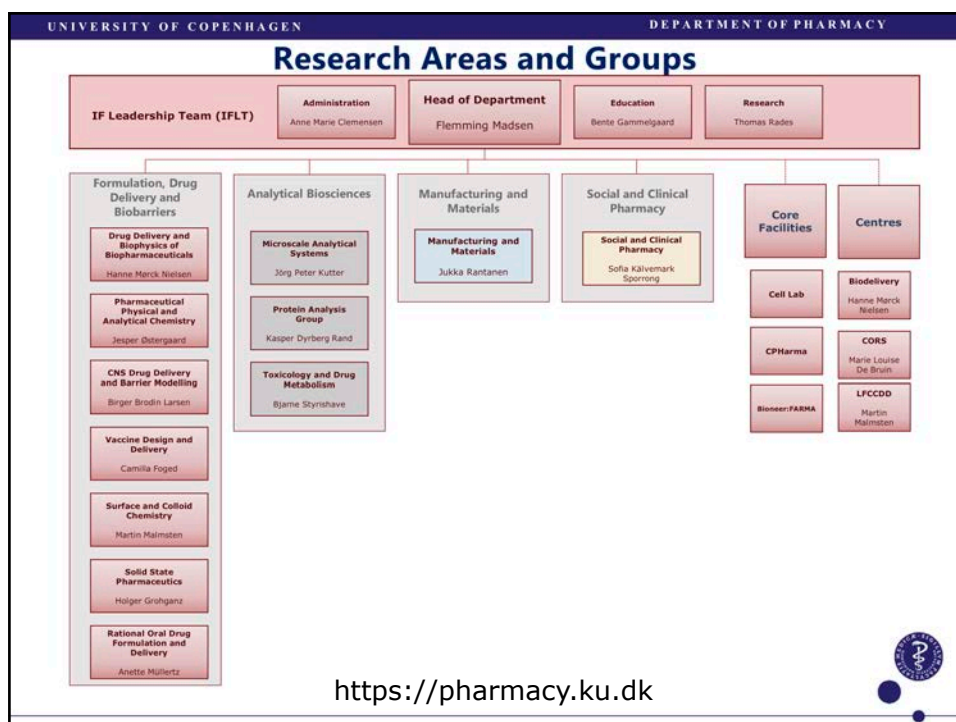
Faculty of Health and Medical Sciences
University of Copenhagen



UNIVERSITY OF COPENHAGEN

The North Campus – a biomedical hub





LEO Foundation Center for Cutaneous Drug Delivery



<https://pharmacy.ku.dk/research/lfccdd>



VISION

Within a 10-year period, LFCCDD should be recognized as an international excellence center within cutaneous delivery

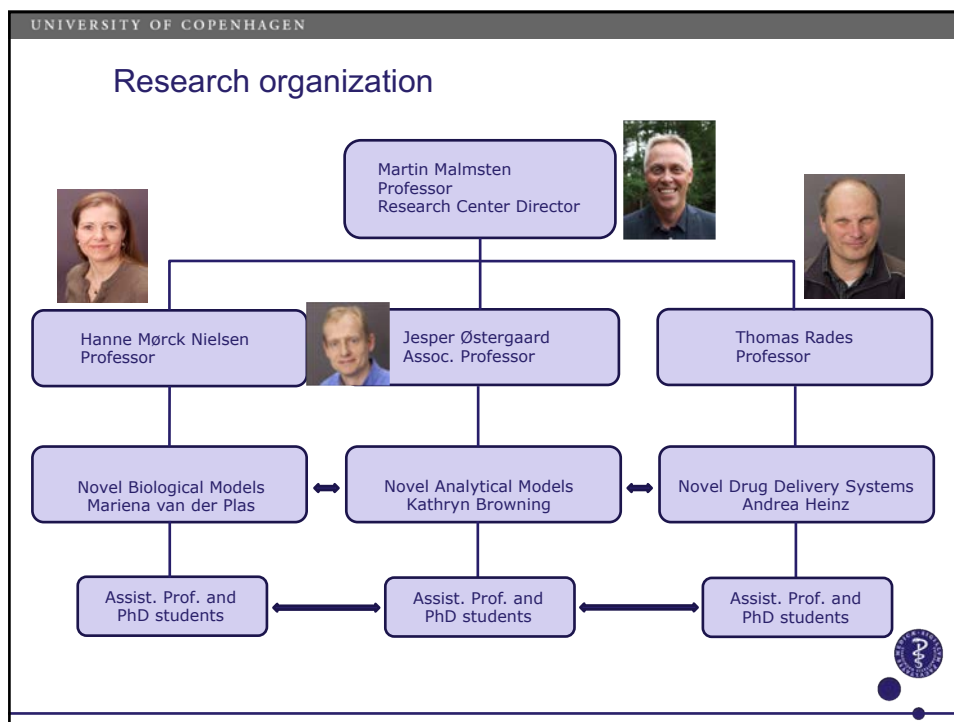
Scientific platform

Built on integrative physicochemical approaches, including pharmaceuticals, as well as novel opportunities in nanotechnology, advanced analytical methodologies, and biological models.

Positioning

- Built on a 10-year funding base (LEO Foundation and University of Copenhagen).





UNIVERSITY OF COPENHAGEN

Center for Biopharmaceuticals and Biobarriers in Drug Delivery

The Vision and Mission

Our vision is to establish a world-class center for oral drug delivery of biopharmaceuticals. We will study how to overcome biological barriers by formulation design through interdisciplinary research collaborations.

The mission is to provide an improved fundamental understanding of novel methods pursuing oral delivery of biopharmaceuticals through tailoring of drug delivery systems and advanced assessment tools.

BioDelivery Center

Hanne Mørck Nielsen
Project leader, PI

Urs O. Häfeli
PI

Knud J. Jensen
PI, Dept. Chem., UCPH

Jesper Glückstad
PI, Dept. Photonics. Eng., DTU

novo nordisk fonden

UNIVERSITY OF COPENHAGEN

The Copenhagen Centre for Regulatory Science (CORS)

About the Centre

The Vision

The Copenhagen Centre for Regulatory Science (CORS) aims at being the international partner for academic leadership in regulatory science, research and education and to participate in building the regulatory framework that will make innovative medicinal products available to patients.

The Mission

The Copenhagen Centre for Regulatory Science will become a powerful Centre for Regulatory Science, influencing and conducting regulatory research and education in an international perspective. The research and education of the Centre makes a clear mark on regulatory decision-making – to the benefit of stakeholders such as patients, authorities, payers and industry.

Partners

University of Copenhagen Faculty of Health and Medical Sciences: Dept. of Pharmacy Dept. of Drug Design and Pharmacology Dept. of Clinical Medicine Dept. of Public Health Biopeople	Faculty of Law: Centre for Information and Innovation Law Faculty of Humanities: Dept. of Media, Cognition and Communication Faculty of Social Sciences	Pharmaceutical Industry Novo Nordisk A/S H. Lundbeck A/S Ferring Pharmaceuticals LEO Pharma A/S Authorities Danish Medicines Agency
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<https://pharmacy.ku.dk/research/cors>

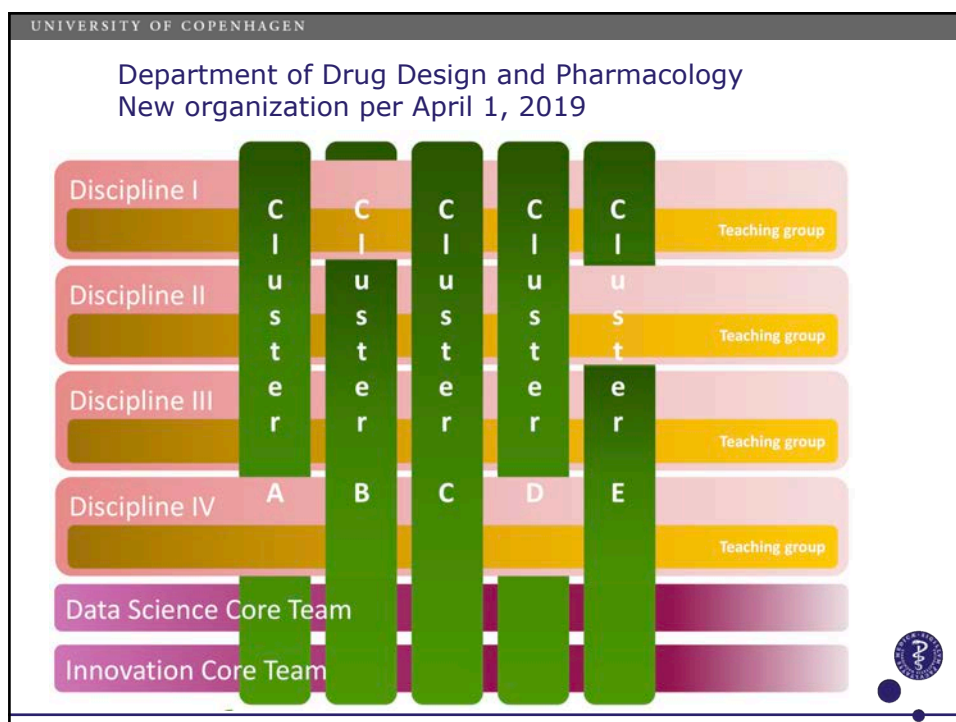
Marie Louise (Marieke) De Bruin
 Professor
 marieke.debruin@sund.ku.dk
 + 45 35 33 08 18

Christine Erikstrup Hallgreen
 Assistant Professor
 christine.hallgreen@sund.ku.dk
 +45 35 33 70 79

Pharmacovigilance group
Head of Unit
Morten Andersen
 Professor
































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
Disciplines














Translational Pharmacology
































Fælles Faciliteter








































Molecular and Cellular Pharmacology






























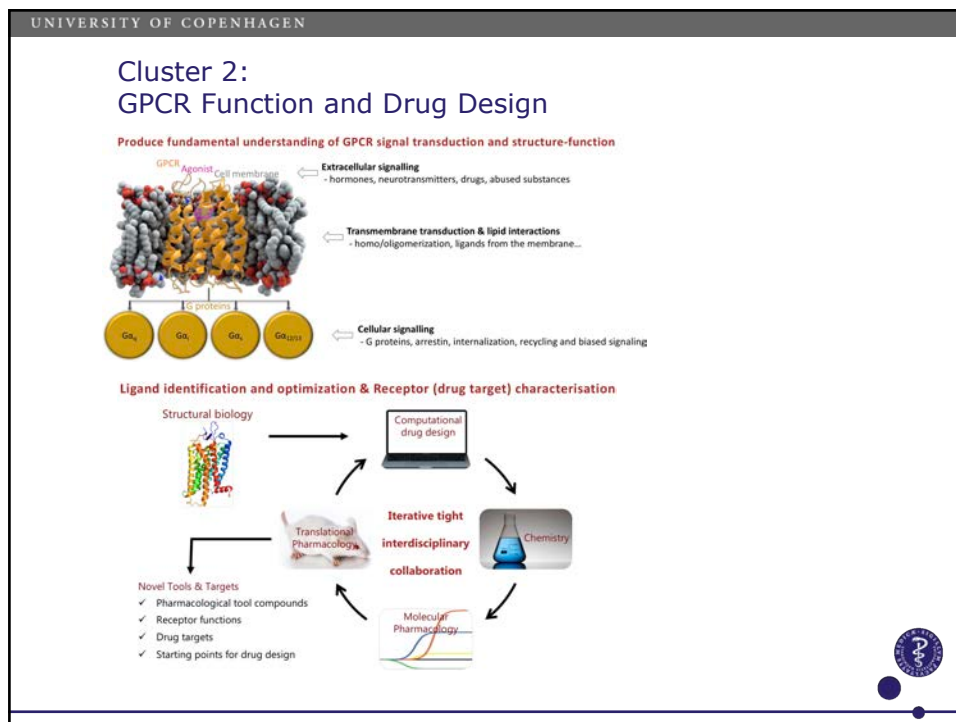
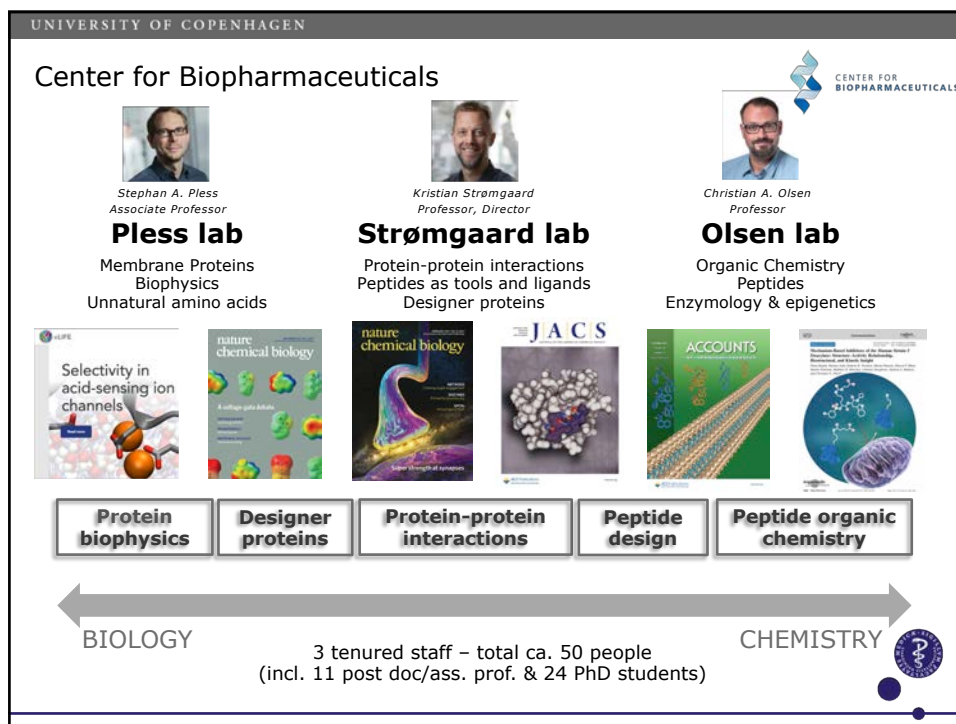






Medicinal Chemistry

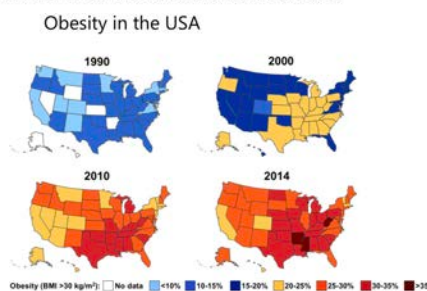
Peptides and Proteins



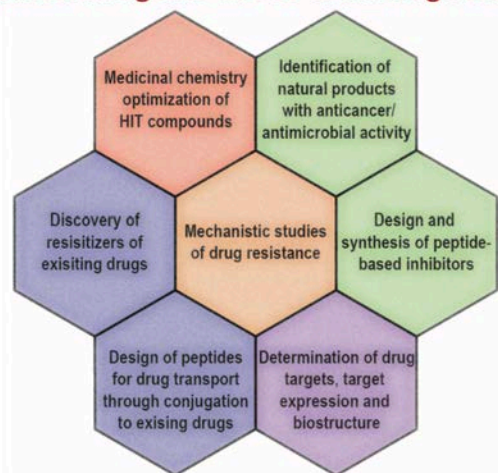
Cluster 3: Metabolism and Inflammation

- Create an environment for cutting-edge research on metabolism & inflammation
- Facilitate interdisciplinary collaborations between complementary research groups
- Contribute high-impact research to solve critical needs
 - Investigate biochemical processes
 - Identify and validate new targets
 - Provide tool compounds
 - Facilitate drug discovery



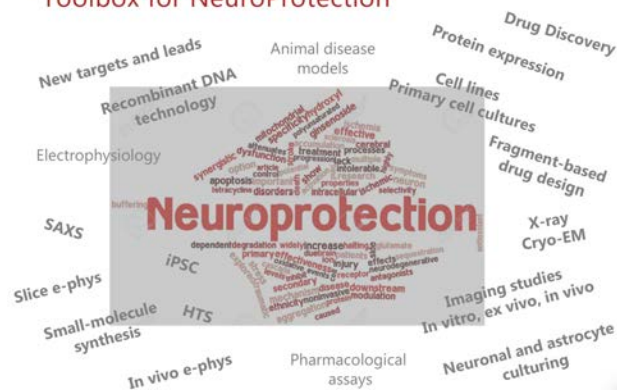
Cluster 4: Cancer and infectious diseases

Addressing the unmet need for novel anticancer and antibacterial agents due to multidrug resistance.



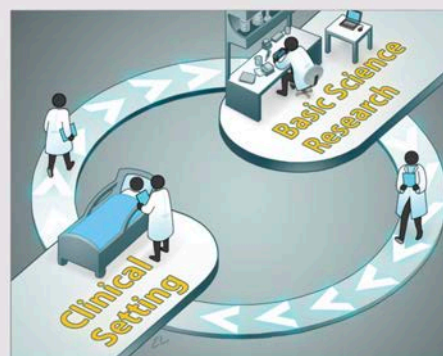
MISSION:

Toolbox for NeuroProtection



To investigate and modulate neurotransmission in cognition, emotion and pain.

- Identify and explore new putative therapeutic targets involved in **NiCEP**
- Identify and develop new assays to explore new targets
- Identify new chemical entities (NCEs) with therapeutic potential
- Employ and optimize *in vivo* models to investigate the therapeutic potential of NCEs
- Establish platforms for translation to the clinic



Cluster 7: Personalized Medicine

“Bridging Molecules and Patients”

- Pharmacoepidemiology
- Population PK/PD modeling
- Clinical phenotyping
- Patient stratifications
- Patient-relevant disease models
- Big data and machine learning
- Omics healthcare data integration
- Molecular mechanistic profiling
- Computational & systems biology
- Chemoinformatics



HELSINKI



UNIVERSITY OF HELSINKI

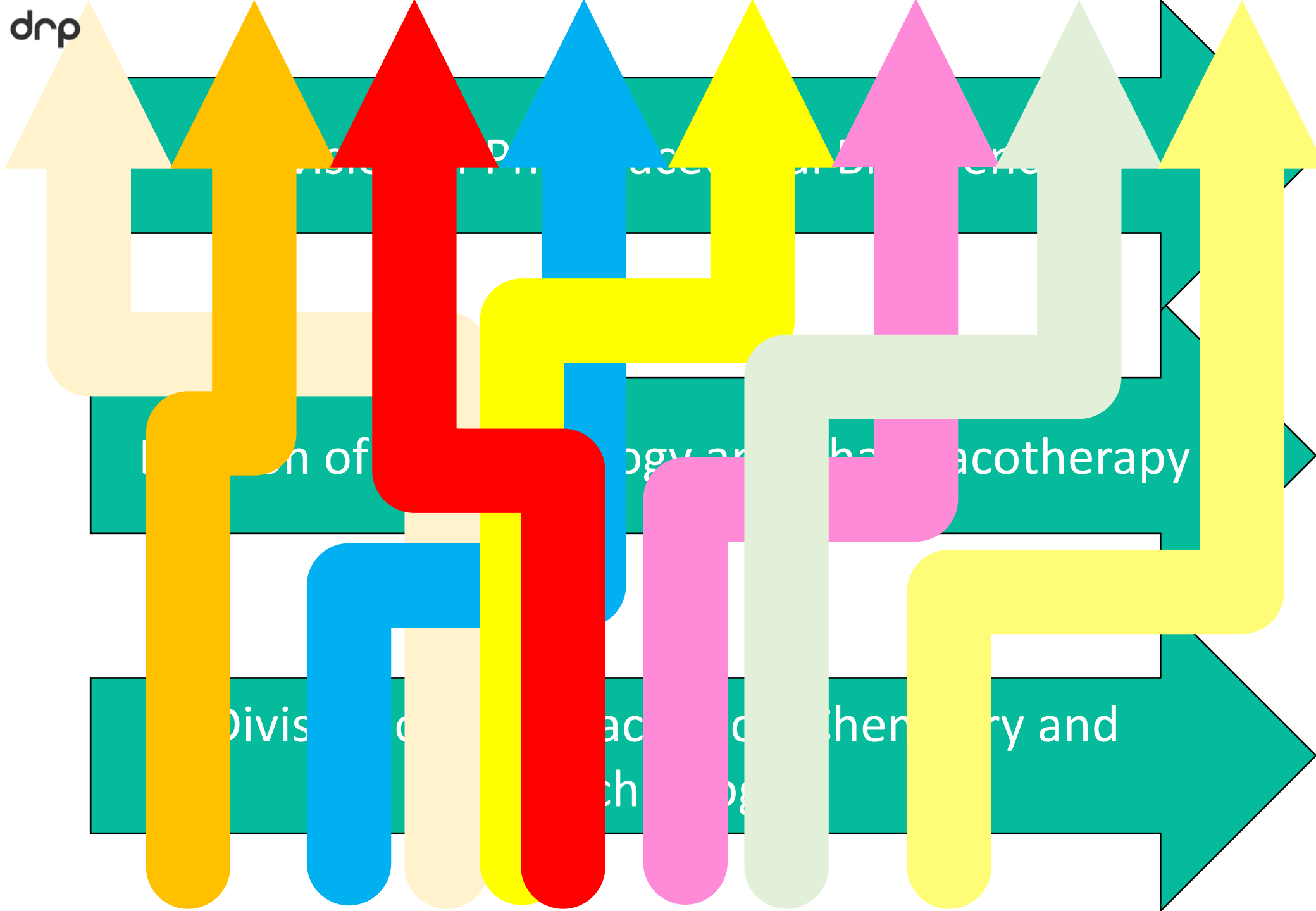
FACULTY OF PHARMACY

drp

DRUG RESEARCH PROGRAM

Vincenzo Cerullo, PhD
Head of Drug Research Program
Associate professor - tenure-track
Group leader at IVTLab and Co-founder of VALO therapeutics
HiLIFE fellow, University of Helsinki





DRUG RESEARCH PROGRAM

- 9 Units
- 35 research groups (220 researchers)
- 30 million euros
- 2000 publications
- 30 patents
- 120 PhD dissertations



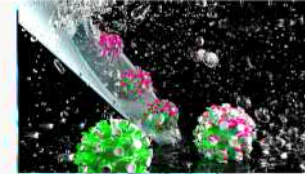
Bioactivity screening

Our research focuses on enhancing antimicrobial drug discovery - covering aspects from early target validation to detailed characterisation...



Biopharmaceutics

x



Cancer Unit for Research on Experimental Drugs

The Unit CURED aims to co-develop novel class of anti-cancer immunotherapy combining fundamental science on transcription factors and...



Drug Delivery

x



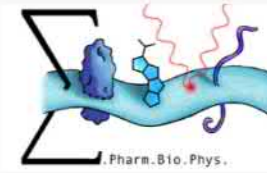
Mass Spectrometry and Metabolomics

The research focus of the Mass spectrometry and metabolomics group involves the development of novel and more sensitive, selective and...



Pharmaceutical Design and Discovery

The Pharmaceutical Design and Discovery Unit in the interface between chemistry, biology and pharmaceutical technology integrates a strong...



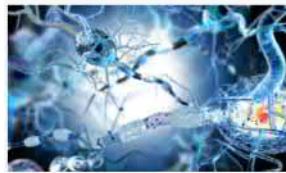
Pharmaceutical Biophysics

Pharmaceutical research has fallen into a rut known as "Erooms Law": while the resources expended increase exponentially the number of new...



Preclinical drug formulation and analysis group

We are a very multidisciplinary research group of life sciences and medical technology that comprises pharmacists, engineers, chemists,...



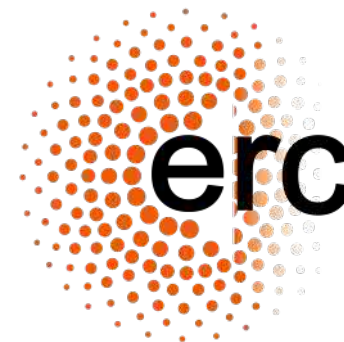
Regenerative pharmacology

Regenerative Pharmacology group has its focus on novel drug targets and experimental drugs to reveal the basis of disease modifying...



Drug delivery and formulation:

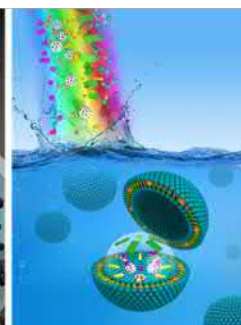
Hélder Santos, Assoc. Professor & ERC investigator
Jouni Hirvonen, Professor and Dean of the Faculty
Leena Peltonen, University Lecturer



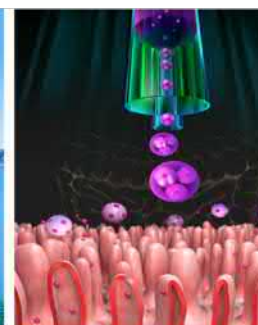
Liu et al. Adv. Mater. **2015**, 27, 2298–2304



Herranz-Blanco et al. Adv. Funct. Mater. **2015**, 25, 1448–1497



Kong et al., Adv. Funct. Mater. **2015**, 25, 3330–3340



Araújo et al., ACS Nano **2015**, 9, 8291–8302.

PRECLINICAL DRUG FORMULATION AND ANALYSIS RESEARCH ACTIVITIES

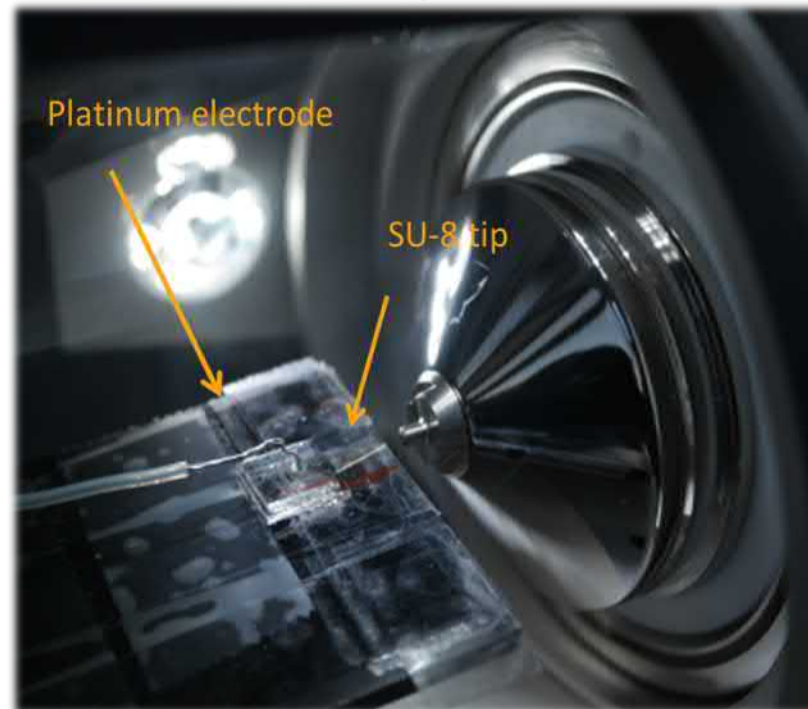
Drug characterization and analysis:

Clare Strachan, Associate Professor - Raman Spectroscopy

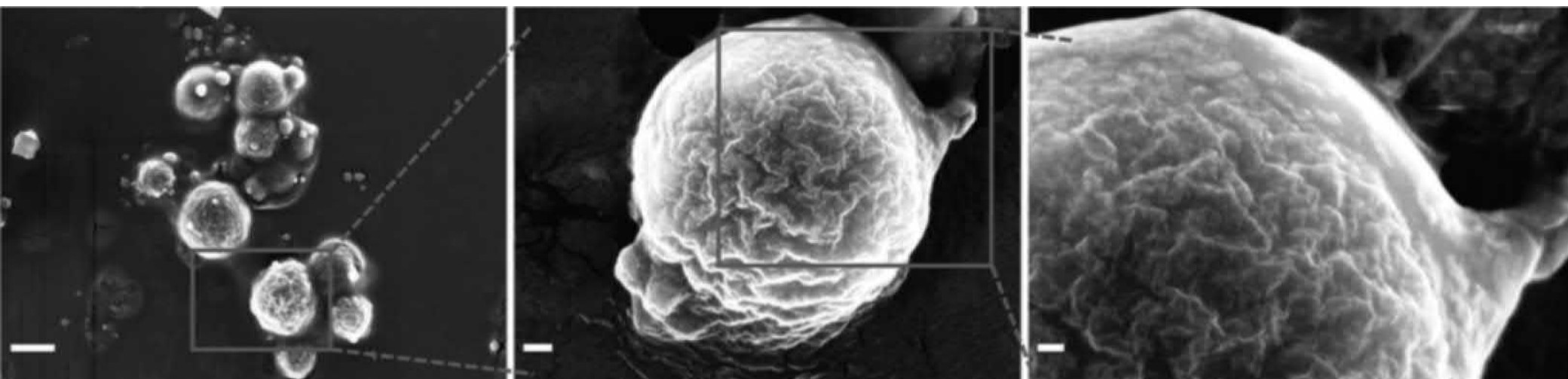
Tiina Sikanen, Assoc. Prof. & ERC investigator - microfluidics

Tapio Kotiaho, Professor - Single Cell Mass Spectrometry

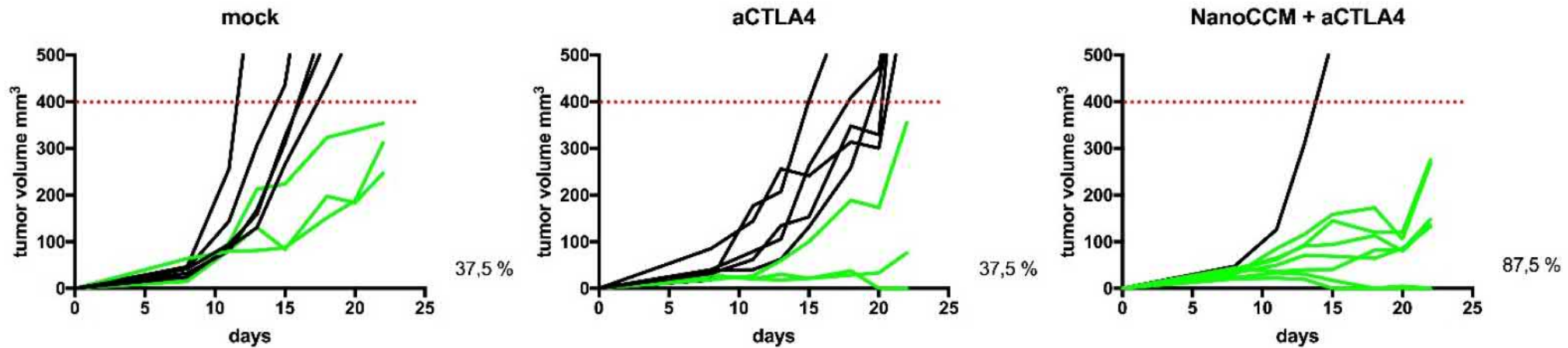
Jouko Yliruusi, Professor - Single Cell Mass Spectrometry



PRECLINICAL DRUG FORMULATION AND ANALYSIS RESEARCH ACTIVITIES



Fontana et al., Adv. Mater. 2017, 29, 1603239,

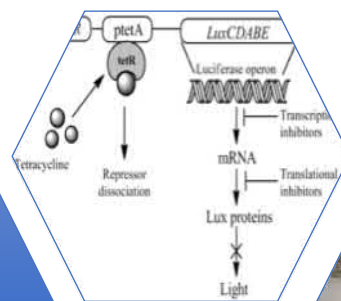


Capasso/Fontana et al., Nature Comm, *under review*

BIOACTIVITY SCREENING UNIT



Paivi Tammela, PhD
Head of Div. Pharmaceutical Biosciences
Head of Unit

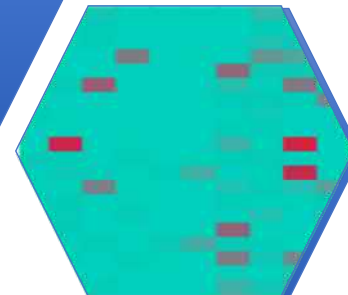
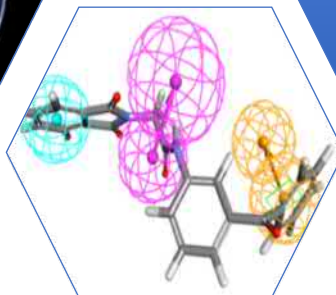
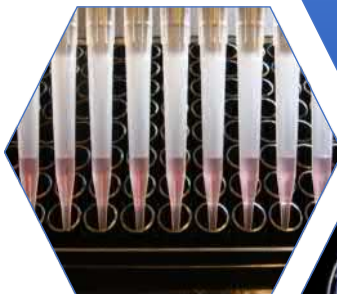


Development of
new approaches
for *in vitro*
screening and
follow-up studies

Focus on
antimicrobial
targets and
natural products

Applications
ranging from
simple
biochemical to
complex cell-
based assays

Head: Docent
Päivi Tammela,
PhD (Pharm),
Academy
Research Fellow

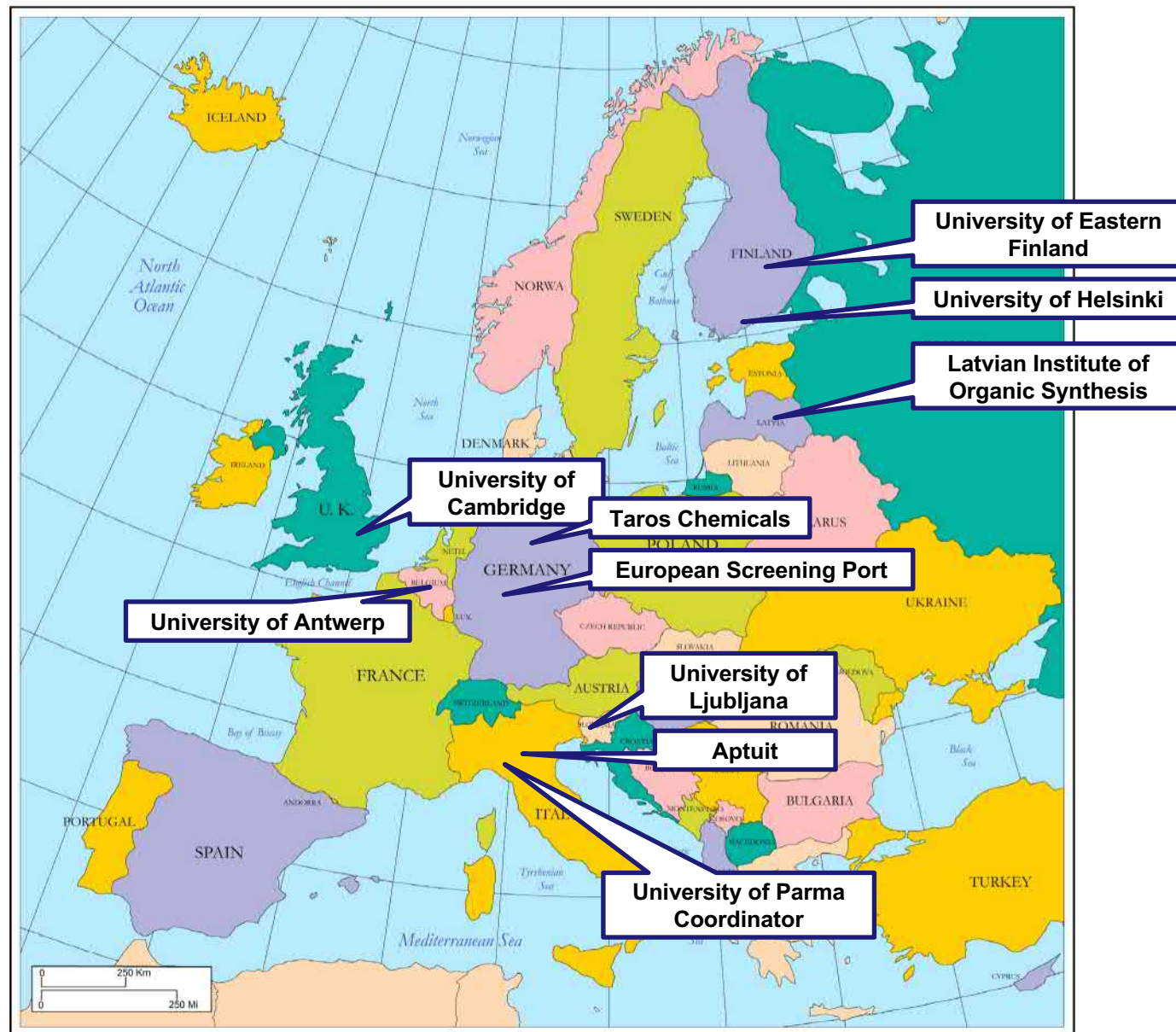


More information at:

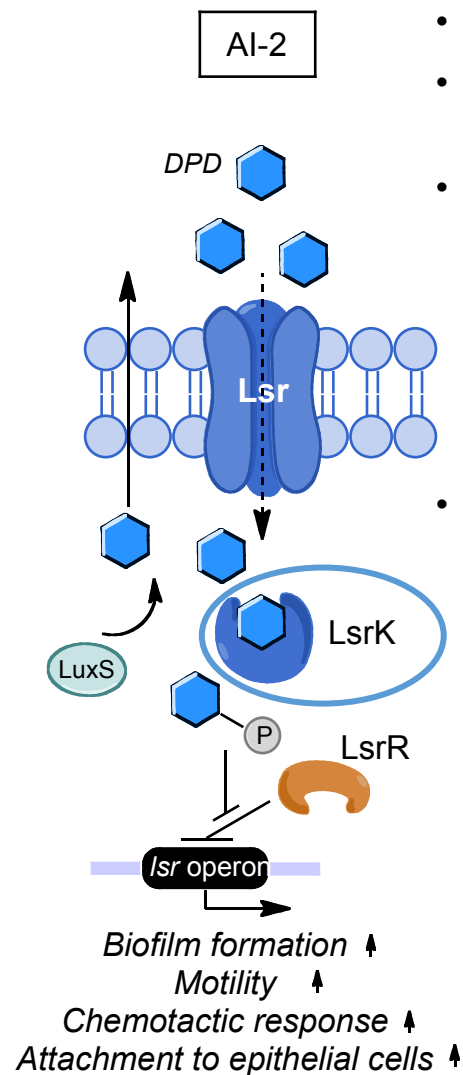
<https://www.helsinki.fi/bioactivity-screening>



INTEGRATE beneficiaries



Quorum sensing inhibitors targeting LsrK



- Target overexpression in *E. coli*
- Kinase assay miniaturisation, validation and automation in 384-well plate format
- Collaboration with University of Eastern Finland (Antti Poso et al.), TAROS Chemicals GmbH, and University of Ljubljana

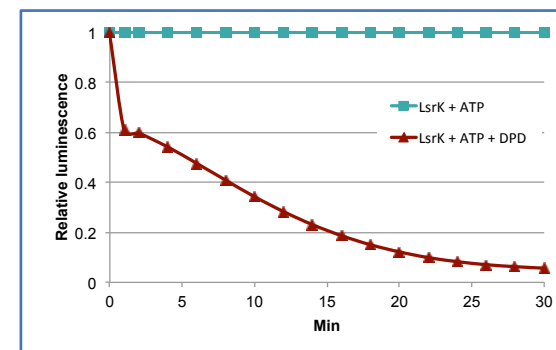
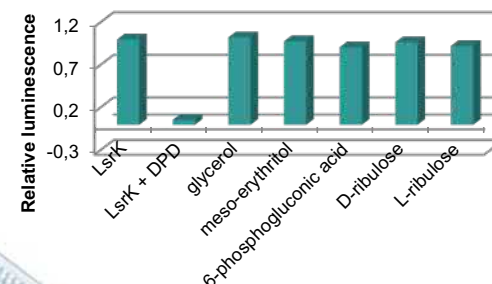


- We have screened:
 - 1) DPD analogs synthesized by TAROS
 - 2) Compounds selected by UEF through homology modelling
 - 3) A library of >2000 known bioactive compounds



SEVERAL POTENT INHIBITORS IDENTIFIED

Substrate specificity



DRUG DELIVERY UNIT



Main aims of research

- Improved drug delivery to the posterior eye segment
- Quantitative understanding and modeling of ocular PK/PD

Main approaches

- Delivery: Light activated liposomes, melanin targeting, targeted conjugates
- PK/PD: Experimental work and follow-up modeling

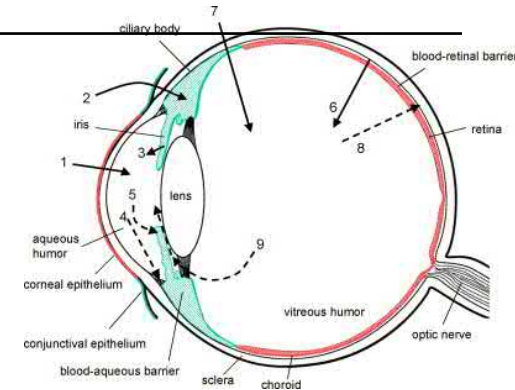
Size and funding of the research program

Research group located at University of Helsinki, University of Eastern Finland and St. Petersburg State University.

Annual grant funding is about 2 M€/year. Main sources: Academy of Finland, TEKES, industry, EU, Russian Federation, U.S. FDA, foundations. Size of the group in total about 40 persons.

Recent highlights

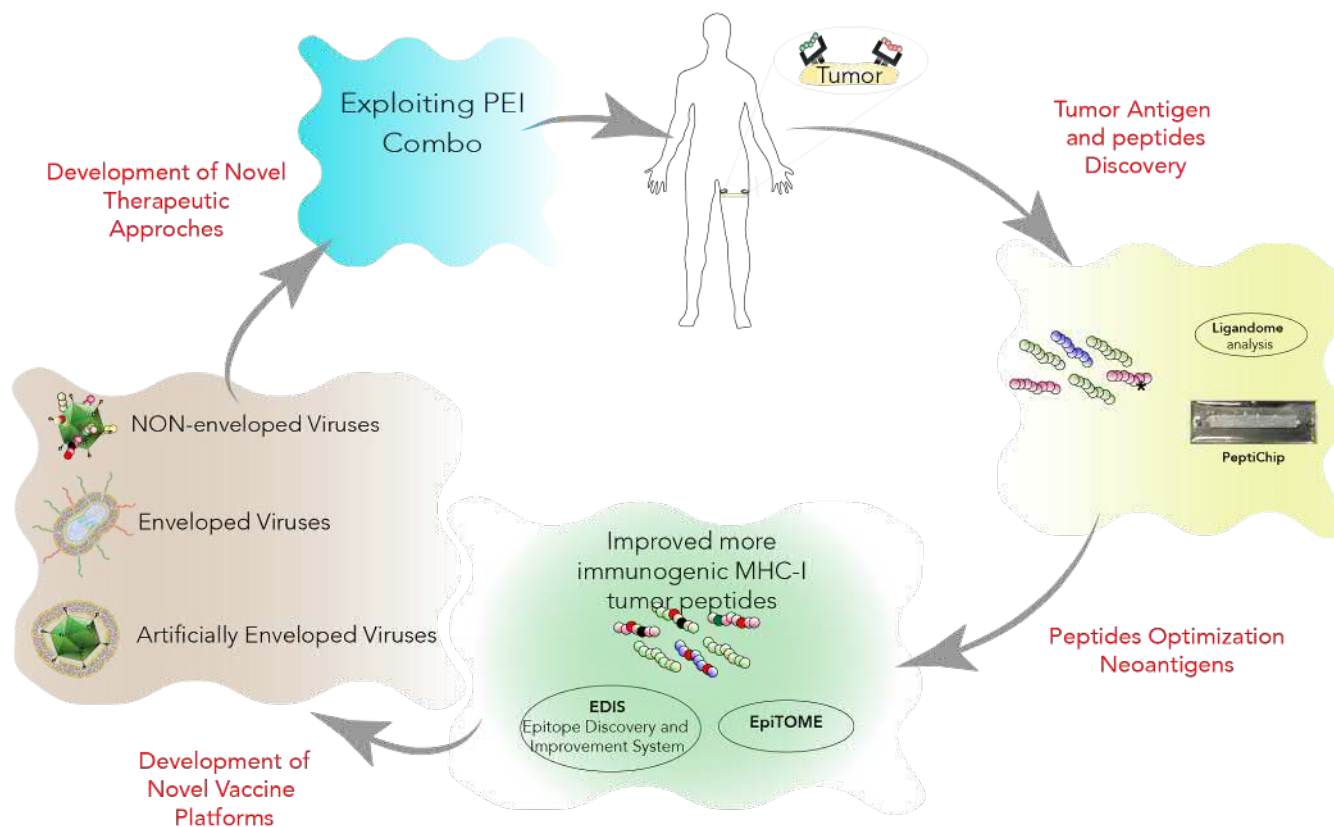
- New light activated liposome technology (Mol Pharm 2016), rationale for melanin based targeting (ADDR 2018), controlled intracellular release based on peptide conjugates (J Control Rel 2017)
- Russian Federation Mega Grant recipient
- Recently in the short list for Center of Excellence and Academy Professor



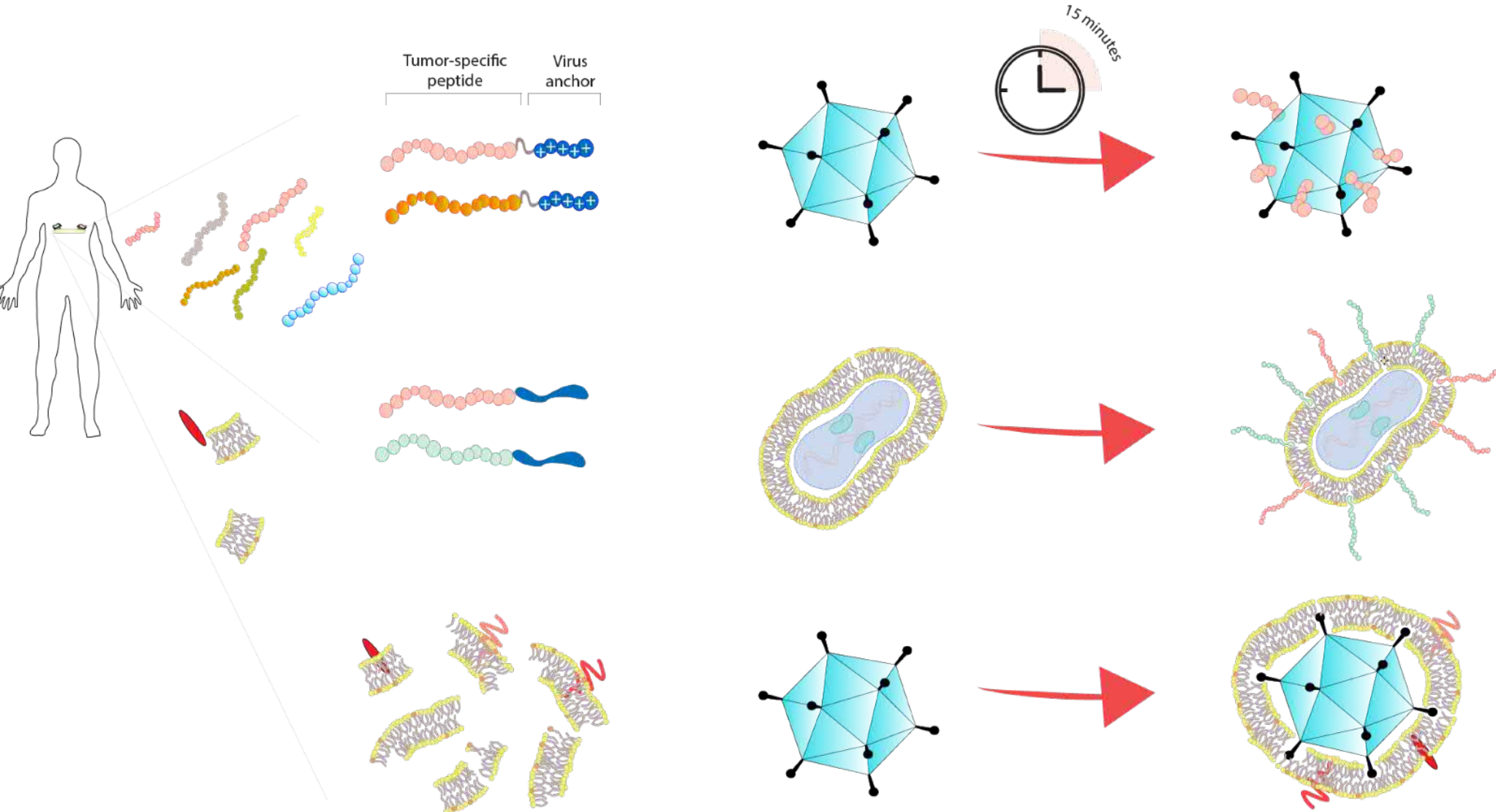
CURED CANCER UNIT for RESEARCH on EXPERIMENTAL DRUGS

Cancer Unit's PIs

Vincenzo Cerullo, Assoc. Professor & ERC investigator
Marikki Laiho, Professor
Pia Siljander, University Lecturer

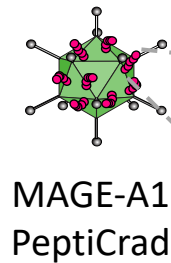
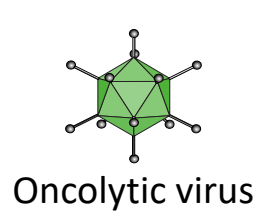
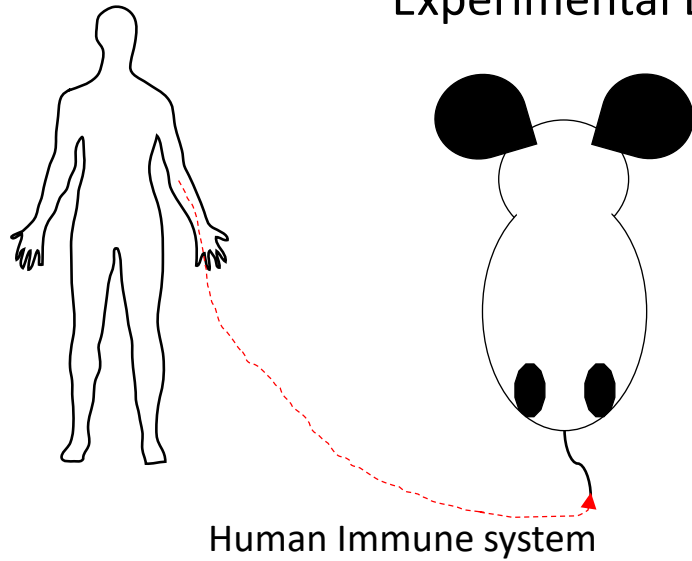


PRECLINICAL DRUG FORMULATION AND ANALYSIS RESEARCH ACTIVITIES



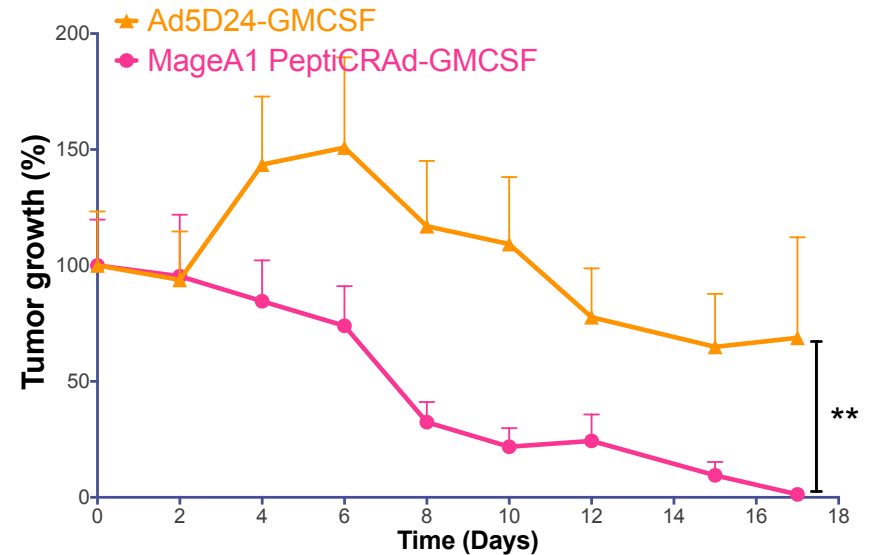
PEPTICRAD - HUMANIZED MICE MODEL

Experimental Design

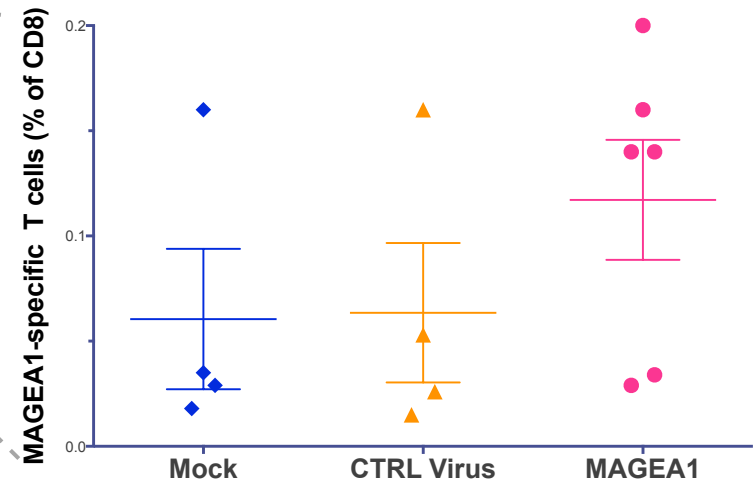


PeptiCrad is efficient in humanized mice bearing human tumor and immune system

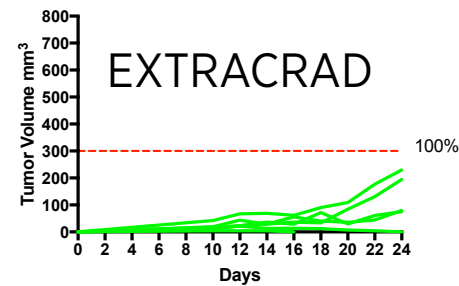
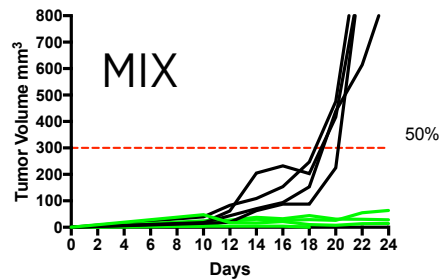
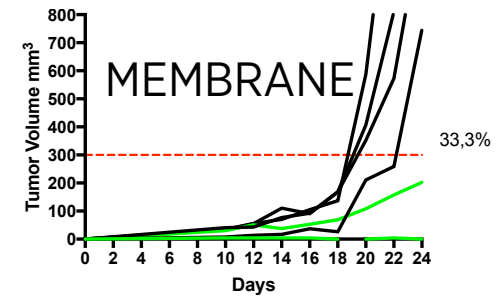
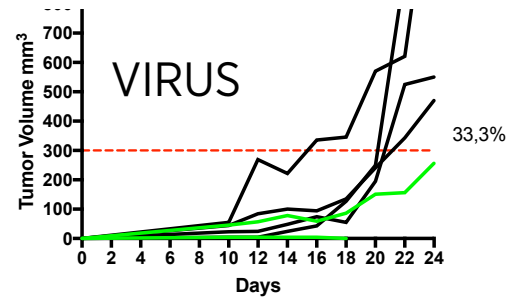
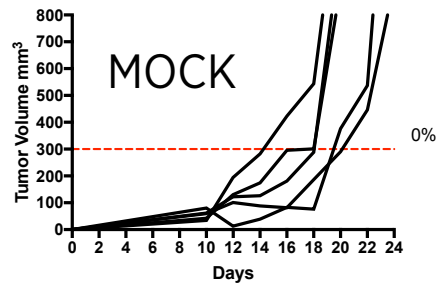
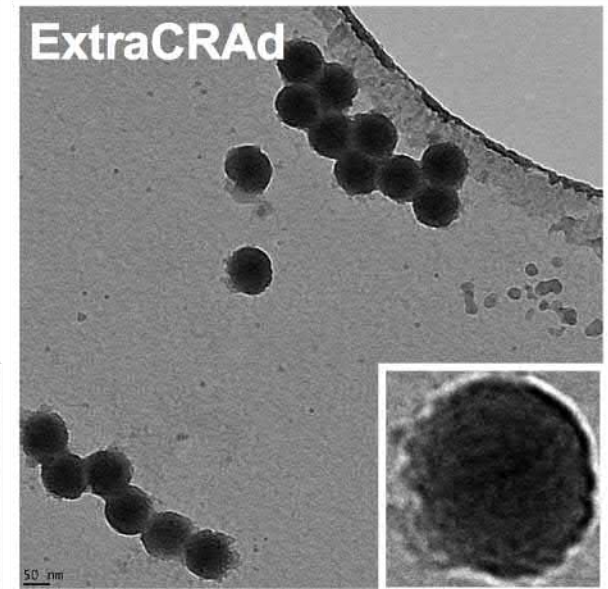
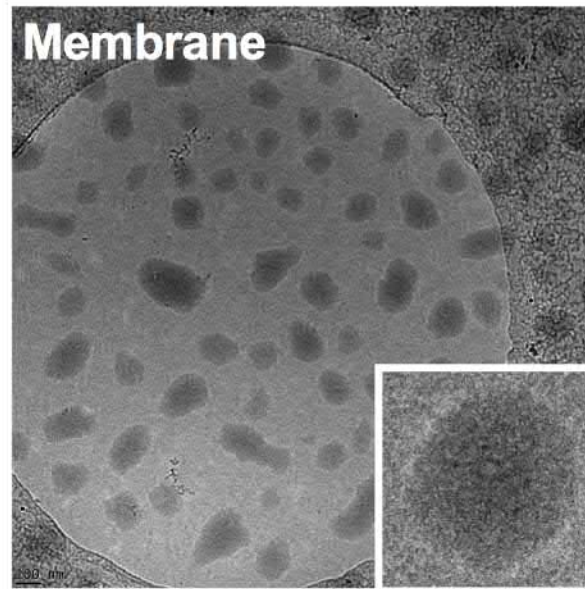
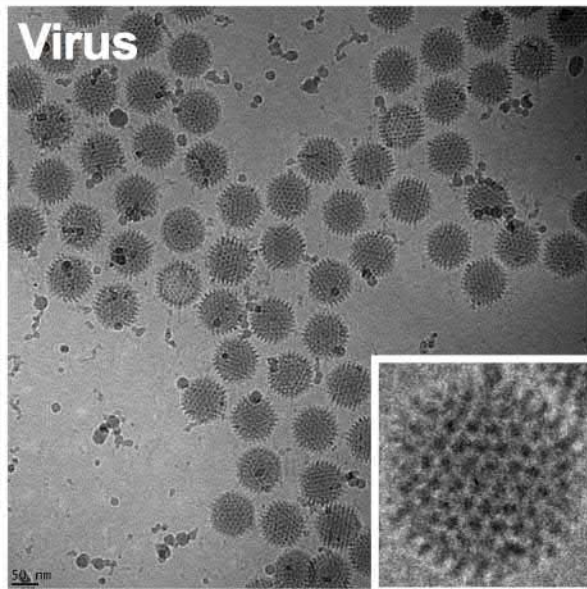
Humanized mice with human Melanoma Human PBMCs - PeptiCrad MAGEA1



MAGE-Specific human T cells (Peptide-specific T cells)



EXTRACRAD - ARTIFICIAL ENVELOPE APPROACH



VALO Therapeutics

Valo Oncolytics for life™

Successful Story in 2016

VINCENZO CERULLO & MICHAEL
STEIN, ProVinceTx

#slushscience16

Petri Virha
VP of CMC

Charlotta Backman
VP Regulatory affairs

Matt Vaughan
Project Manager

Vince Cerullo
Scientific Founder

SLUSH Y SCIENCE

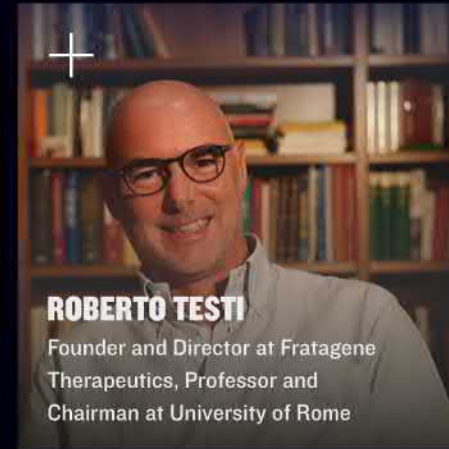
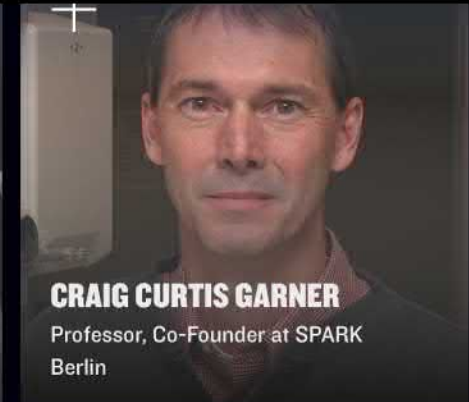
HiLIFE
HELSINKI INSTITUTE OF LIFE SCIENCE



HELSINGIN YLIOPISTO
HELSINGFORS UNIVERSITET
UNIVERSITY OF HELSINKI

1 Million Streaming viewers
20000 attendees
2,600 startups,
1,500 venture capitalists,
600 journalists from 130 countries





www.drphelsinki.fi



LEIDEN

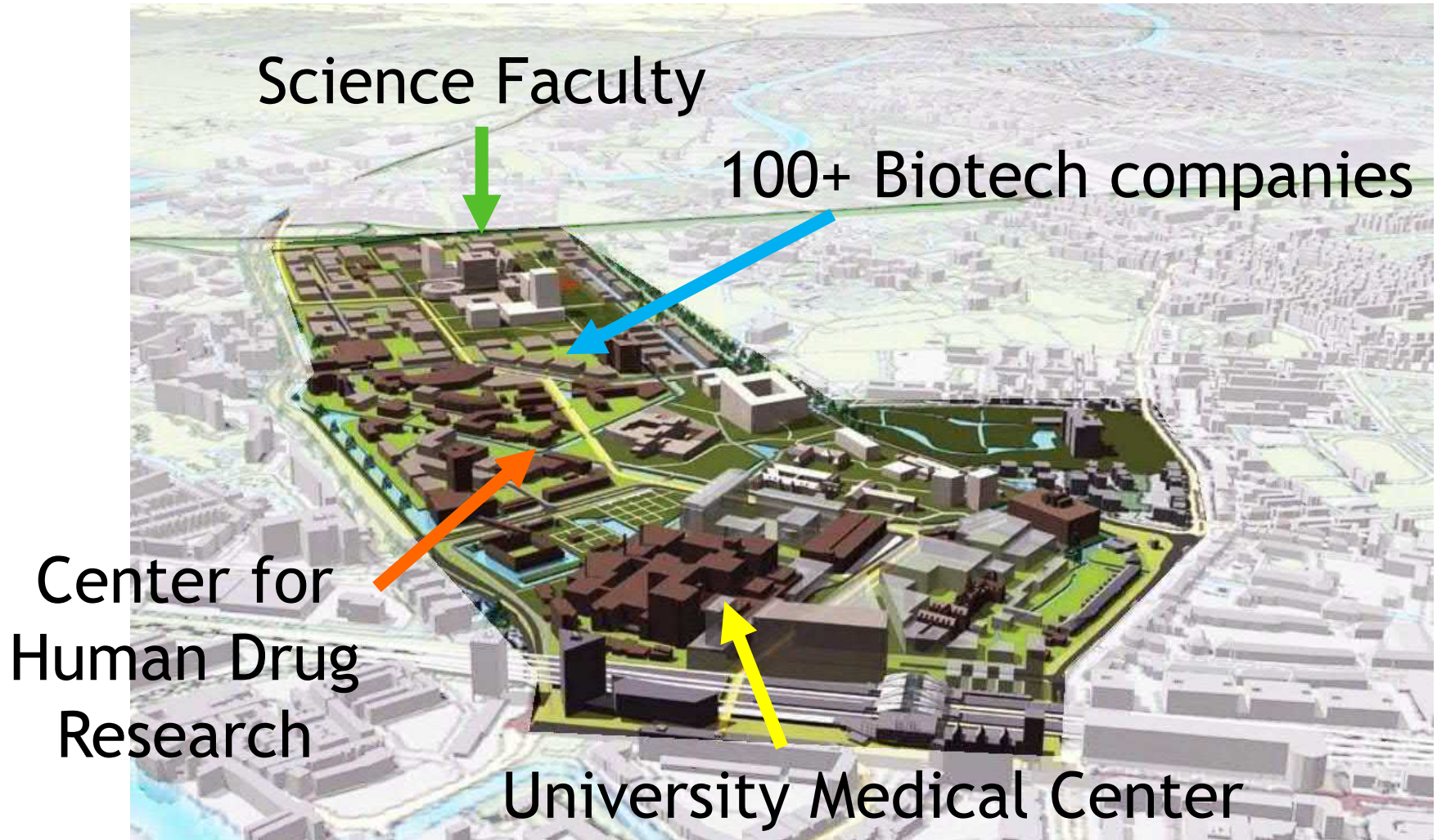
ULLA Presentation

Hubertus Irth
Scientific Director

Leiden Academic Centre for
Drug Research

Faculty of Science
Leiden University

Location: Leiden BioScience Park



LACDR Vision & Mission

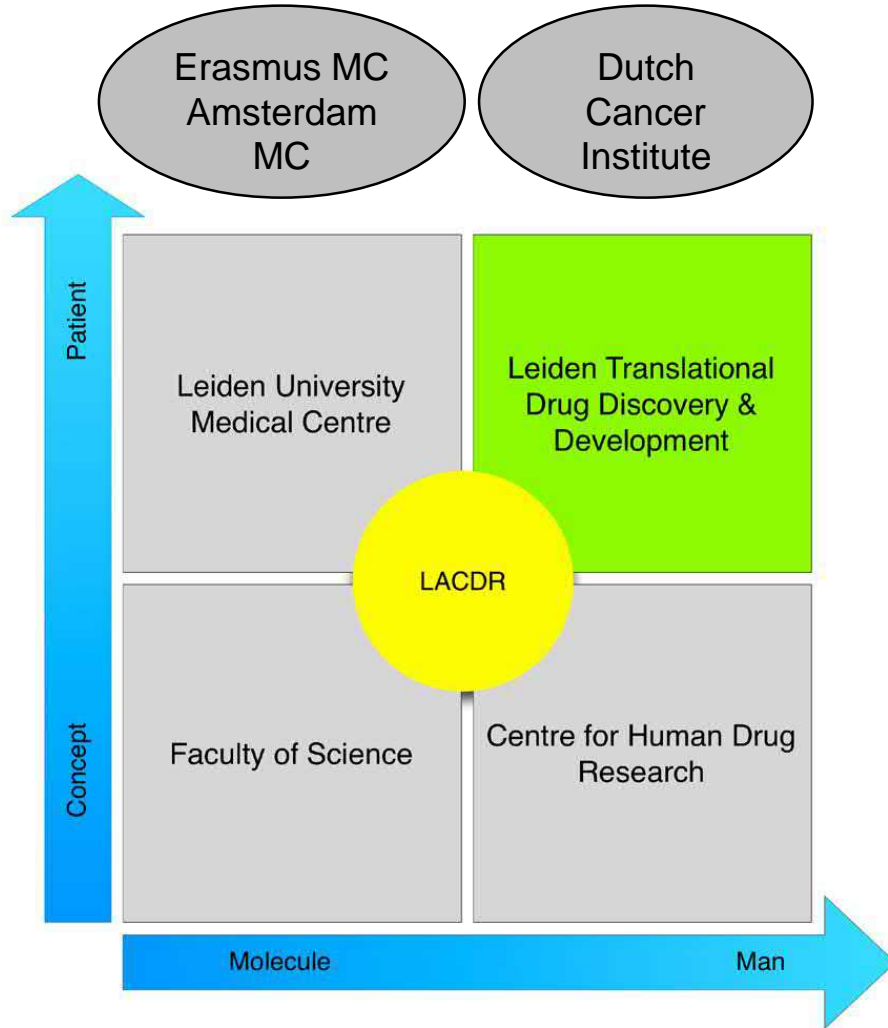
Vision

To be at the frontline of the development of novel concepts in fundamental and translational drug research

Mission

Discovery and optimization of drugs and personalised medicines
Education and training of scientists who can further this cause

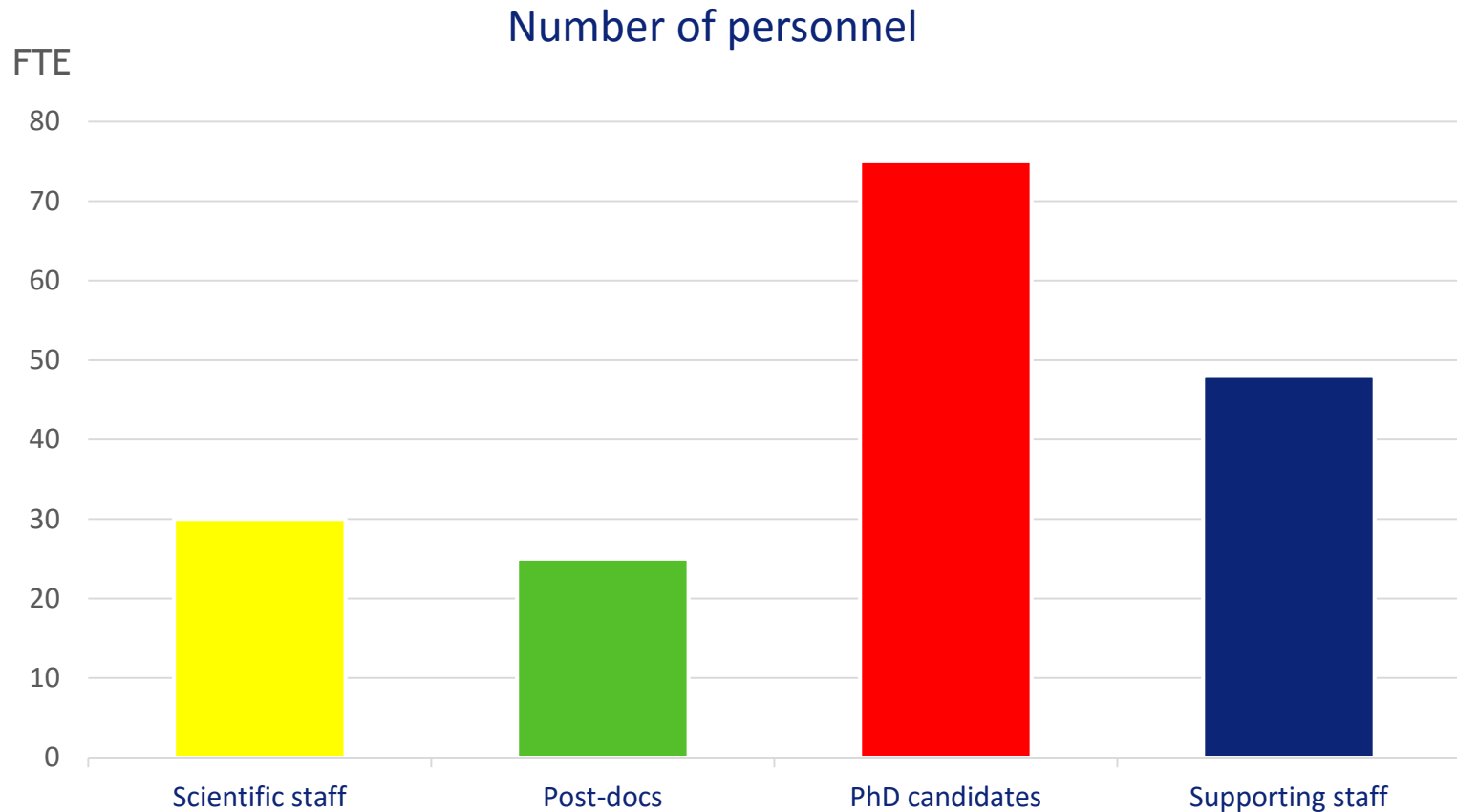
Imbedding in Medical Delta environment



Strong partnerships via

- joint research programmes
- joint appointments
- sharing of key infrastructure

LACDR Key Facts: Personnel



Ca. 170 employees, 15 Mio Euro annual turnover

LACDR Research Divisions

Advancing innovative biopharmaceutical
concepts to intervene in auto-immune-like
disorders

BioTherapeutics

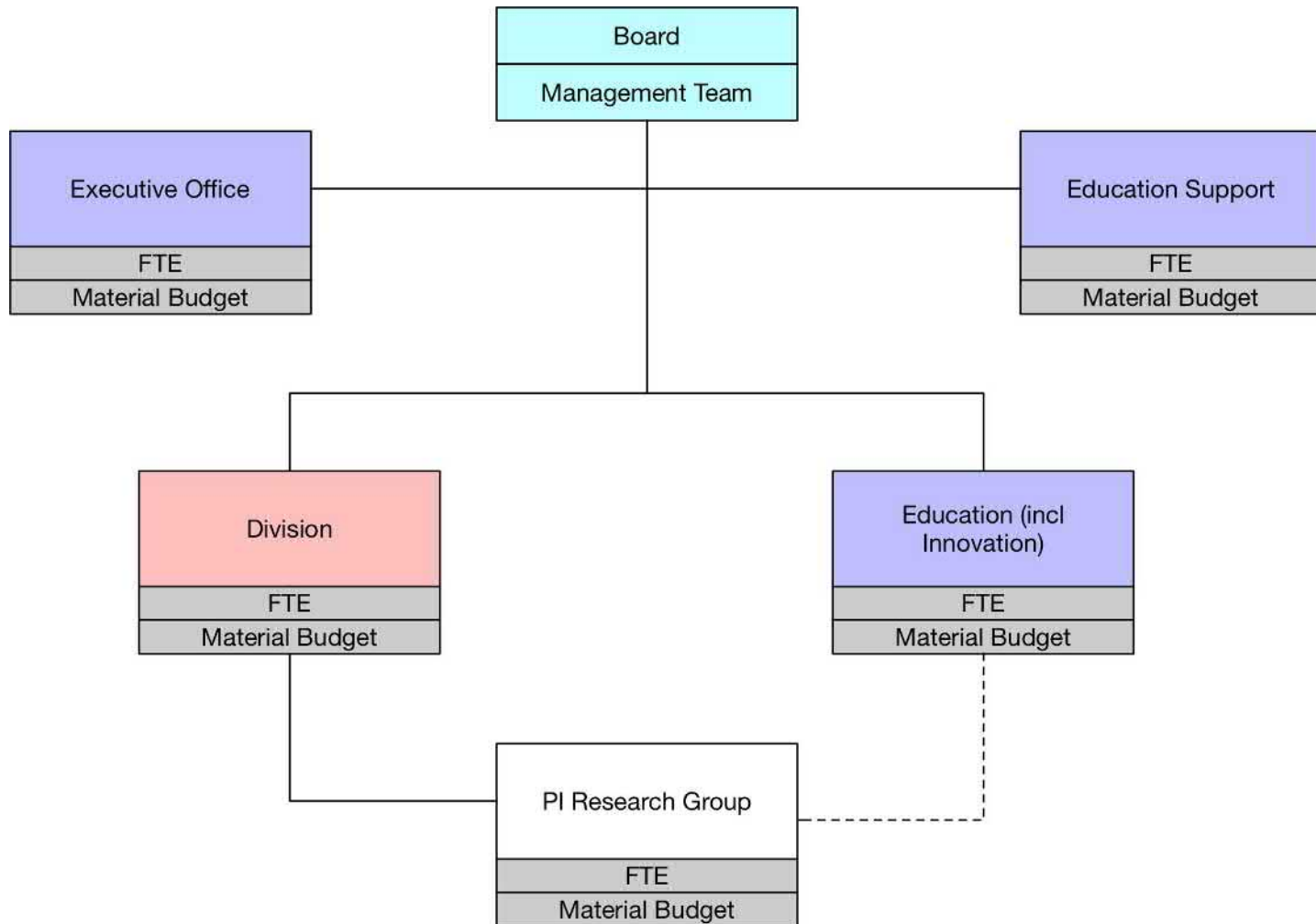
Drug
Discovery &
Safety

Optimizing the desired therapeutic
effect and minimizing adverse
reactions of the drugs of tomorrow.

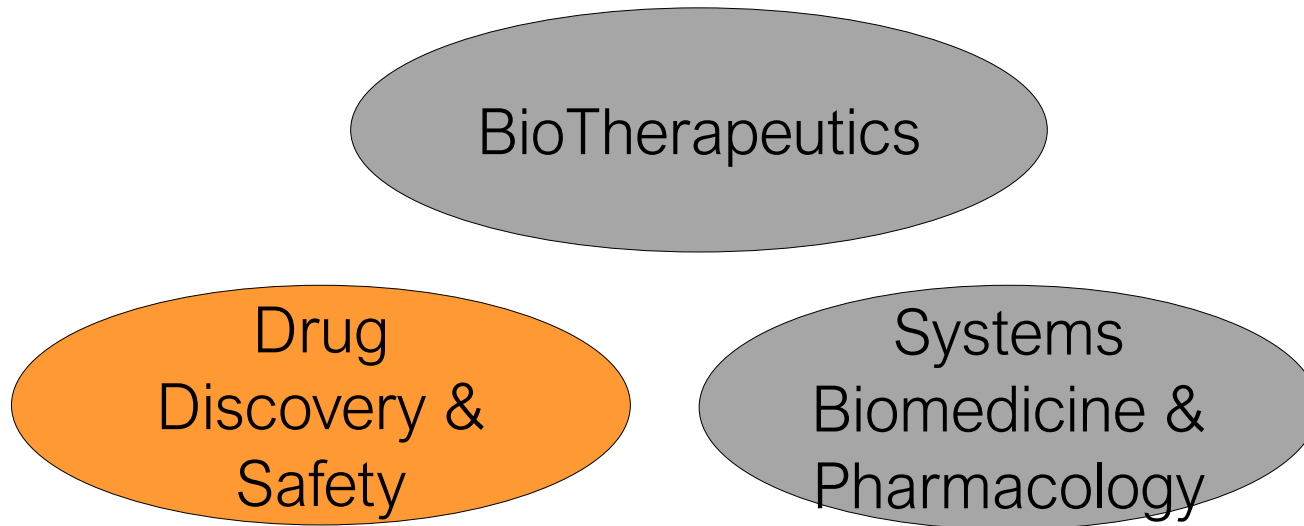
Systems
Biomedicine &
Pharmacology

Developing personalised medicine
strategies and systems-based
approaches in translational/clinical
pharmacology

Sep 2017: Formal implementation of new organizational structure

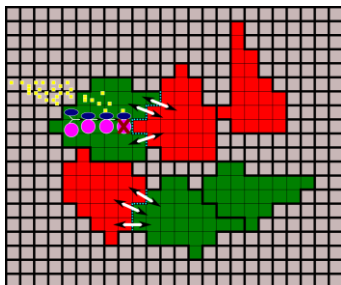


LACDR Research Divisions

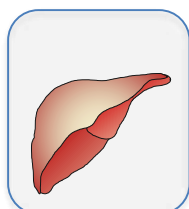


Cluster Drug & Target Discovery: *integrated concepts for drug discovery cycle*

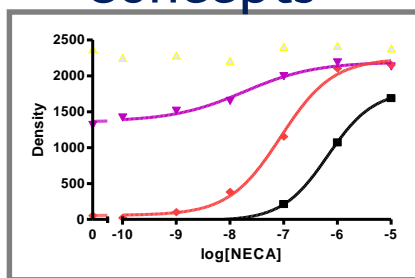
6. Computational Biology



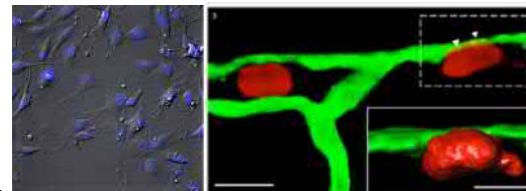
5. Drug Safety



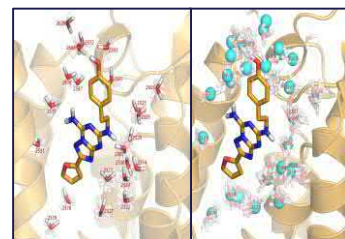
4. Receptor Concepts



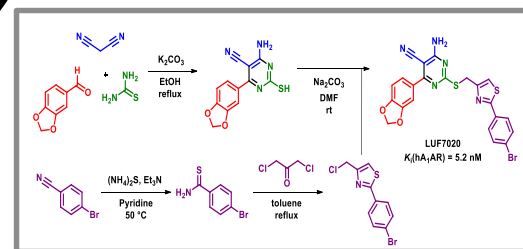
1. Drug Target Discovery



2. Computational Chemical Biology



3. GPCR Ligands



*Establish Concepts for
Drug Discovery Cycle*

PIs and their research lines

- Drug Safety Sciences

- Bob van de Water



- Better Ligands for GPCRs

- Ad IJzerman



- Cancer Drug Target Discovery

- Erik Danen



- Novel Receptor Concepts

- Laura Heitman



- Computational Biology

- Joost Beltman



- Computational Chemical Biology

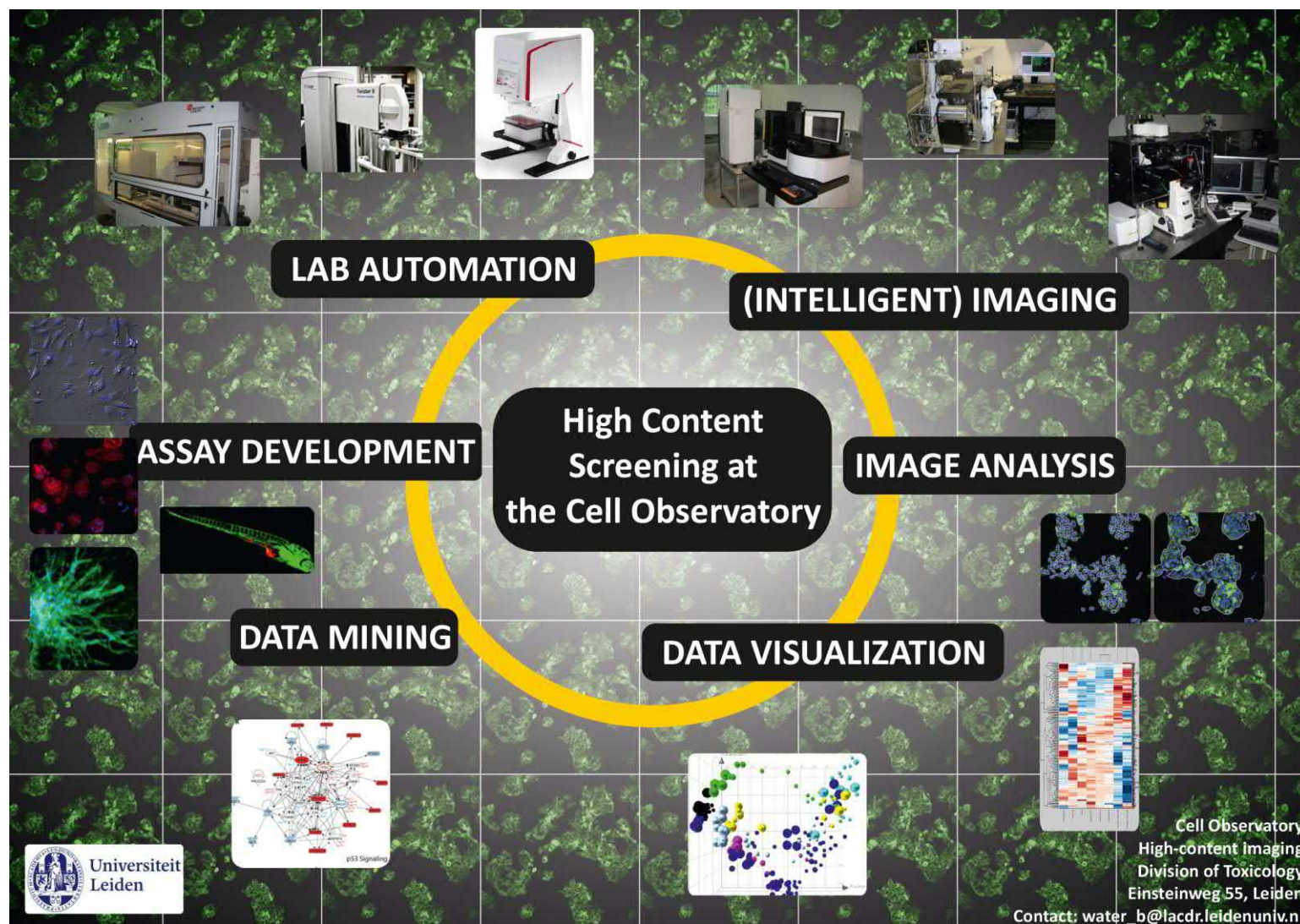
- Gerard van Westen



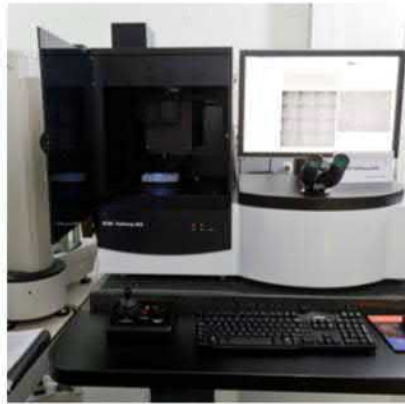
Extraordinary professors:

Jos Jonkers & Aroud Sonnenberg (Neth. Cancer Inst.), Herman van Vlijmen (Janssen)

LACDR Key Infrastructure: Cell Observatory



Functional screening infrastructure Cell Observatory



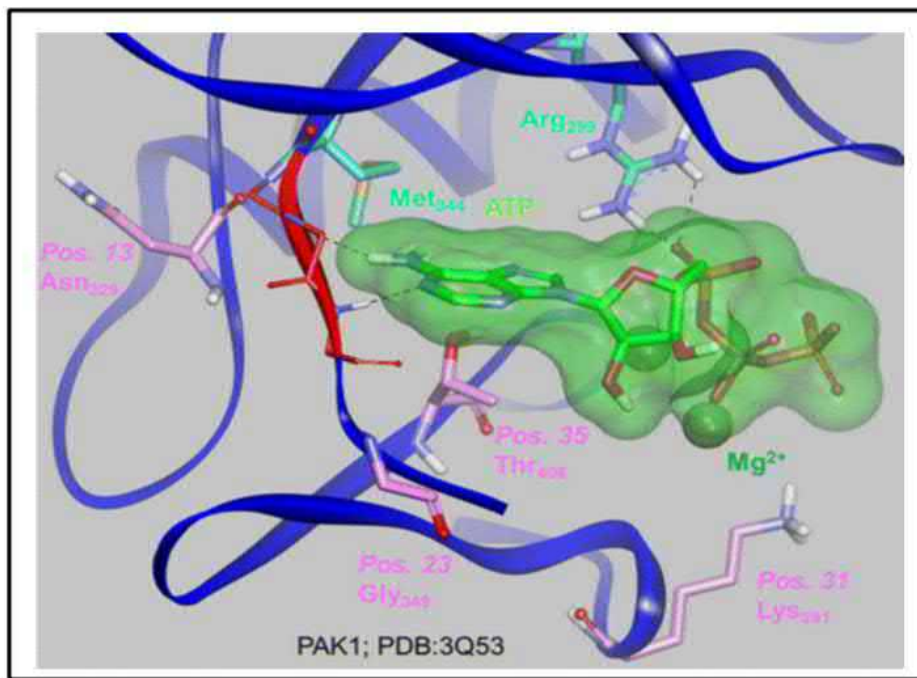
BD Pathway 855
automated highthroughput
epi microscope



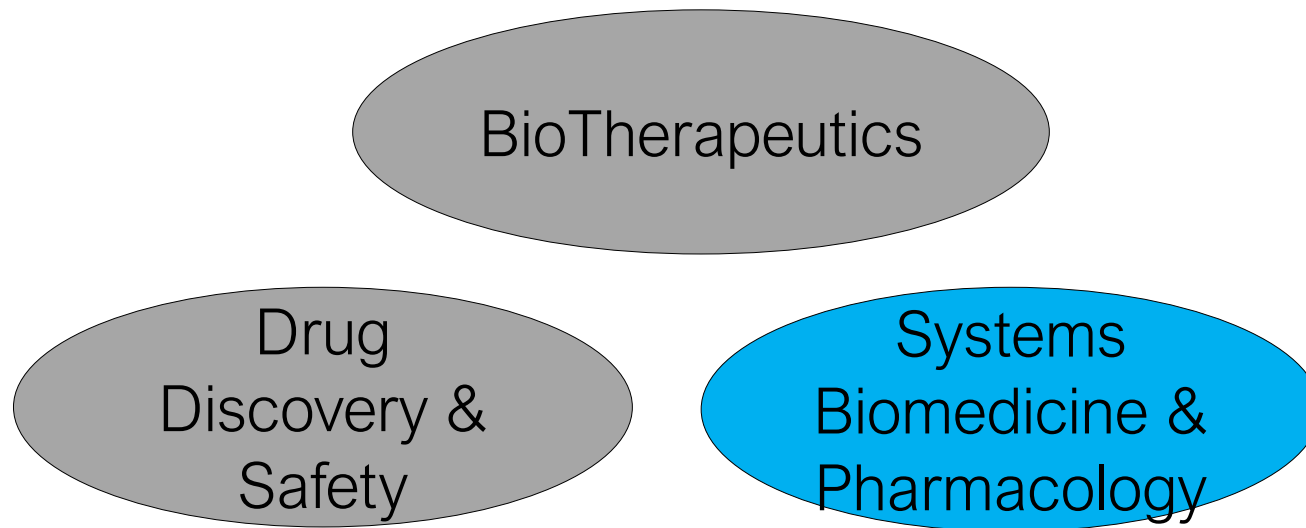
Nikon confocal / epi microscopes with incubators and automated stages,
4 laser lines and GaAsp detectors

LACDR Key Research Focus: Computational Sciences in Pharma

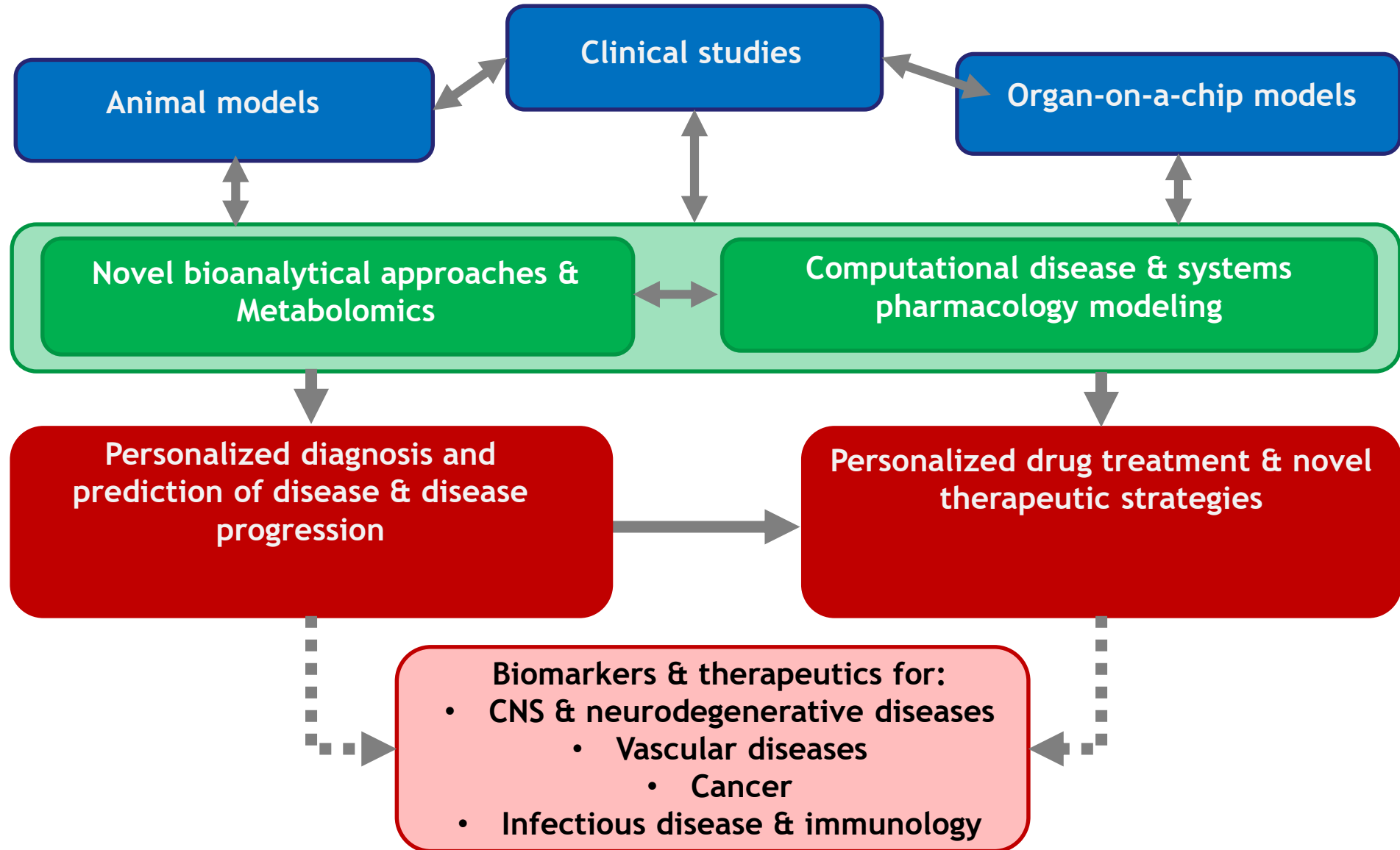
- We aim to apply computational chemical biology for the prediction of drug-target interaction as well as drug efficacy and safety
 - 'Big Data' for precision medicine by combining cheminformatics and bioinformatics: e.g. cancer drug responses
 - Structure-based and statistical methods: e.g. kinase inhibitor drug selectivity



LACDR Research Divisions



Mission: Systems pharmacology approaches to enable personalized medicine



Division of Systems Biomedicine and Pharmacology

Principal investigators



Thomas Hankemeier
*Analytical
Biosciences and
Metabolomics*



Liesbeth de Lange
*Quantitative and
Translational
pharmacology*



Catherijne Knibbe
*Individualized
drug treatment/
Clinical
pharmacology*



Piet van der Graaf
*Systems
Pharmacology*



Rawi Ramautar
*Biomedical
Microscale
Analytics*



Alireza Mashaghi
*Laboratory
for Medical
Systems
Biophysics*



Coen van Hasselt
*Quantitative
Systems
Pharmacology*

Research & Education



Elke Krekels
*Clinical
Pharmacology*



Isabelle Kohler
*Analytical
Biosciences and
Metabolomics*

Extraordinary Professors



Cornelia Van Duijn
ErasmusMC



Koos Burggraaf
CHDR



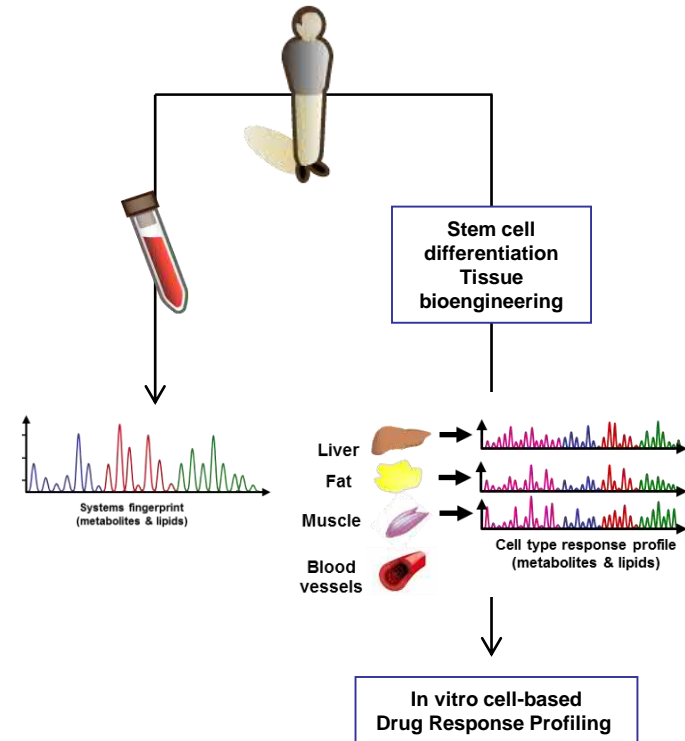
Henk-Jan Guchelaar
LUMC



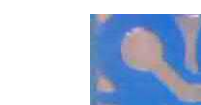
LACDR Key Infrastructure: Metabolomics lab

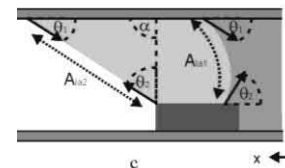
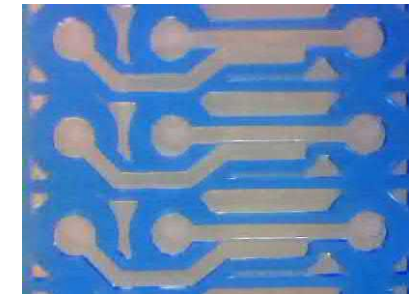


12-04-2018: 3 Mio Euro funding from National Roadmap

From human to models | Organ-on-a-chip

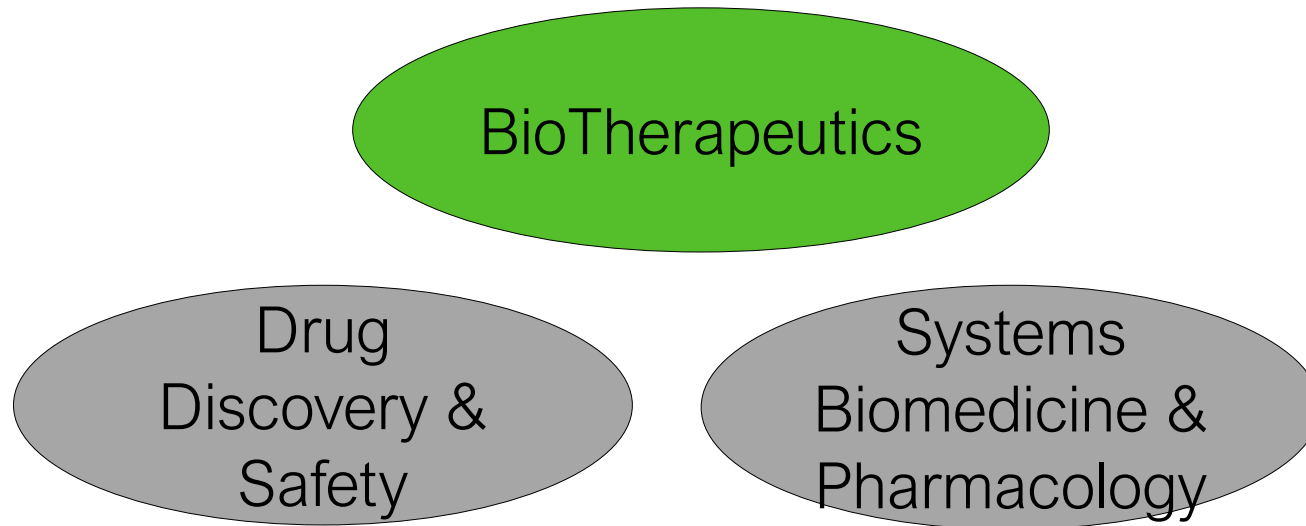


- Organ and tissue functionality
 - Perfusion
 - High throughput
 - Low reagent consumption
 - Fully passive liquid control
 - Easy filling of any shape
 - Liquid & gel patterning
 - Gradient formation



Vulto et al., Lab Chip 11 (2011) 1596

LACDR Research Divisions



Research approach Cluster BioTherapeutics

Vaccine
development



Gideon Kersten

Novel concepts for
formulation, delivery
and targeting



Wim Jiskoot

Innovative
vaccines



Bram Slütter

Adaptive immune response CVD
Novel biologics in humanized
mouse models



Johan Kuiper

**TRANSLATION
TO CLINIC**

Modulation of lipid
Metabolism
Drug delivery, cellular
therapy

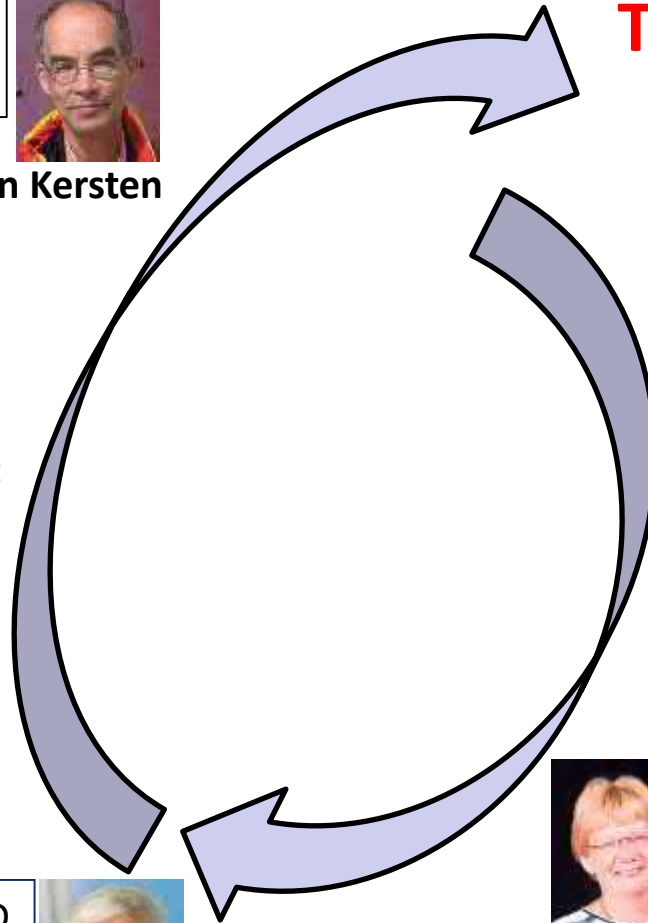


Miranda van Eck

Modulation of lipid
metabolism in inflammatory
skin disease
Intradermal vaccine delivery



Joke Bouwstra



Mission of the cluster BioTherapeutics

Translate cutting edge research in complex immune based diseases into advanced targeted therapies based on biologics

Identify targets for therapy in complex immune based diseases

Cardiovascular disease

Inflammatory skin disease

Translation

From preclinical humanized mouse models of cardiovascular disease and from in vitro skin models to perform First-In-Humans clinical trials

Therapy: focus is on biologics

Therapeutic vaccines in atherosclerosis

Therapeutic proteins

Targeted

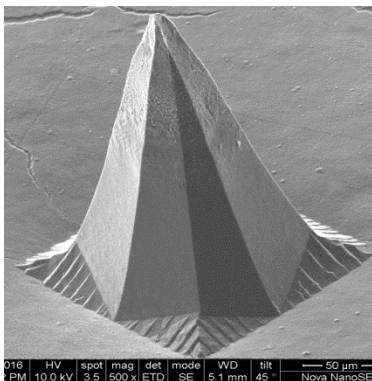
Specific delivery of biologics and vaccines (including route of administration)



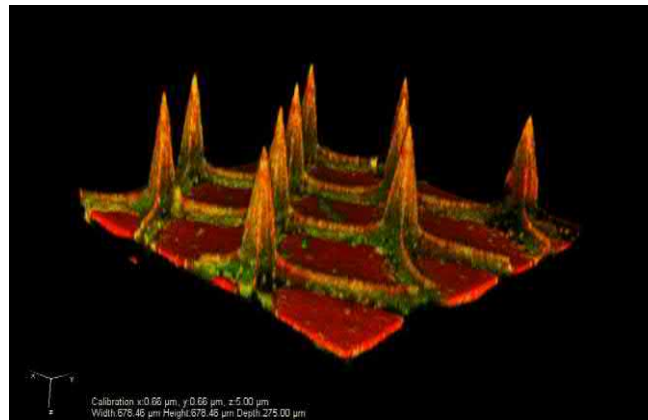
Aim: improved vaccination by the intradermal route

- Approach: microneedles pierce the skin barrier and deliver the vaccine into the dermis
 - Dissolvable, vaccine coated and hollow microneedles are developed
 - Nanoparticles are used to improve the immune response
 - Vaccination without pain sensation

Microneedle that
dissolves in the skin
and releases antigen



IPV coated microneedle arrays,
length of 200 µm



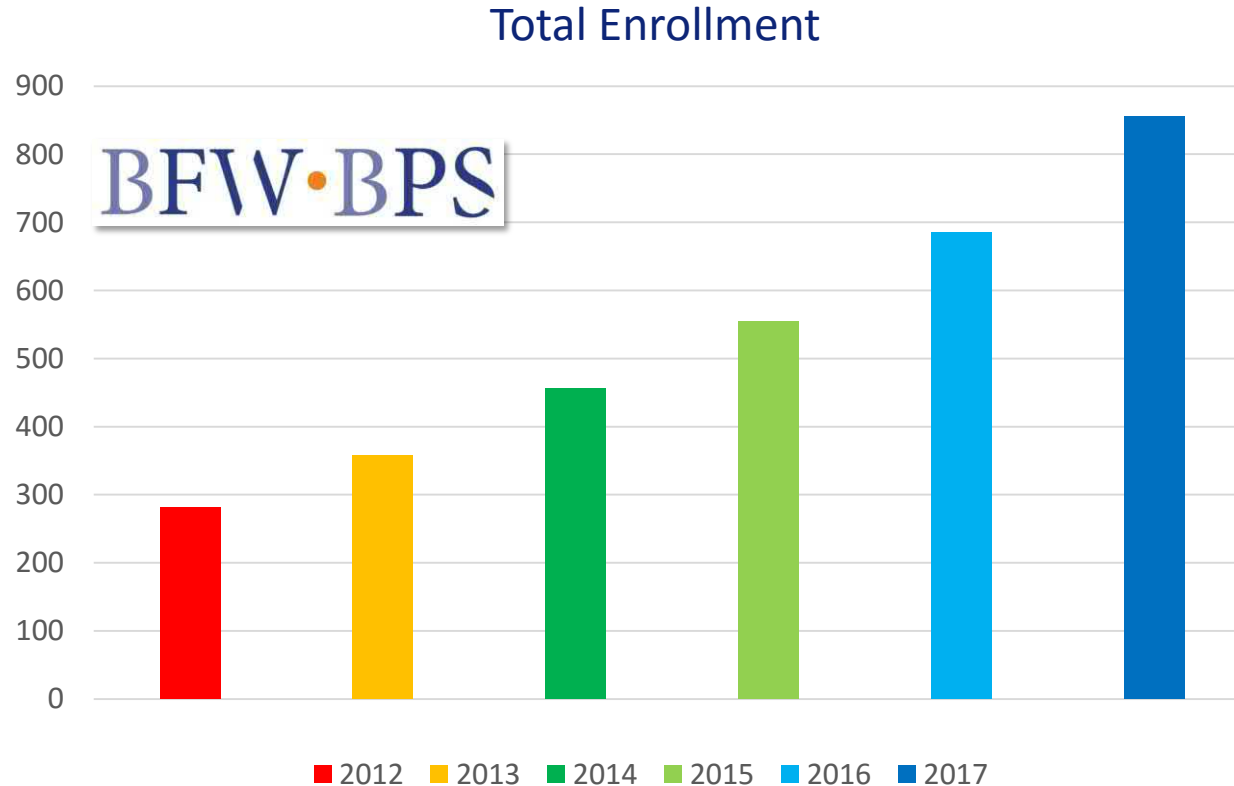
Hollow microneedle arrays
injection depth variation (50-800
µm)





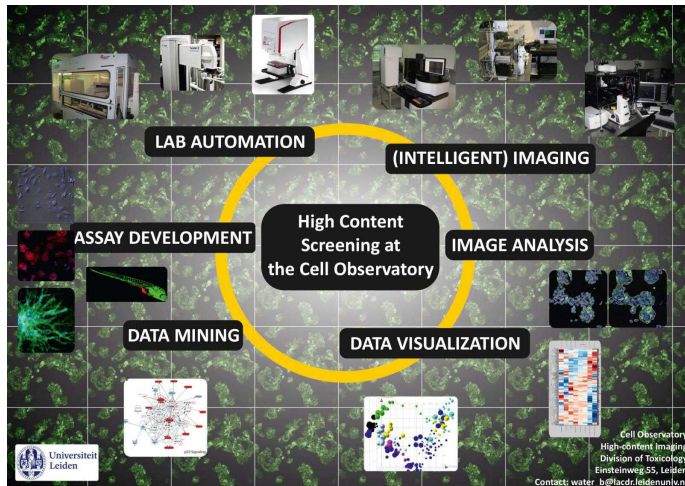
- BSc programme Bio-Farmaceutische Wetenschappen (BFV)
 - Broad academic training in drug research
 - Limited specialisation (minor)
 - Stepwise and integrated Academic Learning in three study years
- MSc programme Bio-Farmaceutische Wetenschappen (BPS)
 - Deepening and specialisation
 - Preparation for labour market (60% → PhD)
- MSc programme Pharmacy
 - Jointly with LUMC

Since 2014: Strong increase in student enrollment



Bio-Pharmaceutical Sciences has become an immensely popular education programme

Leiden Bioscience Park - LACDR



LEUVEN

Department of Pharmaceutical and Pharmacological Sciences



KU Leuven – ON2 building



Rega Institute –
MedChem division

Cloud 1 – Target Validation and Drug Discovery



Cell Metabolism

Prof. Myriam Baes



Molecular Virology & Gene Therapy

Prof. Zeger Debyser



Prof. Rik Gijsbers



Biocrystallography

Prof. Sergei Strelkov



Molecular Biodiscovery

Prof. Peter de Witte



Toxicology & Pharmacology

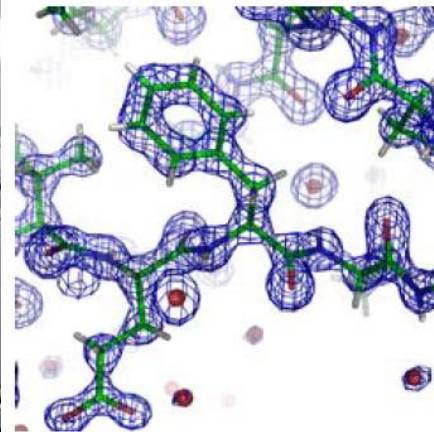
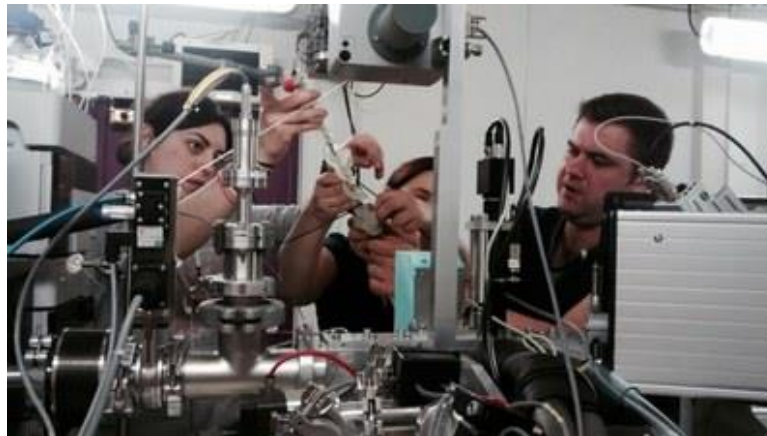
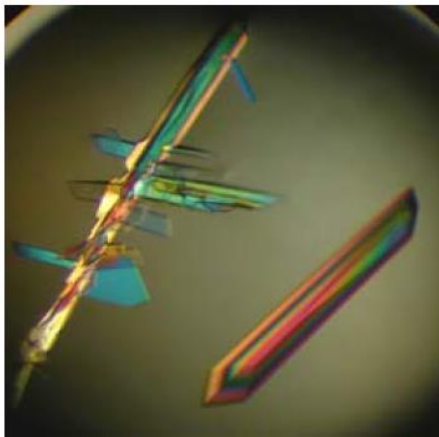
Prof. Jan Tytgat



Prof. Eva Cuypers



Biocrystallography



Techniques:

X-ray crystallography, SAXS, macromolecular modeling and drug design, biotechnology, biochemistry, mass spectrometry, EM



Prof. Dr. S. Strelkov and Dr. S. Weeks
sergei.strelkov@kuleuven.be
stephen.weeks@kuleuven.be



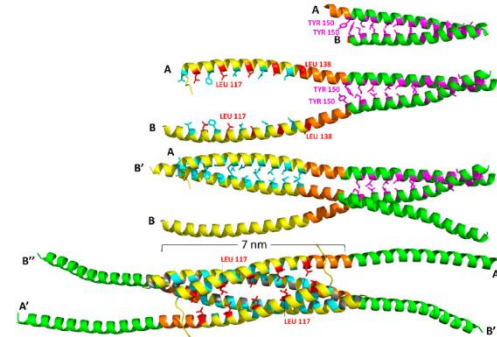
Biocrystallography (Scientific Highlights)

- **Ongoing research on cytoskeletal intermediate filaments**

Chernyatina et al (2015) Curr Opin Cell Biol. 32:65-72;

Clemen et al (2013) Acta Neuropathol. 125(1):47-75;

Chernyatina et al (2012) Proc Natl Acad Sci U S A. 109(34):13620-5.



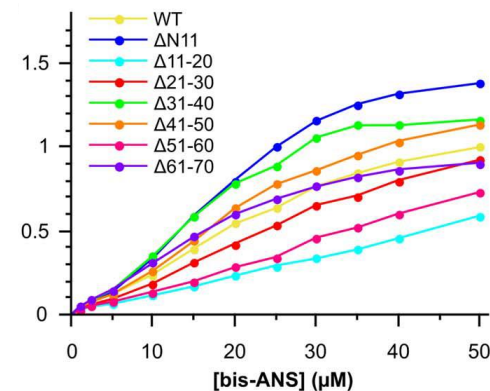
- **Ongoing structural studies of small heat-shock proteins**

Heirbaut et al (2014) PLoS One. Aug 26;9(8):e105892.

- **Past and recently started structural projects aimed at drug design -- novel antivirals and antibiotics (tRNA synthetases)**

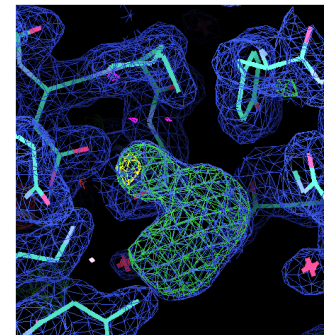
Christ et al (2010) Nat Chem Biol. 6(6):442-8.

Zhang et al (2018) EJMECH, 148, 384-396



- **Methods development**

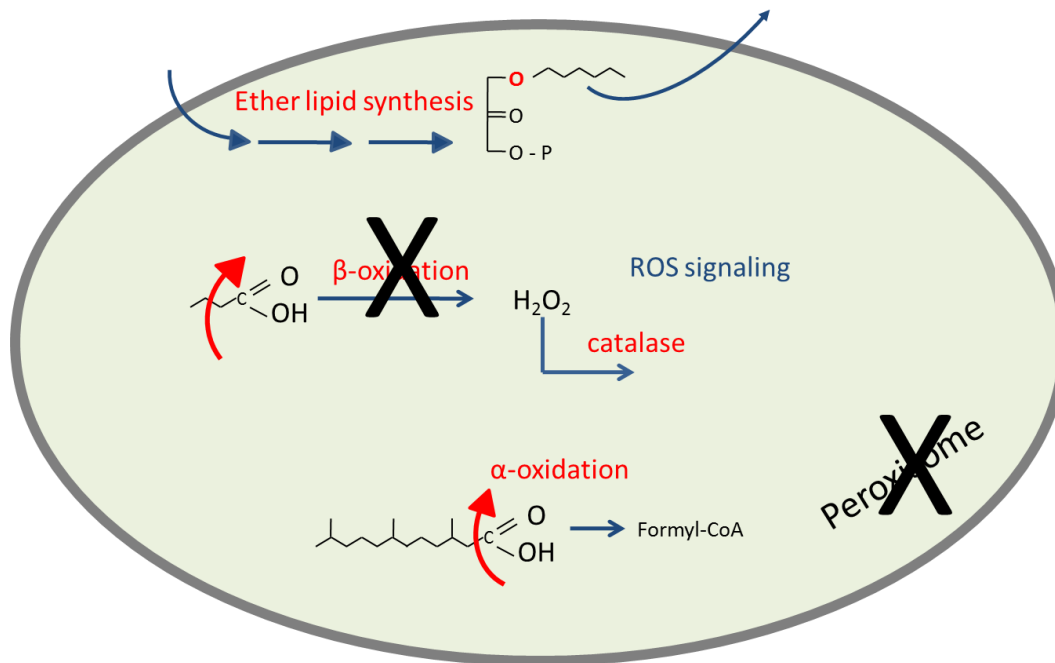
Guzenko & Strelkov (2016) Bioinformatics, pii: btw628.



Cell Metabolism

Peroxisomes: targets in rare and common diseases?

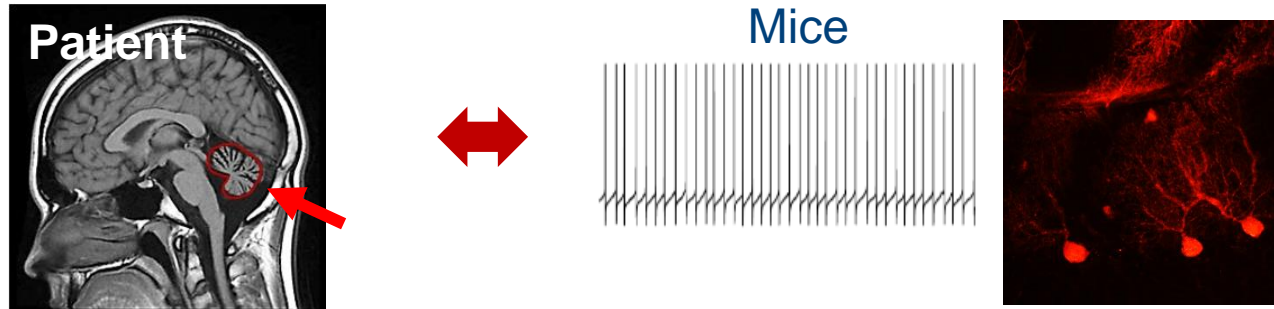
- Role in tissue functioning
- Pathogenesis using loss of function approaches in mice



Prof. Dr. M. Baes
myriam.baes@kuleuven.be

Cell Metabolism (Highlights and outlook)

- *Neurobiol of Disease, 2016* : Purkinje cell dysfunction and degeneration causing ataxia



- *Glia, 2015* : MFP2 deficiency causes neuro-inflammation



- Peroxisomes are essential in **β -cells** of pancreas : mechanisms?
- Peroxisomal β -oxidation is necessary for **retinal** integrity: mechanisms?
- **Microglia** : can manipulation of metabolism determine detrimental vs neuroprotective features?

Molecular Virology & Gene Therapy (Scientific Highlights)

Molecular Virology and drug discovery

- **A novel strategy for a functional cure of HIV infection**

(Vranckx et al., *EBiomedicine*. 2016 Jun;8:248-64.)

- **A technology platform for single virus imaging**

(Dirix et al., *Scientific Reports*, 2016)

- **MLL-LEDGF interaction as drug target for treatment of leukemia**

(Cermakova et al., *Trends Pharmacol Sci*. 2016 Aug;37(8):660-71)



Gene Therapy

- **A gene therapeutic strategy for cystic fibrosis**

(Vidovic, Carlon et al. *Am J Respir Crit Care Med*. 2016 Feb 1;193(3):288-98)



Prof. Dr. Z. Debyser

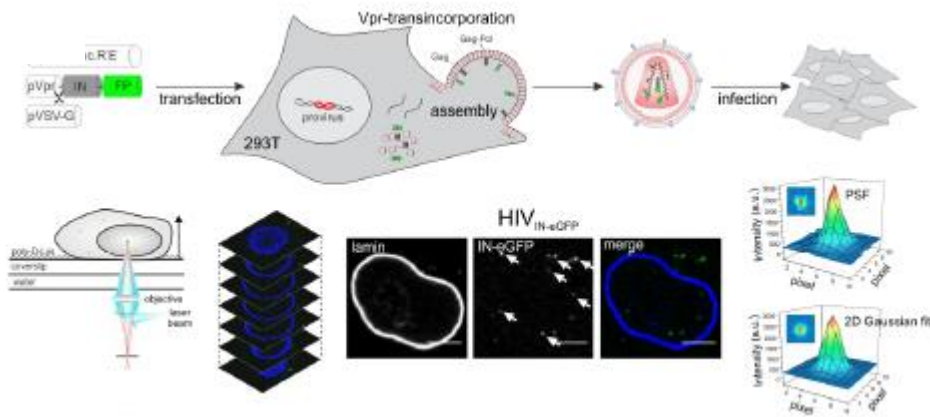
zeger.debyser@kuleuven.be

Prof. Dr. R. Gijsbers

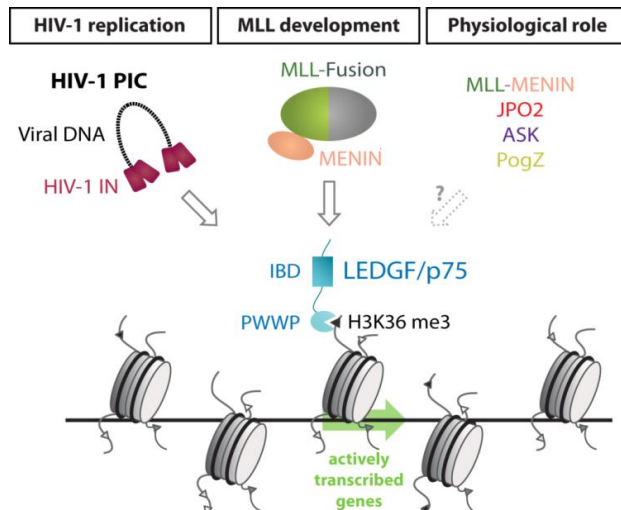
rik.gijsbers@kuleuven.be

Molecular Virology & Gene Therapy (Research lines)

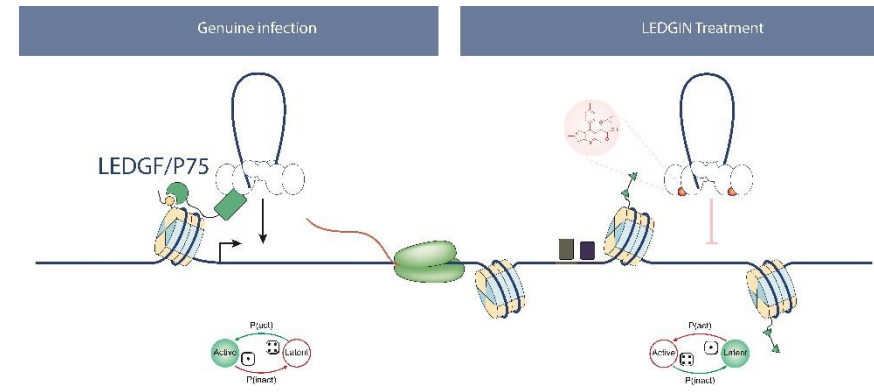
Single virus imaging of HIV



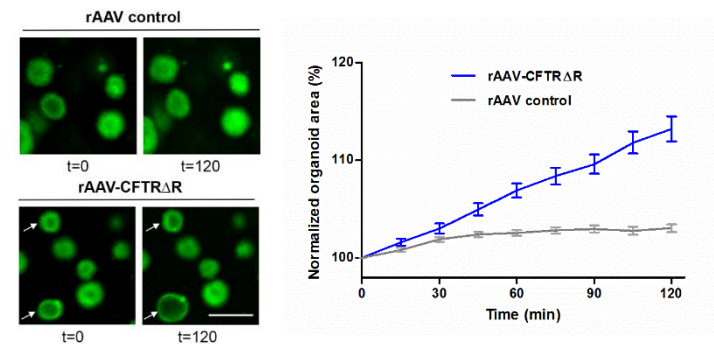
HIV points the way towards precision treatment of mixed lineage leukemia



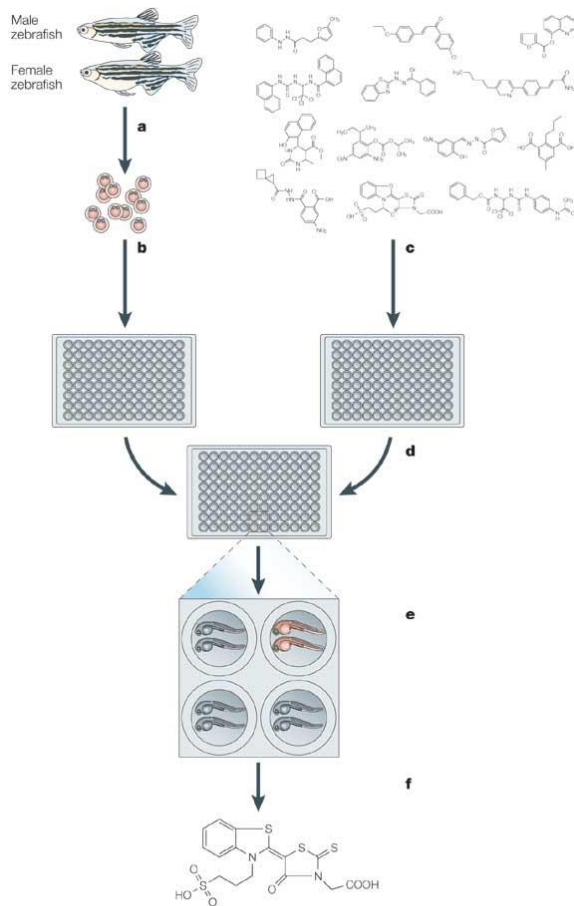
Towards a functional cure of HIV



rAAV-CFTRΔR gene transfer rescues CF phenotype in CF organoids



Molecular Biodiscovery



Nature Reviews | Drug Discovery



- zebrafish transgenic lines for toxicity testing (hepato, cardio, nephro, neuro)
- Medaka reporter line (endocrine disruption)
- zebrafish transgenic and mutant lines as models for human disease (epilepsy, kidney fibrosis, cancer immunology, viral disease)
- 66 tanks, 1200 liter

Molecular Biodiscovery

Prof. Dr. P. de Witte

peter.dewitte@kuleuven.be

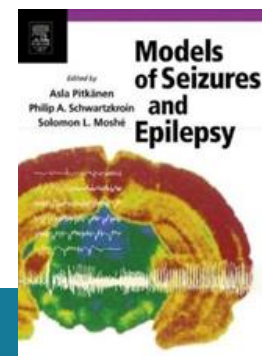


Toxicity Testing

- **Are zebrafish larvae suitable for assessing the hepatotoxicity potential of drug candidates?** (*Mesens et al, J Appl Toxicol. 2015 Sep;35(9):1017-29*)
- **Use of zebrafish larvae as a multi-endpoint platform to characterize the toxicity profile of silica nanoparticles** (*Pham et al, Scientific Reports, minor revision*)

Epilepsy models

- **Mutations in STX1B, encoding a presynaptic protein, cause fever-associated epilepsy syndromes** (*Schubert et al, Nat Genet 2014 Dec;46(12):1327-32*)
- **Gain-of-function FHF1 mutation causes early-onset epileptic encephalopathy with cerebellar atrophy** (*Siekierska et al, Neurology 2016 Jun 7;86(23):2162-70*)
- **Zebrafish models of epilepsy and epileptic seizures**
(*Copmans, Siekierska, de Witte, in print, 2nd ed, Elsevier*)



KU LEUVEN

Toxicology and Pharmacology

General Research Topics:

- Drug Discovery starting from biodiversity, marine and terrestrial organisms, including purification, structure determination, and functional assays (electrophysiology, voltage clamp)
- Structure-function research of ligands (peptides, toxins, small molecules, drugs) interacting with ion channels and receptors
- Transcriptomics of venomous animals (PCR-based)
- Peptidomimetics (cyclic peptides, miniaturized scaffolds)

Prof. Dr. Jan Tytgat
jan.tytgat@kuleuven.be



Prof. Dr. Eva Cuypers
eva.cuypers@kuleuven.be



Toxicology and Pharmacology

Scientific Highlights

- Structure-function research of ion channels and receptors
(*Nijs, M. et al., PNAS. 2016, in press*)
- Toxin bio-portides: novel generation of cell penetrating medicines
(*Kerkis, I. et al., CMLS. 2016, e-pub ahead of print*)
- Discovery of novel insecticides
(*Zhu, S. et al., Mol Biol Evol. 2016, 33(8):1907-20*)

Objectives:

- Structure-function research of ligands - ion channels and receptors
- Peptidomimetics: cyclic peptides and miniaturized scaffolds grafted with pharmacological epitopes for novel medicines

Cloud 2 – Development of therapeutics & diagnostics



Therapeutic & Diagnostic Antibodies

P Declerck
A Gils

5 ATP, ± 7 PhD, ± 4 PostDoc

Radiopharmacy

G Bormans

7 ATP, 5 PhD, 5 postdocs

Medicinal Chemistry

P Herdewyn
A Van Aerschot
M Froeyen
J Rozenski
E Lescrinier

3 ATP, ± 20 PhD, ± 15 PostDoc

Therapeutic & Diagnostic Antibodies

Mission: generation of monoclonal antibodies (Mabs), antibody derivatives, nanobodies and diabodies and application as either therapeutics or diagnostics

Research topics:

1. Increasing fibrinolysis

- increased concentrations of **PAI-1** and **TAFI** = decreased fibrinolysis
- development and application of **immunoassays** to measure PAI-1 and TAFI
- generation, production & characterization of an anti-PAI-1/anti-TAFI diabody as a **therapeutic** to increase fibrinolysis



Prof. Dr. Paul Declerck – Dean – paul.declerck@kuleuven.be

2. drug monitoring and immunogenicity of therapeutic antibodies

- development and application of **immunoassays** to **monitor drug concentration** of therapeutic antibodies in the serum of patients
- characterization of **biosimilars**.



Prof. Dr. Ann Gils – ann.gils@kuleuven.be

3. antibody gene transfer

- development of a DNA-based platform for the *in vivo* expression of therapeutic antibodies.

Therapeutic & Diagnostic Antibodies

Pharmabs: spinn-off

Innovation, incubation and valorisation platform on
antibody development founded 2009

Therapeutic antibody development
& Antibody-based diagnostics

EU H2020 Projects and Industrial projects

Outlook:

- Develop a selected diabody as a therapeutic profibrinolyticum
- Sustain the collaboration with diagnostic companies to produce CE-labelled diagnostics & implement TDM in clinical practice
- Grow the Antibody Gene Transfer Program, and launch dedicated spinoff

Radiopharmacy

Mission: development, preclinical validation and translation to clinical use of diagnostic and therapeutic radiopharmaceuticals

Research topics:

1. small molecule based PET radiotracers

neuroinflammation	endocannabinoid system
TSPO, P2X7, GPR-84, CB2, ...	CB2, MAGL, FAAH,...
misfolded proteins	
amyloid, tau, ...	
epigenetic targets	ion channels (M Schönberger)

2. biomolecule based radiotracers

This research focuses on the development, validation and translation to the clinic of **PET tracers based on biomolecules** (peptides, nanobodies, affibodies, antibodies).

- New methodology that allows room temperature radiolabeling using Al18F chelation.
- Application of PeptIns (peptides directed to aggregation-prone regions on proteins) as a new generic platform for visualisation of protein expression .

Radiopharmacy

MIRaCLE

State of the art platform for translational PET research



GMP accredited
production lab

preclinical

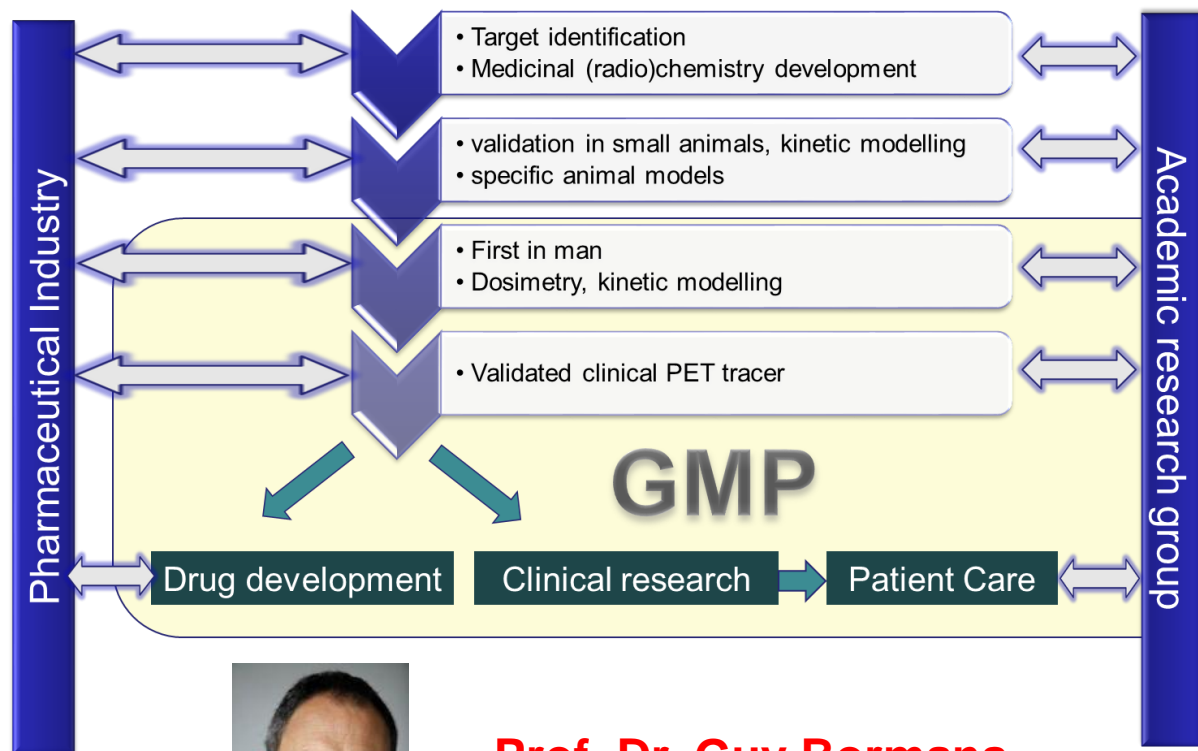


clinical



PET/MR scanners

>15 first in man studies of
novel PET tracers



Prof. Dr. Guy Bormans
guy.bormans@kuleuven.be

KU LEUVEN

Medicinal Chemistry

Mission: transdisciplinary research focusing on lead finding, lead optimization and structure-activity relationships studies on compounds to be used as therapeutics or diagnostics; synthetic biology and directed evolution

Medicinal Chemistry Team - January 2019 status

- 6 Group Leaders
- 14 Postdoctoral researchers
- 20 PhD students
- 3 Support staff

- Combined **38 papers cited more than 100 times**
- **Over EUR 7M in research funding** generated in the last 10 years
- Successful supervision of **26 PhD students**, including many international students in the last 10 years

mathy.froeyen@kuleuven.be

Research Themes

Applied Organic Chemistry



- Small molecules
- Nucleosides
- Oligonucleotide Therapeutics (aptamers)
- XNAs
- tRNA synthetases

piet.herdewijn@kuleuven.be
arthur.vanaerschot@kuleuven.be
Emeriti: 2019 + 2022

- Drug design

Molecular Modelling Computational Chemistry



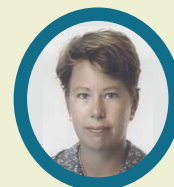
Mass Spectrometry Analytical Chemistry

- Drug metabolism
- RNA modifications
- Electrochemistry



eveline.lescrinier@kuleuven.be

NMR



- Biomolecular NMR (proteins & nucleic acids)
- Structure-based design
- Small molecule characterization

Synthetic Biology



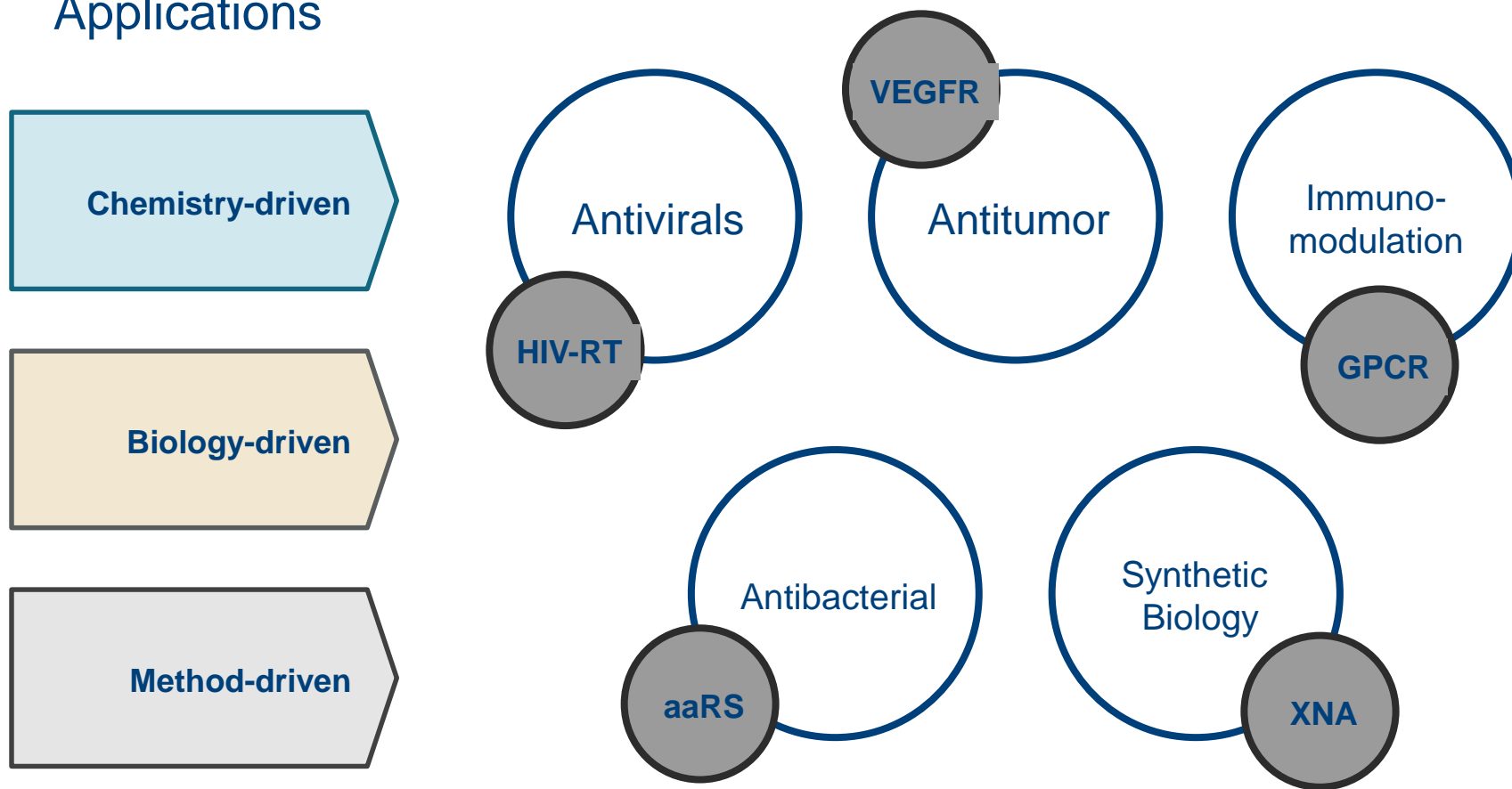
- Directed evolution
- Molecular Biology

vitor.pinheiro@kuleuven.be
jef.rozenski@kuleuven.be

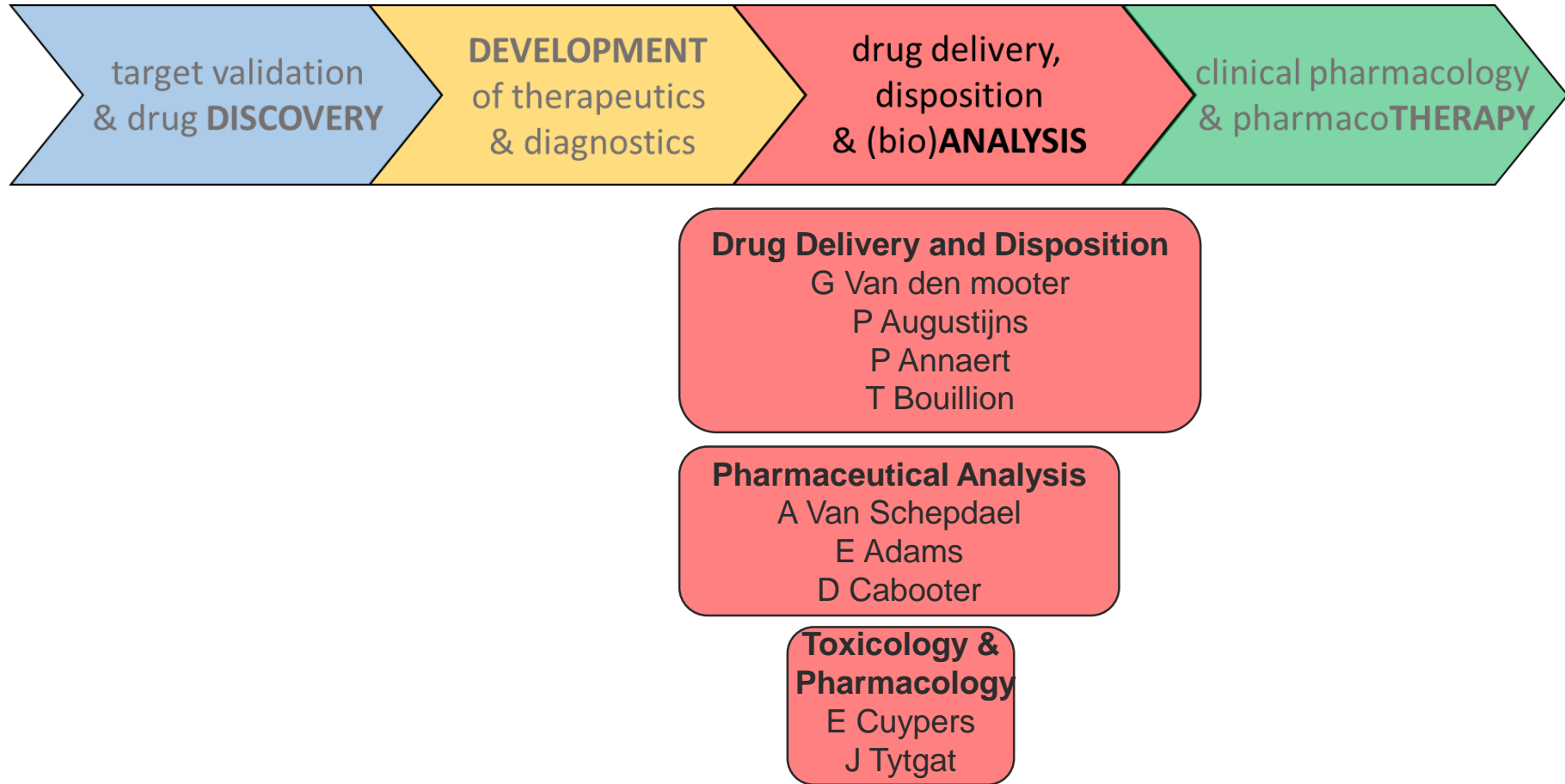
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Medicinal Chemistry

Applications



Cloud 3 – Drug delivery, disposition and (bio)analysis

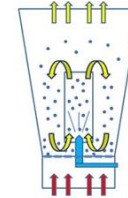
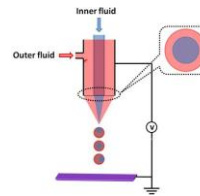
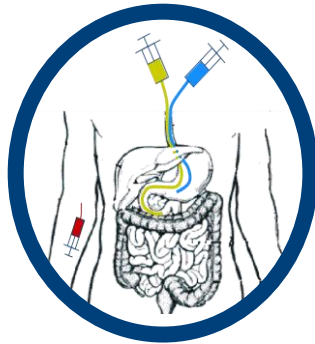


Drug Delivery and Disposition



**Patrick
Augustijns**

patrick.augustijns@kuleuven.be



**Guy Van den
Mooter**

guy.vandenmooter@kuleuven.be

✓ General Research Topics:

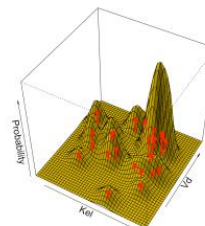
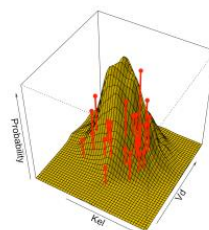
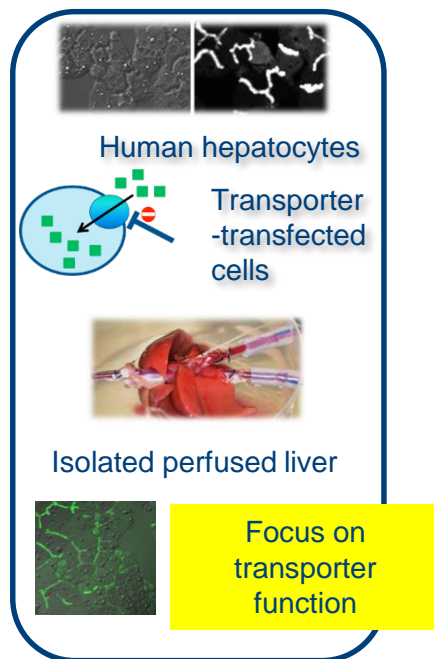
- ✓ **Intestinal drug disposition:** Exploring intestinal drug and formulation behavior using a unique intestinal sampling technique
- ✓ **Pharmaceutical technology – physical pharmacy:** API characteristics and formulation parameters; amorphous solid dispersions; coated nanocrystals; mAb; mesoporous silica

Drug Delivery and Disposition



**Pieter
Annaert**

pieter.annaert@
kuleuven.be



**Thomas
Bouillon**

thomas.bouillon@kuleuven.be

✓ General Research Topics:

- ✓ **Hepatic drug disposition – hepatotoxicity:** focus on transporter function; PBPK modeling; prediction and simulation of drug exposure
- ✓ **Pharmacometrics:** PKPD relationships; transition from parametric to nonparametric methods --> optimal dose as ultimate target of modeling efforts

Pharmaceutical analysis



**Ann Van
Schepdael**

ann.vanschepdael@kuleuven.be

Advances in Capillary Electrophoresis

- **On-line screening of enzyme inhibitors**
 - Electrophoretically mediated microanalysis (EMMA)
 - Capillary electrophoresis coupled to ESI mass spectrometry
 - Development of immobilized enzyme reactors based on magnetic nanoparticles

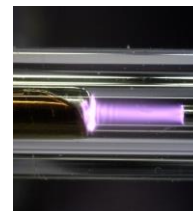
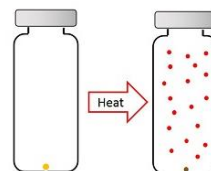


Erwin Adams

erwin.adams@kuleuven.be

Improved sampling and detection in GC analysis

- Full evaporation technique and thermal desorption
- New detection concept based on a microplasma
- Analysis of aqueous samples, high boiling RS, halogenated VOCs,...as impurities in drugs



KU LEUVEN

Pharmaceutical analysis

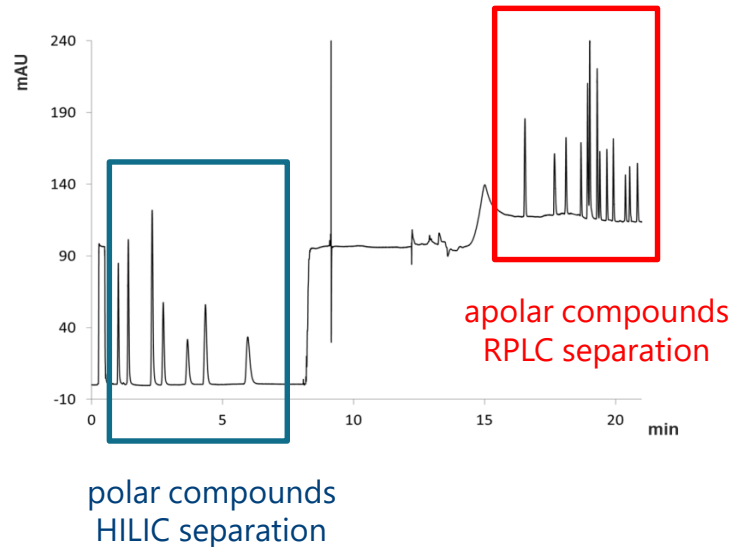


**Deirdre
Cabooter**

deirdre.cabooter@kuleuven.be



- **Novel hardware solutions for the analysis of complex samples**
 - Coupling highly orthogonal columns in series to separate polar & apolar compounds
 - Development of innovative mixing unit for online solvent exchange
 - Applications in environmental, pharmaceutical, bio-analysis...



Toxicology and Pharmacology

➤ PI's:



Jan Tytgat

jan.tytgat@kuleuven.be



Eva Cuypers

eva.cuypers@kuleuven.be

➤ General Research Topics:

- Discovery of buried cadavers using detection and analysis of volatile decomposition compounds
- The use of color tests for new generation psychoactive substances
- Alternative matrices and task-specific ionic liquids in Postmortem Forensic Toxicology
- Imaging mass spectrometry on hair
- Medical and forensic mass spectrometry imaging

Advances in human decomposition

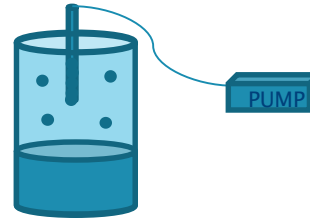
✓ TD-GC/MS: Method development and validation

Anal Bioanal Chem (2014) 406:3611–3619
DOI 10.1007/s00216-014-7741-8

RESEARCH PAPER

Development and validation of a new TD-GC/MS method and its applicability in the search for human and animal decomposition products

E. Rosier · E. Cuypers · M. Dekens · R. Verplaetse ·
W. Develter · W. Van de Voorde · D. Maes · J. Tytgat



✓ Human versus animal decomposition

PLOS ONE

RESEARCH ARTICLE

The Search for a Volatile Human Specific Marker in the Decomposition Process

E. Rosier¹, S. Loix¹, W. Develter², W. Van de Voorde², J. Tytgat¹, E. Cuypers^{1*}

¹ Department of Pharmaceutical and Pharmacological Sciences, Toxicology and Pharmacology, University of Leuven (KU Leuven), Leuven, Belgium; ² Imaging & Pathology Department, Division Forensic Biomedical Sciences, University of Leuven (KU Leuven), Leuven, Belgium

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Contents lists available at ScienceDirect

Forensic Science International

journal homepage: www.elsevier.com/locate/forensi



Time-dependent VOC-profile of decomposed human and animal remains in laboratory environment

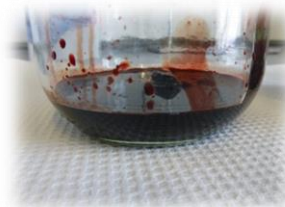
E. Rosier^a, S. Loix^a, W. Develter^b, W. Van de Voorde^b, J. Tytgat^a, E. Cuypers^{a,*}

^a Department of Pharmaceutical and Pharmacological Sciences, Toxicology and Pharmacology, University of Leuven (KU Leuven), Campus Gasthuisberg, O&G2, PO Box 922, Herestraat 49, 3000 Leuven, Belgium

^b Imaging & Pathology Department, Division Forensic Biomedical Sciences, University of Leuven (KU Leuven), Campus Sint-Rafaël, Kapucijnenvoer 33, 3000 Leuven, Belgium



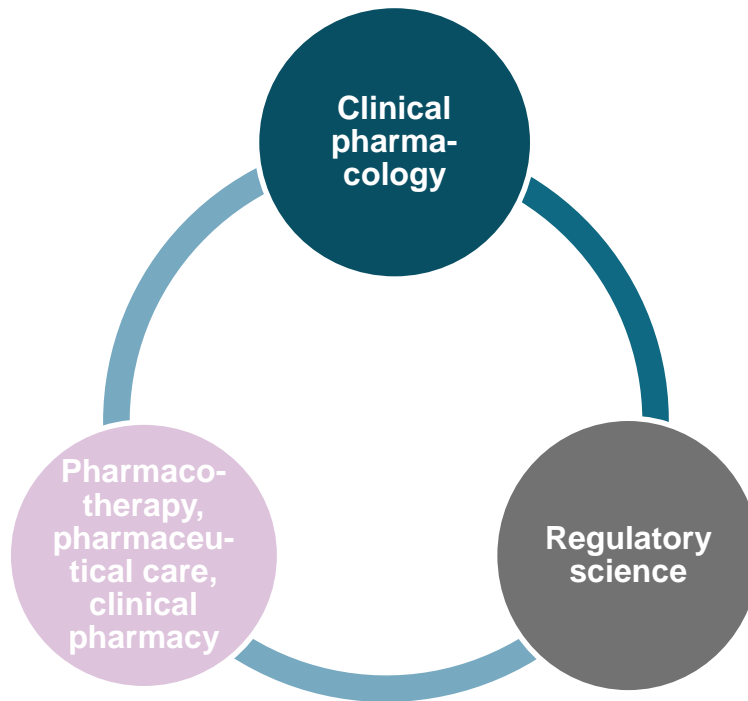
✓ Blood versus tissue



KU LEUVEN

Clinical Pharmacology & Pharmacotherapy

Bridging the gap from molecule to man



Clinical Pharmacology & Pharmacotherapy

M Casteels
J de Hoon
K De Nys
V Foulon
I Huys
S Simoens
I Spriet
C Vandermeulen

Clinical Pharmacology



Jan de Hoon

jan.dehoon
@uzleuven.be



Minne Casteels

minne.casteels@kuleuven.be

- clinical trial activities and clinical drug development,
- involving mainly healthy subjects or well-defined patient populations,
- with an emphasis on research activities in the exploratory phase (phase 0, phase Ia, phase Ib studies)
- special interests:
 - target-engagement biomarker development
 - CNS compounds / PET studies / microdosing
 - pain / analgesics
- GMP certified facilities since 2013
- Important societal roles:
 - Membership of EMA Scientific Advice Working Party (SAWP) and Committee on Herbal Medicinal Products
- Chair of Belgian Drug Reimbursement Committee

Regulatory Science

- regulatory and legal aspects of the development and market access of medicinal products, diagnostics and treatment strategies
- health economic aspects of medicinal products
- Expertise center on regulatory science topics, advising (inter)national authorities and other institutions
- Several chairs funded by industry (generics, biologics, biosimilars); various EU and IMI participations



isabelle.huys@kuleuven.be



steven.simoens@kuleuven.be

Pharmacotherapy, Pharmaceutical Care, Clinical Pharmacy

- **Pharmacotherapy:** with focus on the **rational, efficient and safe use of medicinal products in daily patient care** (both ambulatory and hospital setting).
- **Pharmaceutical Care / Clinical Pharmacy:** exploring the role of the pharmacist in the rational use of medicinal products in the ambulatory setting as well as in the hospital.
- Leadership role in developing the role of the pharmacist in research and teaching in Belgium.
- Many opportunities for collaboration around clinical PK/PD research in University Hospitals Leuven.
- Large involvement in society / committees, taking leading roles.



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Hospital

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KU LEUVEN

Clinical Pharmacology & Pharmacotherapy:

From research to societal relevance – a brief overview

- Membership of EMA Scientific Advice Working Party (SAWP) and Committee on Herbal Medicinal Products (HMPC)
- Chair of Belgian Drug Reimbursement Committee
- Chair of Belgian Chamber of Pharmacists
- Chair of Ethics committee UZ KU Leuven/Research
- Past Chair of European Society for Clinical Pharmacy (ESCP)
- Past Secretary of Pharmaceutical Care Network Europe (PCNE)
- Membership of BBMRI-ERIC (European Biobank Network) ELSI (ethical-legal-social) Board
- Membership of the Superior Health Council



LONDON

UCL School of Pharmacy ULLA – ExCo Parma 2019:

Research 2010

Michael Heinrich

Research Group

'Pharmacognosy and
Phytotherapy'

UCL School of Pharmacy,
Univ. London

29 - 39 Brunswick Sq.

London WC1N 1AX



London
02/03/2018

- Created in 1842 as the “School of Pharmacy of the Pharmaceutical Society of Great Britain”
- In 1926, it was incorporated into the University of London and was known as the School of Pharmacy, University of London (“The Square”)
- A very special School – not just in terms of achievements but also in terms of flagship status and professional outreach
- Since 2012 part of University College London
- Currently rated 7th in world for pharmacy and pharmacology (both QS and Shanghai)

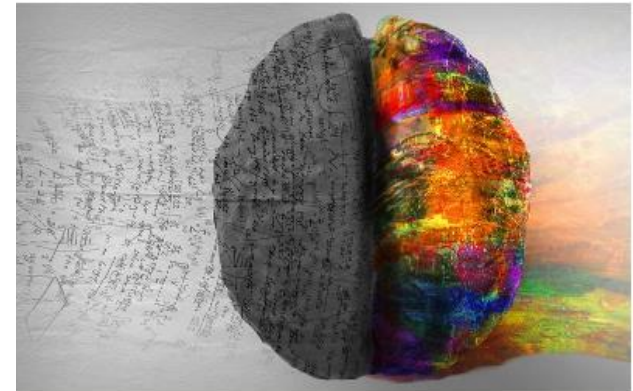




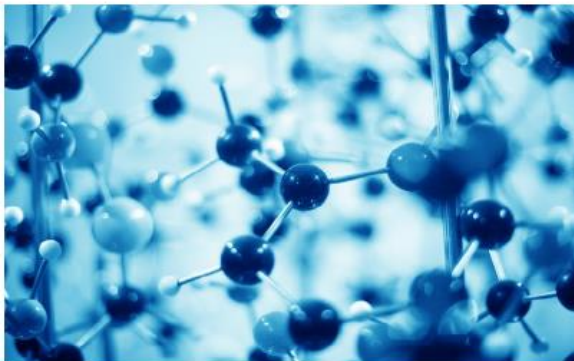
**Age-Related Medicines
Development And Use**



**Drug Discovery And
Therapeutic Target
Identification**



Translational Neuroscience



**Fabrication And Synthetic
Technologies For Advanced
Drug Delivery**



**Medicines Use And
Optimisation**



**Pharmacoepidemiology And
Medication Safety**

Age Related Medicines Development and Use

- Age appropriate formulation design (Orodispersibles, Multiparticulates, Taste masked formulations)
- Fixed dose combinations
- Age and gender related oral biopharmaceutics
- Preventive interventions (herbal substances)

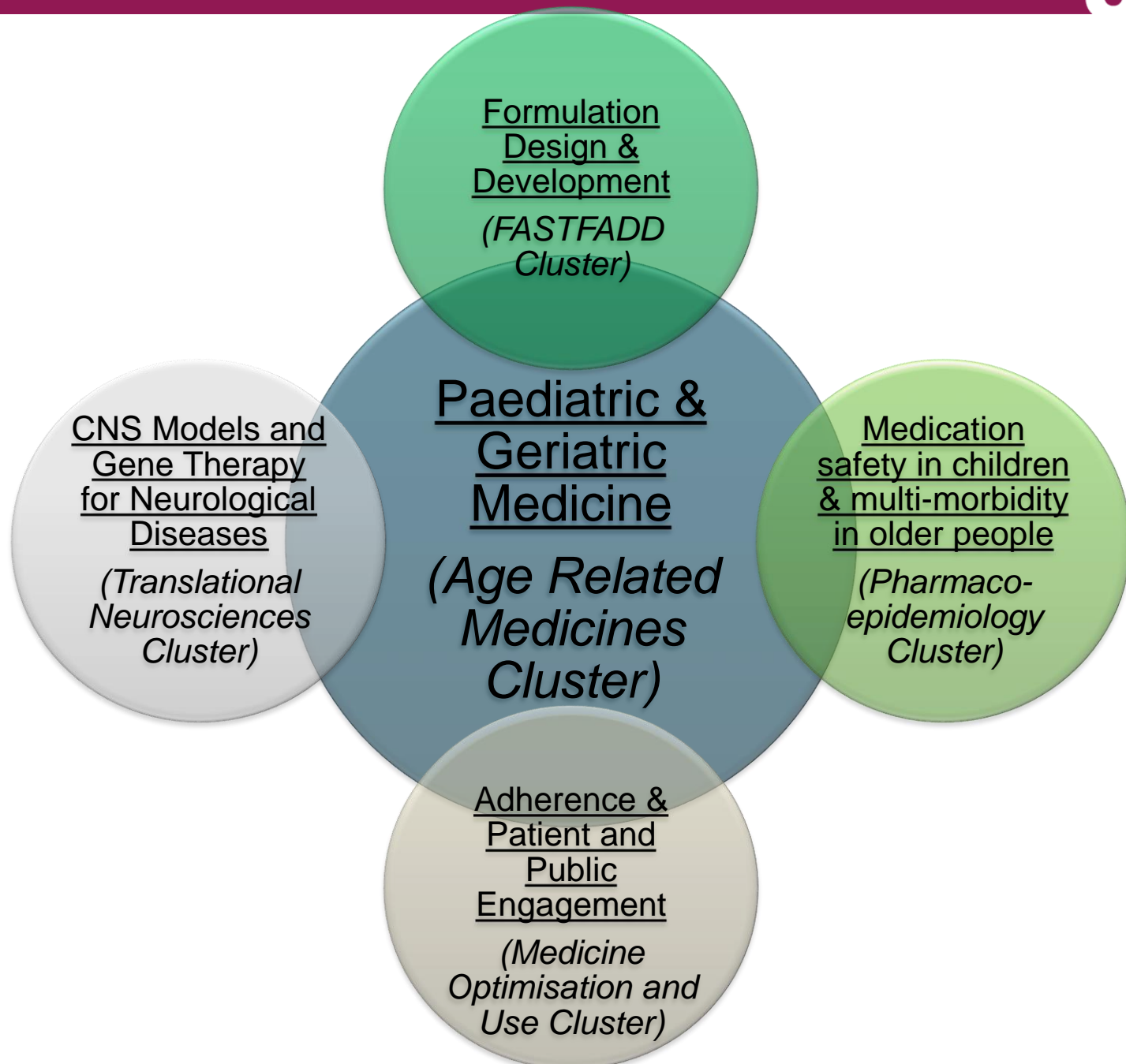
Formulation Development & Biopharmaceutics

Formulation Testing

- In vitro sensory evaluation of formulations
- Brief Access Taste Aversion (BATA) model
- Human panel studies

- Pharmacometrics and paediatric PKPD modelling
- Dose rationale and clinical trial design for novel therapeutic interventions in special populations, paediatrics, geriatrics and rare diseases

Clinical Pharmacology & Translational Research



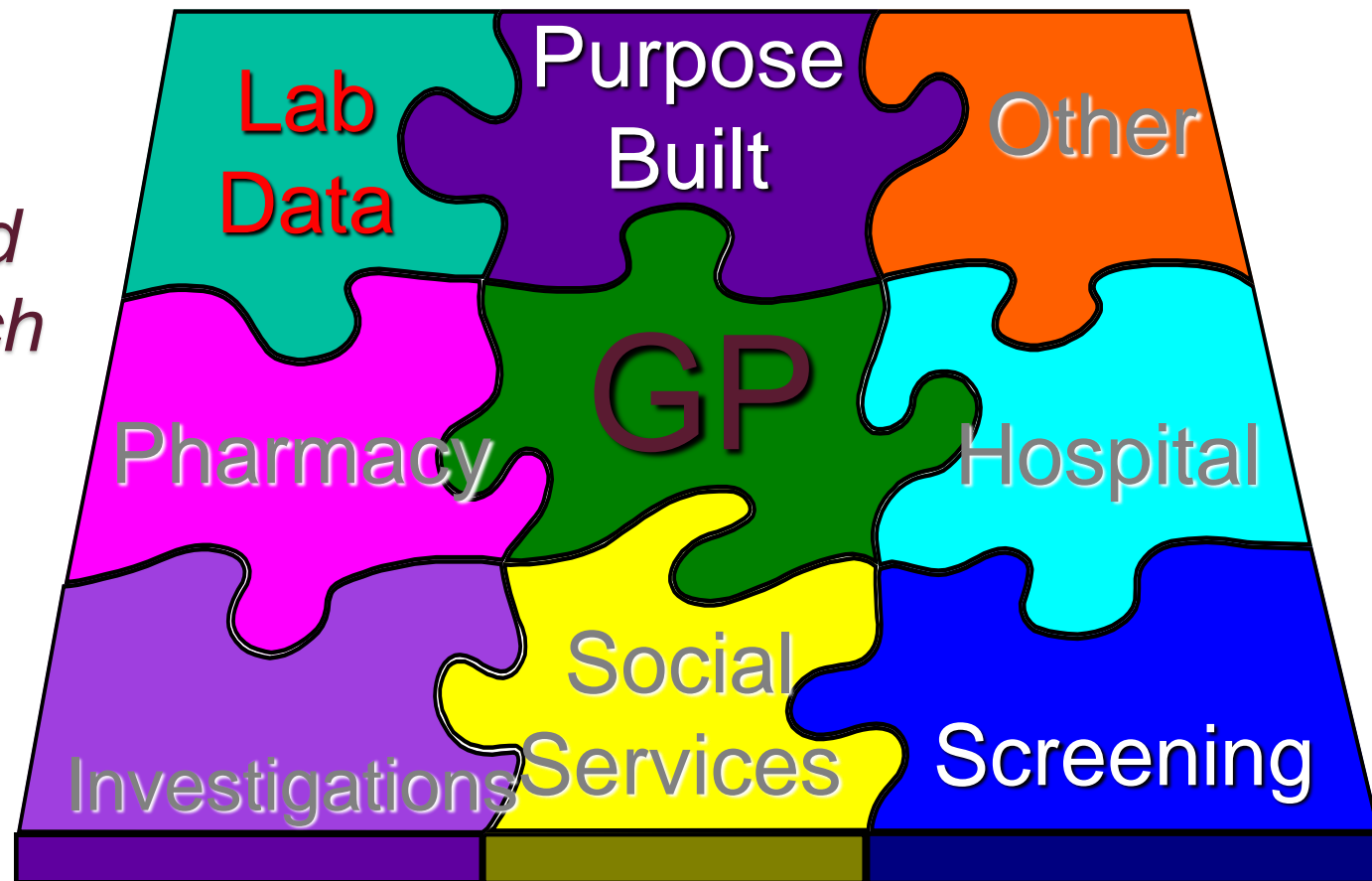
Projects (recently completed & ongoing)

- Assessing the taste of medicines with the rat “BATA” model; insight into the physiological aspect of taste
- Effective administration of multiparticulates to paediatric patients
- Advanced Therapeutics for Parkinson’s Disease Using Cell and Tissue Engineering and Biomaterials Technology
- Development of 3D printing technology for in-situ verification of dose
- Biopharmaceutics of excipients in paediatric medicines
-

Pharmacoepidemiology and medication safety

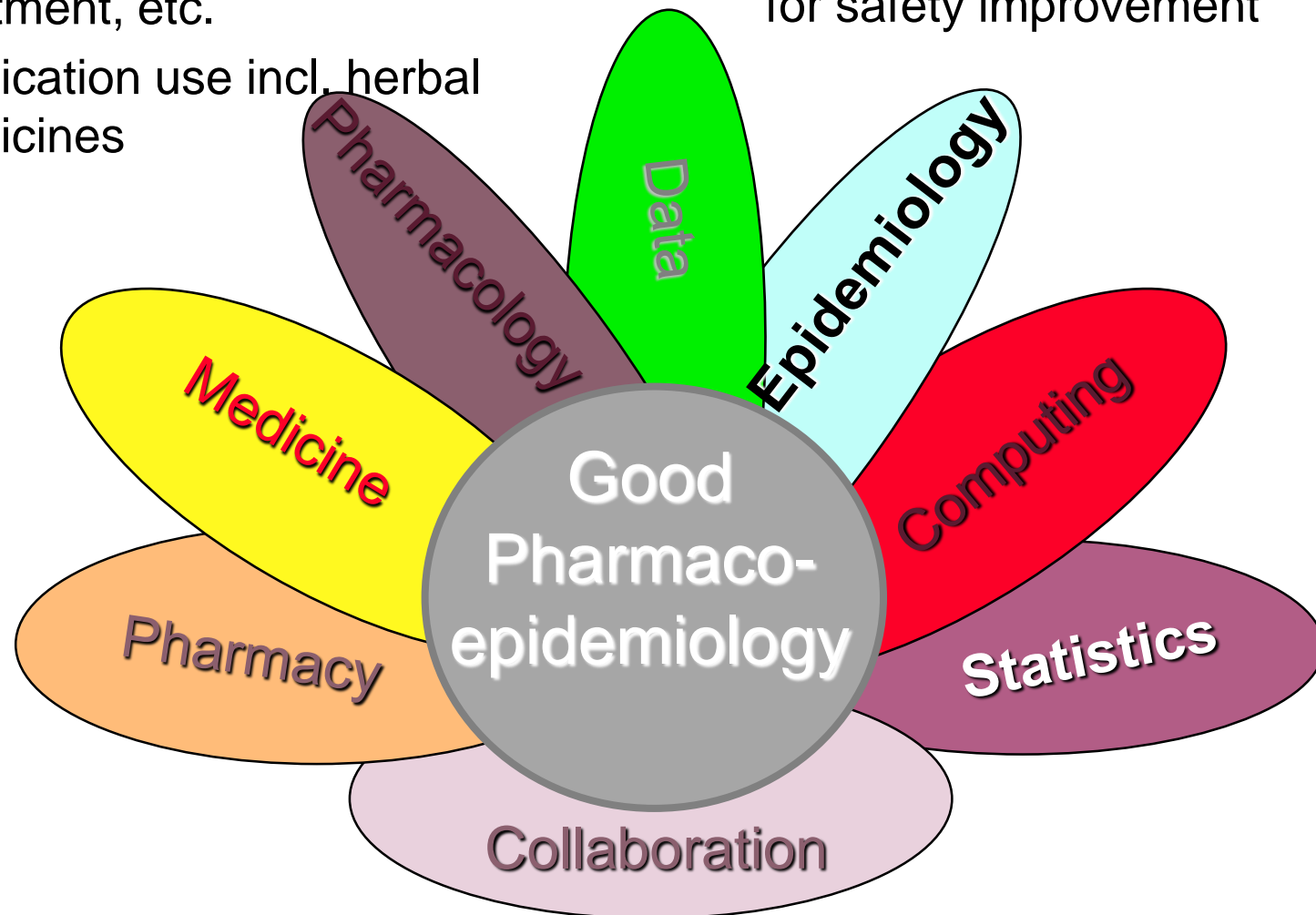
Informing and influencing policies to improve
safety and benefit outcomes in the use of
medicines

*through
record-linked
data research*



Research focus

- Cardiovascular disease, diabetes and mental health disorders and treatment, etc.
- Medication use incl. herbal medicines
- Medication errors and evaluation of pharmacy practice and technologies for safety improvement



Quality and safety of medicines, herbal medicines and related substances

Key c **Tweets**

Tweets & replies

Media

erns

 UCL Fight The Fakes Retweeted



Oksana Pyzik @OksanaPyzikUCL · 19h

Great to meet with passionate professionals in #politics #healthcare & #tech dedicated to improving #healthsystems & #patientsafety at @EUParl_EN 🙌
Mike Isles ED of @ASOP_Europe keep fighting the good fight 🌟 @FightTheFakes @EU_Health @GiraudSylvain @School_Pharmacy @IAPOvoice



Vytenis Andriukaitis, José Inácio Faria, Aaron C and 7 others



Tomat



Potatoes



Rice



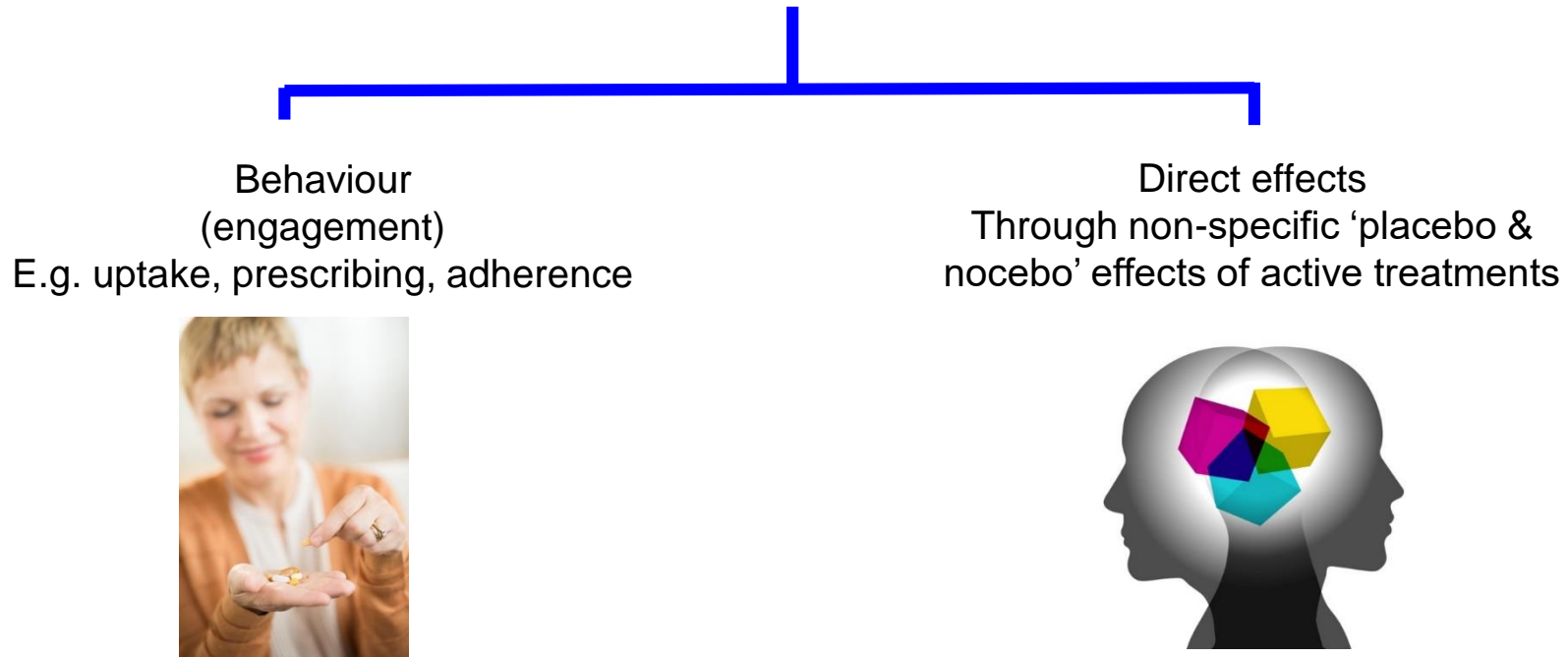
Simvastatin



Codeine

Medicines Use And Optimisation / Behavioural Medicine

Creating new knowledge to make healthcare more efficient and sustainable by understanding and addressing the psychosocial and behavioural factors explaining variation in response to treatment.



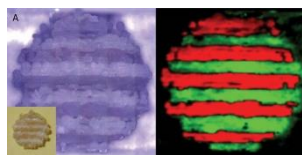
Research programme

- Arrange of validated assessment tools for quantifying patients' perspectives of illness and treatment
- Application of these tools in explanatory studies has identified the key modifiable determinants of treatment engagement (initiation, adherence and persistence) across long-term conditions
- This has informed the development of pragmatic interventions to help get the best form treatments by changing behaviour optimising engagement
- We have recently developed a new programme of research examining the behavioural aspects of antimicrobial stewardship
- Research has impact informing national treatment guidelines and the NHS New Medicines Service. UCL-Business spinout company applying research into practice



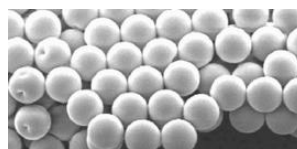
Fabrication & Synthetic Technologies for Advanced Drug Delivery

Pharmaceutical technologies



Macro

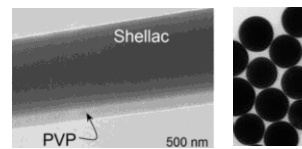
3D printing
Inkjet printing
Crystal engineering
Hot melt extrusion
Tablets/minitables
Coating technologies
Liquid formulations



Micro

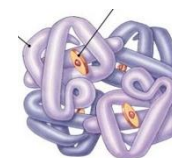
Spray drying
Emulsions
Suspensions

Electrospraying
Nano-in-micro formulations



Nano

Self-assembly
Electrospinning
Inorganic NPs



Molecular engineering

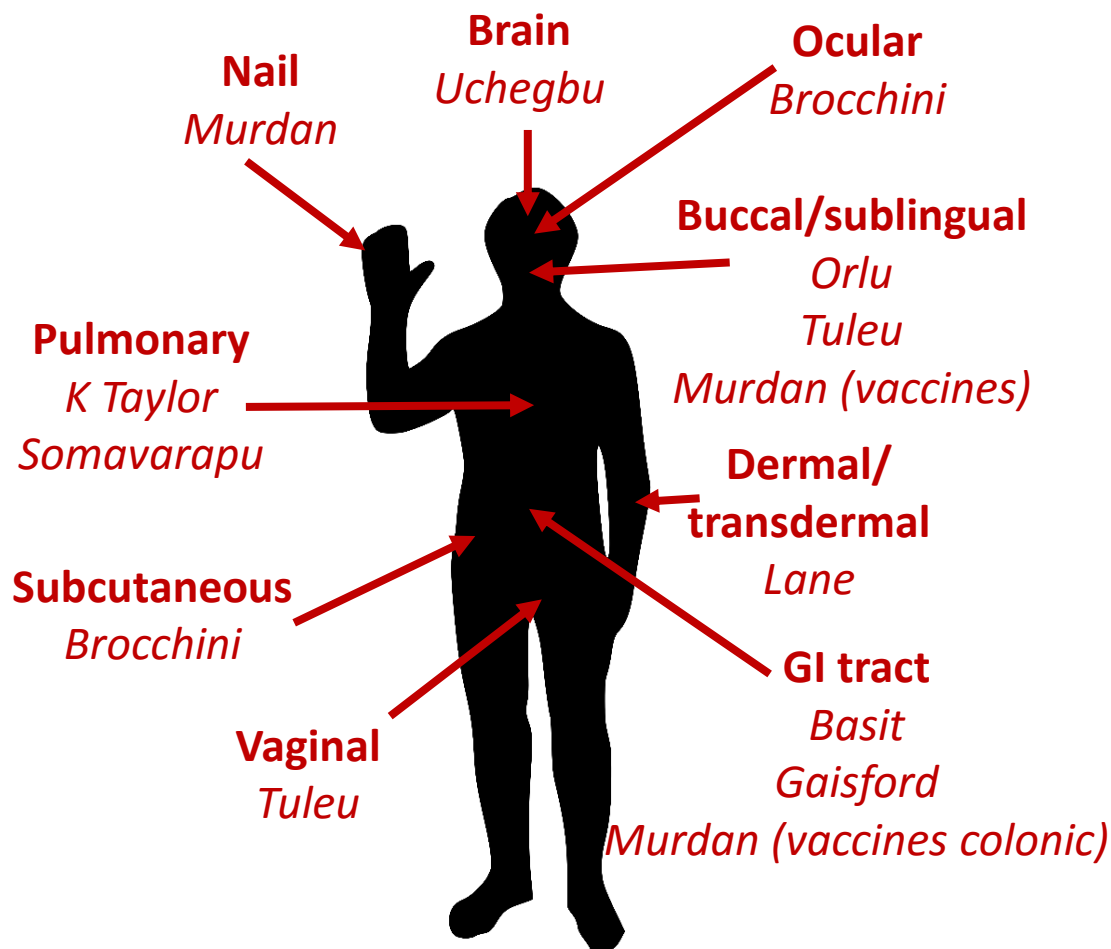
Novel polymers
Protein mimics/conjugates

Materials characterisation

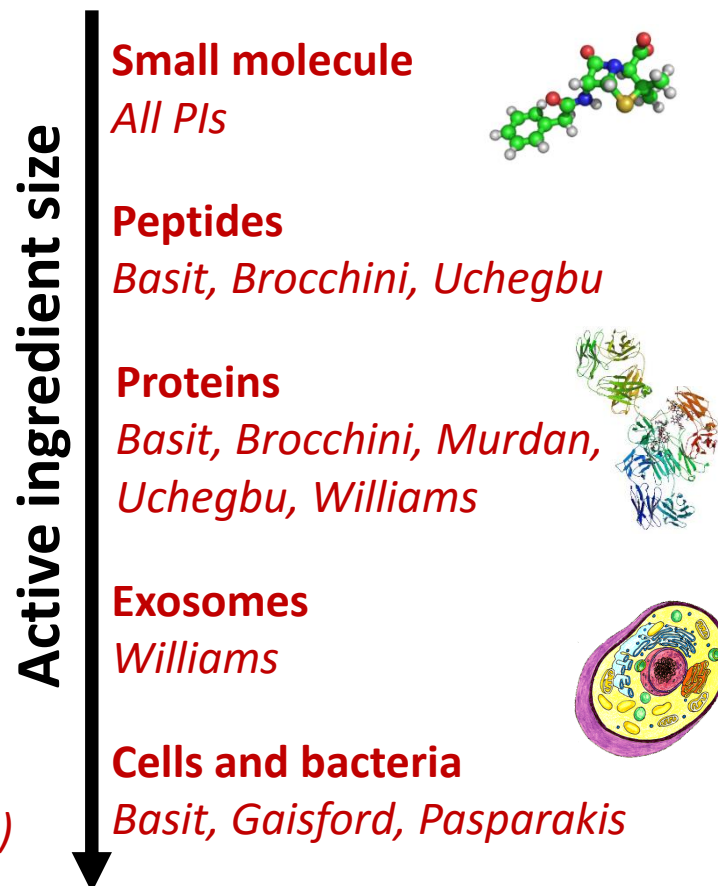
Full gamut of techniques available. Particular expertise in thermal methods, synchrotron X-ray diffraction, electron and derivatised atomic force microscopies, hyphenated approaches, dissolution testing, IVIVC, protein binding, surface analysis

Fabrication & Synthetic Technologies for Advanced Drug Delivery

Routes of administration



Formulation development



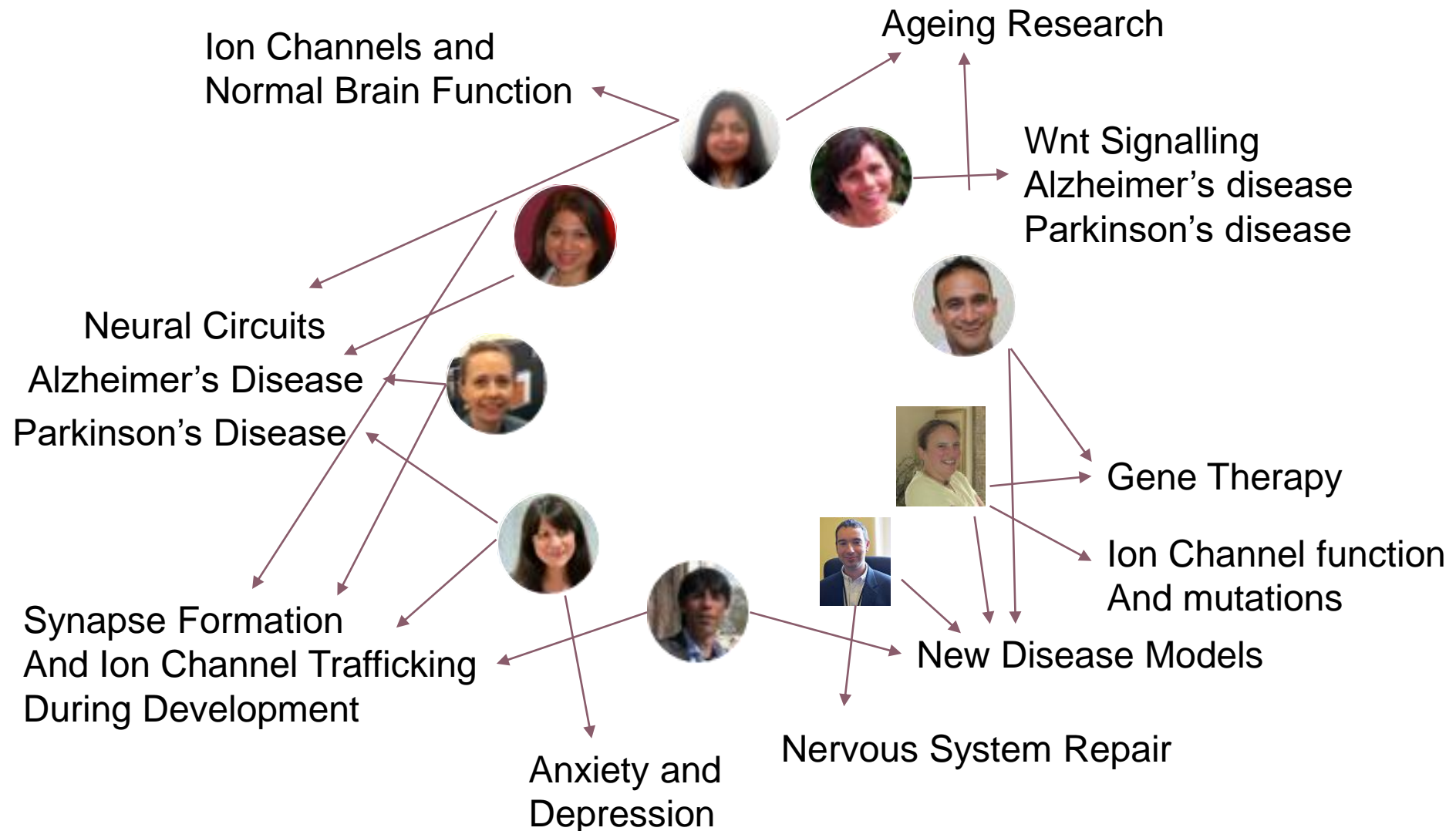
Translational Neuroscience Cluster

Aims

- 1) Understand normal brain function,
- 2) Uncover the fundamental causes of neurological and psychiatric diseases
- 3) Identify novel therapeutic targets for their treatment.



Translational Neuroscience people



Stephanie Schorge - Gene therapy for the treatment of epilepsy

1% of population suffers from epilepsy, of which 25-30% have no effective treatment

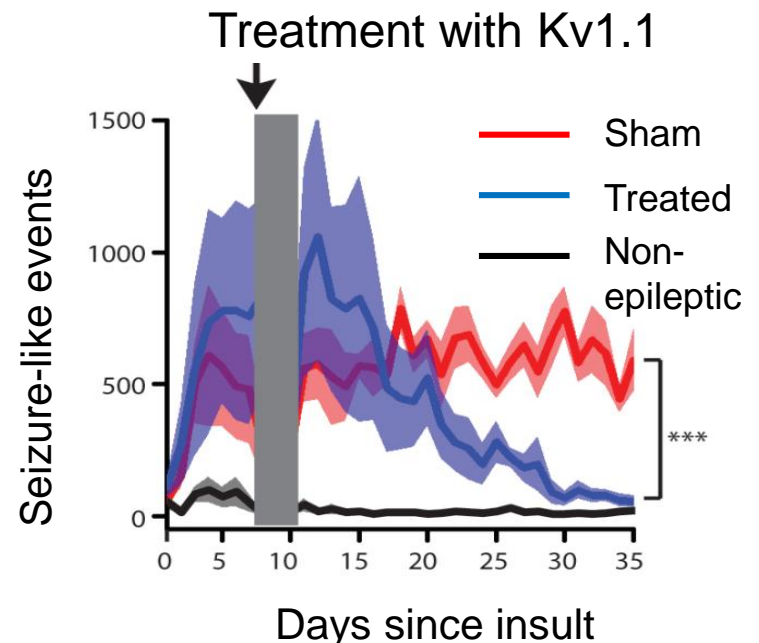
Surgery for refractive epilepsy is dangerous and highly invasive

Gene therapy can be used even for non-genetic epileptic conditions – may be used to manipulate neuronal excitability

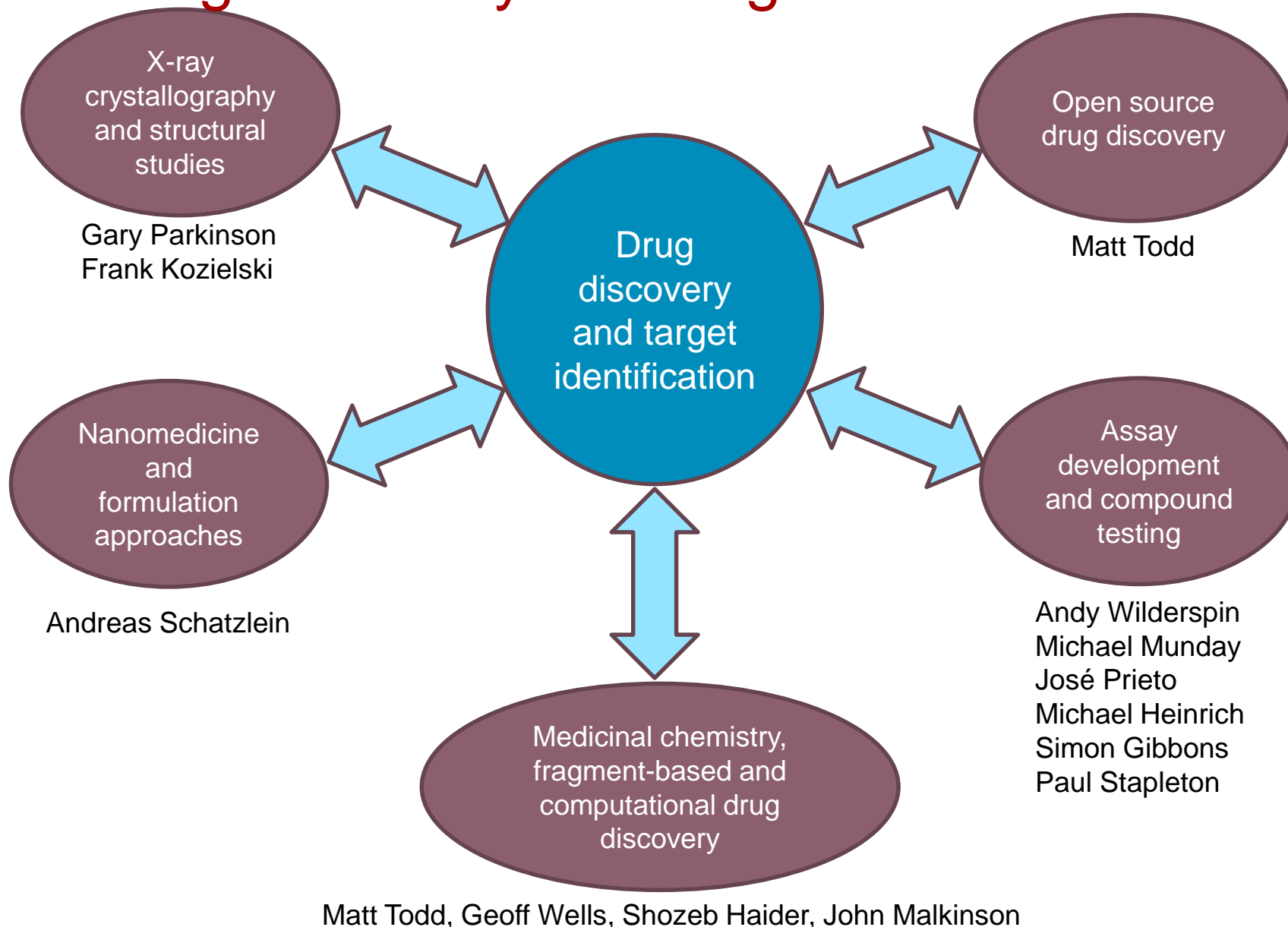
In the animal study, the rat seizures were effectively eradicated (cured?)

Stephanie has been awarded £1.9m by MRC to develop first human trial of this approach

Kätzel et al Chemical-genetic attenuation of focal neocortical seizures. Nat Commun. 2014 May 27;5:3847.



Drug discovery and target identification

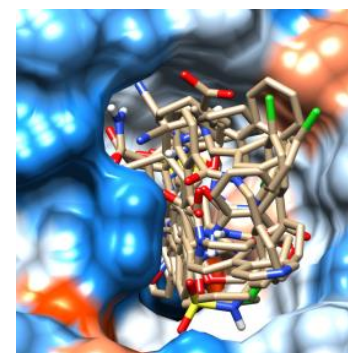
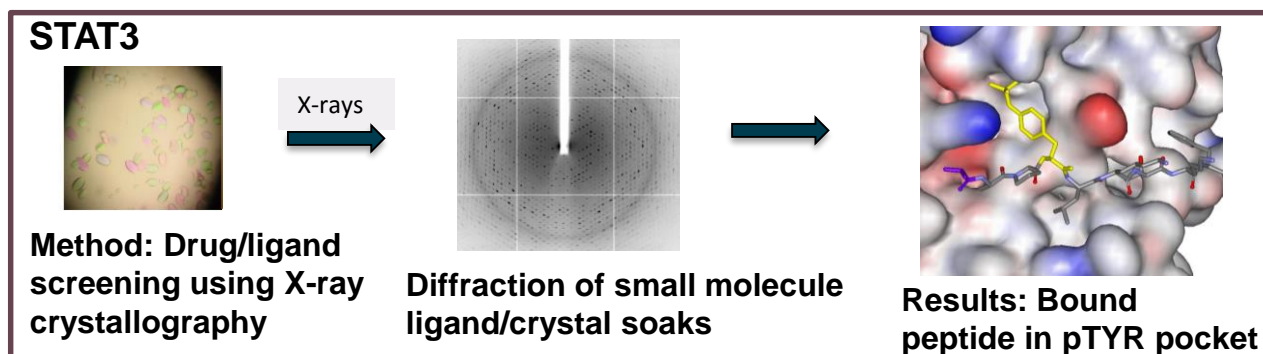


Drug Discovery and Target Identification Therapeutic Focus

Antimicrobial targets e.g. malaria, antibiotic resistance, diabetes (natural products)

Cancer drug discovery e.g. kinesin drug targets, transcription factor targets including STAT3, and Nrf2

Targeted delivery of peptides and small molecules using nanoscale approaches



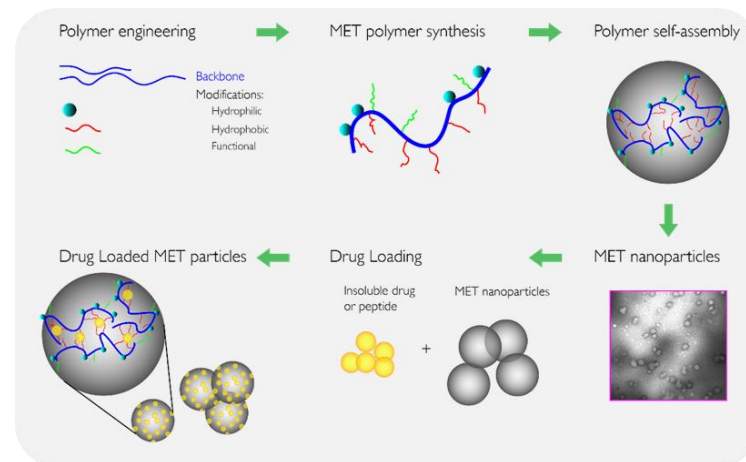
OS M OPEN SOURCE MALARIA
Looking for New Medicines

Also Check Out

- Lab Notebook
- Project Wiki

Catch us on the Daily Show?
If you're here to see more about the **Breaking Good** project, as featured on the Daily Show
[Click here!](#)

The Open Source Malaria project is trying a different approach to curing malaria. Guided by open source



Mat Todd – open source drug discovery

Award winning pioneer of new approach to synthesis and discovery

Principle is that data and ideas are shared via a virtual community. New synthetic routes or new molecules can be developed via a coordinated shared lab book approach




Major initiatives in malaria, tuberculosis but as a model can be applied very widely indeed



NOVEMBER 30 2016

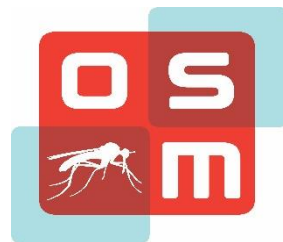
SAVE PRINT LICENSE ARTICLE

Sydney schoolboys take down Martin Shkreli, the 'most hated man in the world'

 Marcus Strom  




Dylan Siow-Lee holding about \$150,000 worth of Daraprim if sold in the US market. Photo: Nic Walker




Open Source
Malaria
Twitter: @O_S_M


MycetOS
Twitter @MycetOS
#OpenScience


Mycetoma
Neglected fungal/bacterial disease that leads to disability and stigma and has no effective treatment


PURPOSE
Develop new medicine to treat fungal mycetoma (eumycetoma) using an Open Pharma approach


CONCEPT



VIRTUAL COMMUNITY
Invite the scientific and global health community to contribute


OPEN ACCESS DATABASE
Drive lead optimization of compounds targeting *Mucorales* mycetomiasis

PROCESS


github
SHARE
DATA
PROJECT FILES


Twitter
COMMUNICATE
RESULTS
NEWS


reddit
FACILITATE
INTERACTIVE DISCUSSION

Free of intellectual property constraints
Launch participants:
University of Sydney - Mat Todd
Erasmus MC - Wendy van de Sande
Drugs for Neglected Diseases Initiative

- 1st Law: All data are open and all ideas are shared
- 2nd Law: Anyone can take part at any level
- 3rd Law: There will be no patents
- 4th Law: Suggestions are the best form of criticism
- 5th Law: Public discussion is much more valuable than private email
- 6th Law: An open project is bigger than, and is not owned by, any given lab

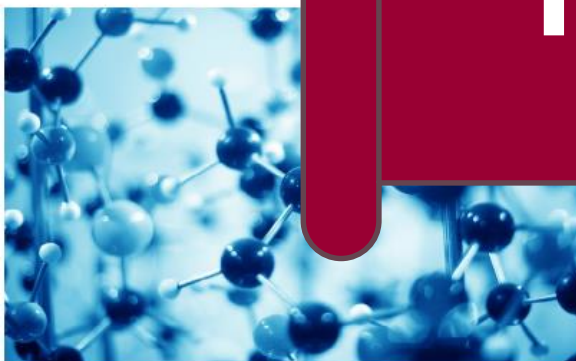


Age-Related Me
Development A



science

Thank you



Fabrication And Synthetic
Technologies For Advanced
Drug Delivery

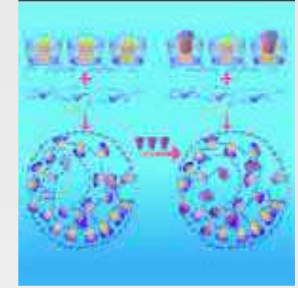
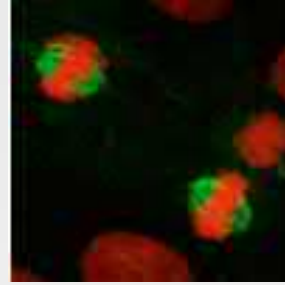
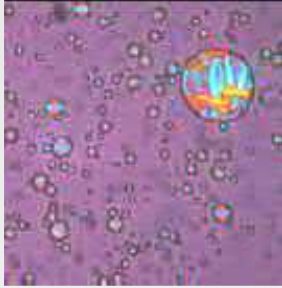


Medicines Use And
Optimisation

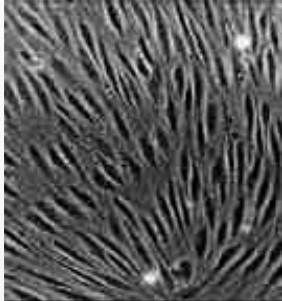
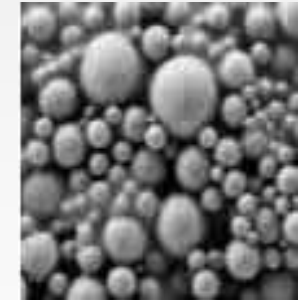


Pharmacoepidemiology And
Medication Safety

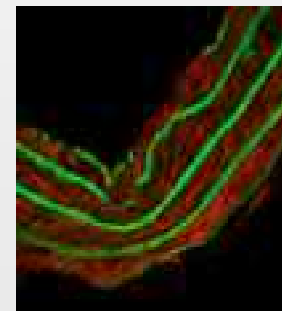
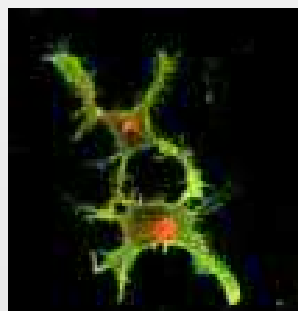
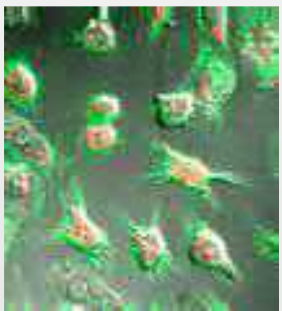
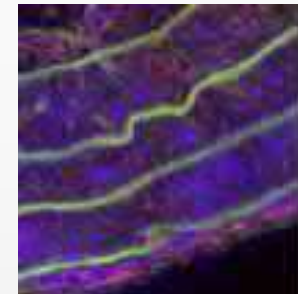
PARIS

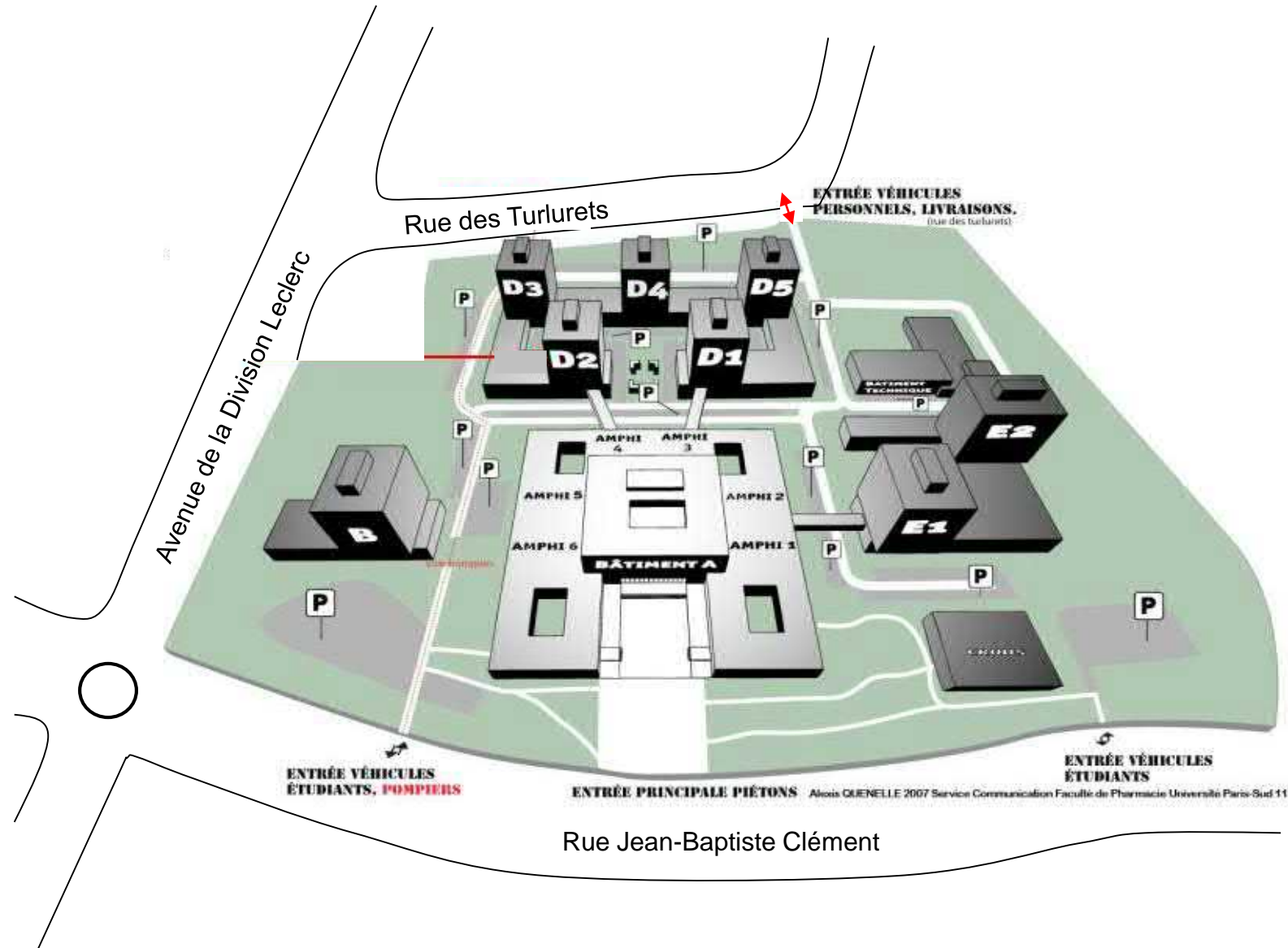


Research activities and organization



FACULTÉ DE PHARMACIE





➤ **12 Research Units**

➤ Composed of 23 teams

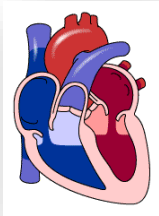
➤ ~ 260 Professors & assistant professors

➤ ~ 30 scientists from CNRS & Inserm

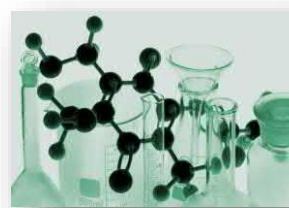
➤ ~ 80 engineers and technicians

➤ ~ 40 post-doctoral fellows

➤ ~ 100 PhDs



UMR INSERM 1180
Dr. Ana Maria GOMEZ



UMR CNRS 8076 BioCIS
Dr. Bruno Figadère



UMR INSERM 1178
Pr. Alain Gardier



EA 4529 Lip(Sys)²
Pr. Pierre Chaminade



EA 4043
Pr. Claire Janoir



UMR CNRS 8612
Institut Galien Paris-Sud
Pr. Elias Fattal



UMR CNRS I2BC
Pr. Audrey Esclatine



EA 401
Pr. Najet Yagoubi



UMR INSERM 1193
Pr. Christian Poüs



UMR CNRS 8079
Pr. Yves Levi



UMR INSERM 996
Pr. Marc Pallardy



EA 7358
Pr. Eric Fouassier

- **UMR-S 1180 - *Signalisation et Physiopathologie Cardiovasculaire*** (Dr. Ana-Maria GOMEZ)
 - *Signalisation énergétique* (Dr. Mathias MERICKSKAY, Pr. Anne GARNIER)
 - *Signalisation des nucléotides cycliques* (Dr. Grégoire VANDECASTEELE, Pr. Véronique LEBLAIS)
 - *Signalisation calcique* (Dr. Jean-Pierre BENITAH, Dr. Ana-Maria GOMEZ)
- **UMR-S 996 - Equipe « Allergie, Immunotoxicologie et Immunopathologie »** (Pr. Marc PALLARDY)
 - rattachée à l'unité INSERM UMRS-996 (Directrice : Dr. Françoise BACHELERIE)
- **UMR-S 1193 Equipe « *Mécanismes cellulaires et moléculaires d'adaptation aux stress et cancérogenèse* »** (Pr. Christian Poüs, Pr. Antoinette Lemoine & Pr. A.M Roque-Afonso)
 - rattachée à l'unité INSERM UMRS-1193 (Directeur : Pr. Didier SAMUEL)
- **UMR-S 1178 Equipe « *Dépression, Plasticité et Résistance aux Antidépresseurs* »** (Pr. Alain GARDIER & Pr. Emmanuelle CORRUBLE), rattachée à l'unité INSERM UMR-S 1178: Santé Mentale et Santé Publique (Directeur : Pr. Bruno FALISSARD)
 - **Equipe MOODS « *Médicaments, Outre-mer, Dépression, Suicide* »** (Responsable : Pr. Alain GARDIER & Pr. Emmanuelle CORRUBLE) du CESP

UMR-8612 - Institut Galien Paris-Sud (Pr. Myriam TAVERNA)

- ❑ *Physico-Chimie des Surfaces* (Pr. Véronique ROSILIO)
- ❑ *Physico-Chimie des Systèmes Polyphasés* (Dr. Vincent FAIVRE)
- ❑ *Physique Pharmaceutique* (Pr. Florence PETIT-AGNELY)
- ❑ *Ingénierie particulière à visée thérapeutique* (Pr Elias FATTAL)
- ❑ *Amélioration du Passage des Barrières par les Molécules Biologiquement Actives* (Pr. Gilles PONCHEL)
- ❑ *Nanomédicaments **innovants** pour le traitement de maladies graves* (Dr. Julien NICOLAS)
- ❑ *Protéines et Nanotechnologies en Sciences Analytiques* (Pr. Myriam TAVERNA)

UMR-8076 - *Biomolécules : Conception, Isolement, Synthèse (BioCIS)* (Dr. Mouad ALAMI)

- ❑ *Chimie des Substances Naturelles* (Pr. Erwan POUPON, Pr. Delphine JOSEPH)
- ❑ *Chimiothérapie antiparasitaire* (Pr. Philippe LOISEAU)
- ❑ *Molécules Fluorées et Chimie Médicinale* (Dr. Benoit CROUSSE, Pr. Sandrine ONGERI)
- ❑ *Conception et Synthèse de Molécules d'Intérêt Thérapeutique (CoSMIT)* (Dr. Samir MESSAOUDI, Pr. Abdallah HAMZE)
- ❑ *Chimie Biologique* (Pr. Thierry BRIGAUD)

UMR CNRS I2BC Equipe « *Virulence et Latence des Herpesvirus* » (Responsable : Pr. Audrey ESCLATINE)

rattachée à l'UMR CNRS I2BC (Directeur : Dr. Thierry MEINNEL) va déménager et intégrer la nouvelle **Equipe « *Autophagy and antiviral immunity* »** (Responsable : Dr. Arnaud MORIS) de l'I2BC

UMR CNRS 8079 Groupe « *Santé Publique – Environnement* » (Responsable : Dr. Sara KAROLAK)

rattaché à l'UMR CNRS 8079 « *Écologie, Systématique, évolution* » (Directrice : Pr. Jane LECOMTE)

EA 4043 UMR-INRA - *Bactéries, Pathogènes et Santé* (Pr. Claire JANOIR)

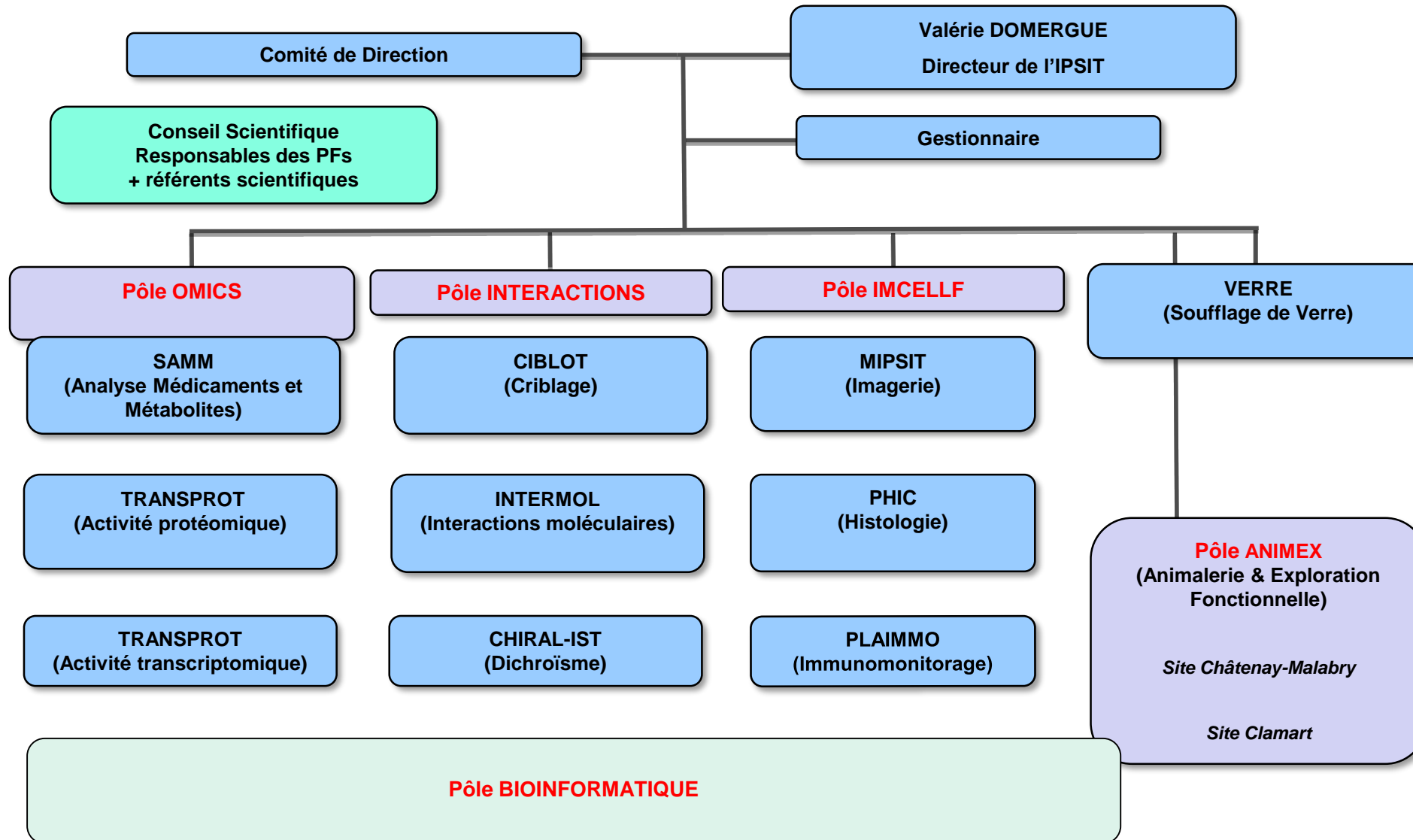
→ rejoint l'unité MICALIS (UMR INRA AgroParisTech et UPSud) pour constituer une équipe qui reste sur le site de l'UFR de Pharmacie

EA 7357 - *Lipides, Systèmes analytiques et Biologiques* (Lip(sys)²) (Pr. Pierre CHAMINADE)

EA 401 - *Matériaux et Santé* (Pr. Najet YAGOUBI)

EA 7358 - *Groupe de Recherche et d'Accueil en Droit et Économie de la Santé* (GRADES) (Pr. Eric FOUASSIER)

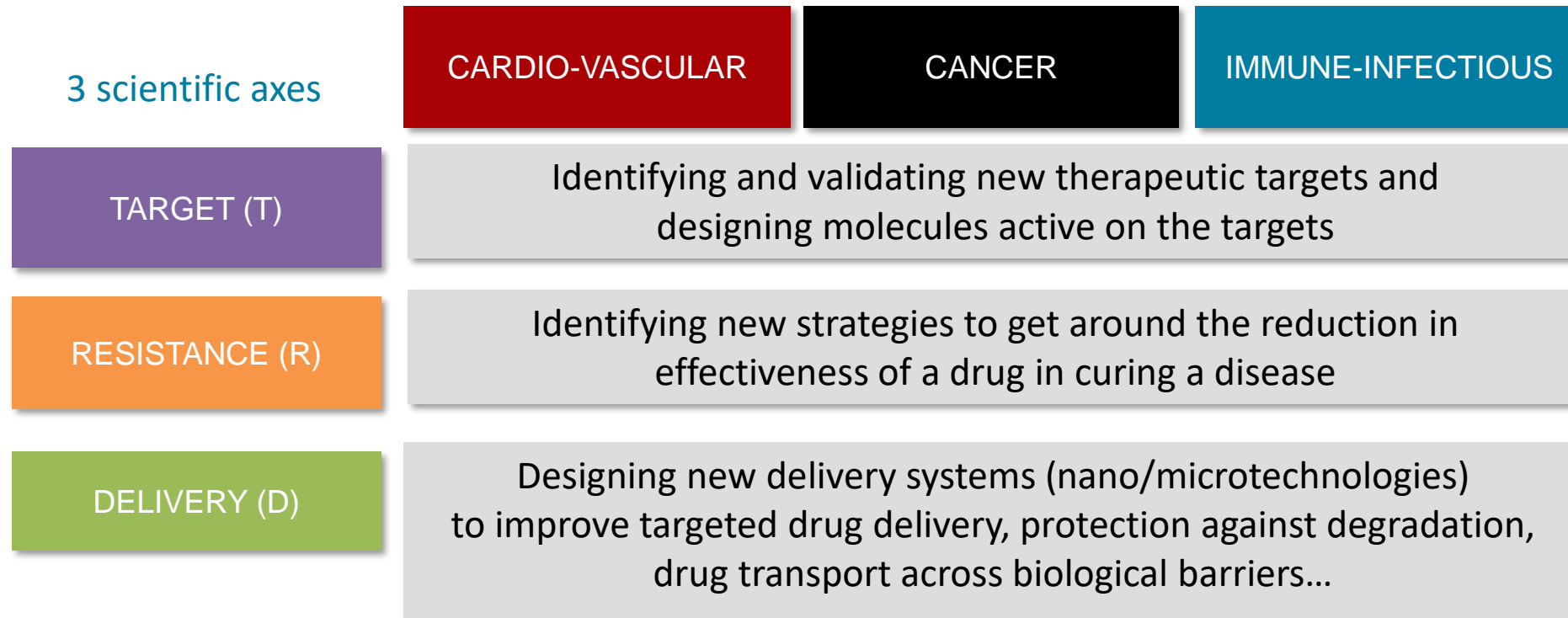
US31-UMS3679-IPSIT – Plateformes technologiques





A consortium of teams in research unites grouped to work on common research projects
Transversal Structure (one project can merge teams from different research units)

New therapeutics to combat 3 major classes of diseases



Renouvellement du LabEx LERMIT



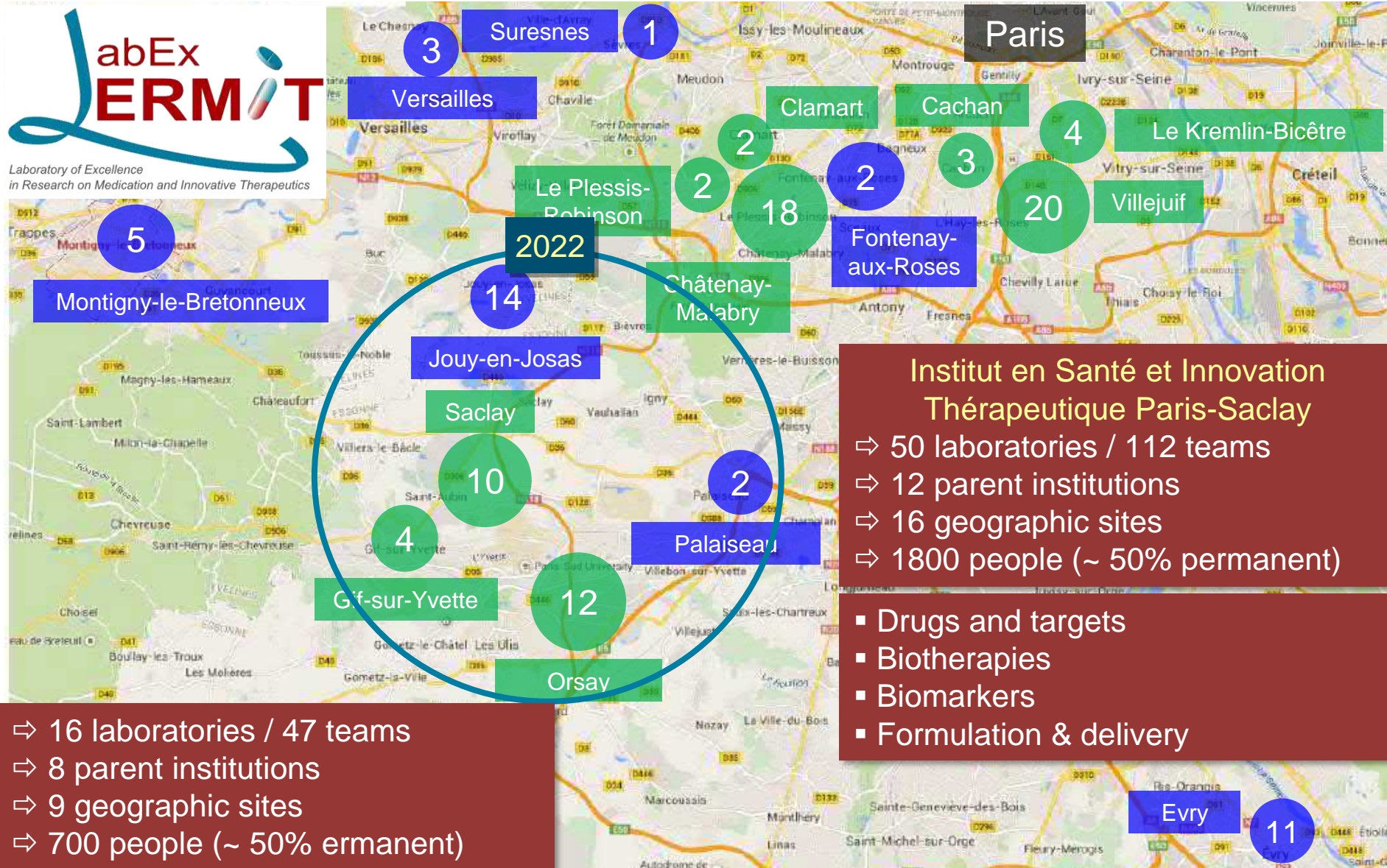
- ⇒ 16 laboratories / 47 teams
- ⇒ 8 parent institutions
- ⇒ 9 geographic sites
- ⇒ 700 people (~ 50% permanent)



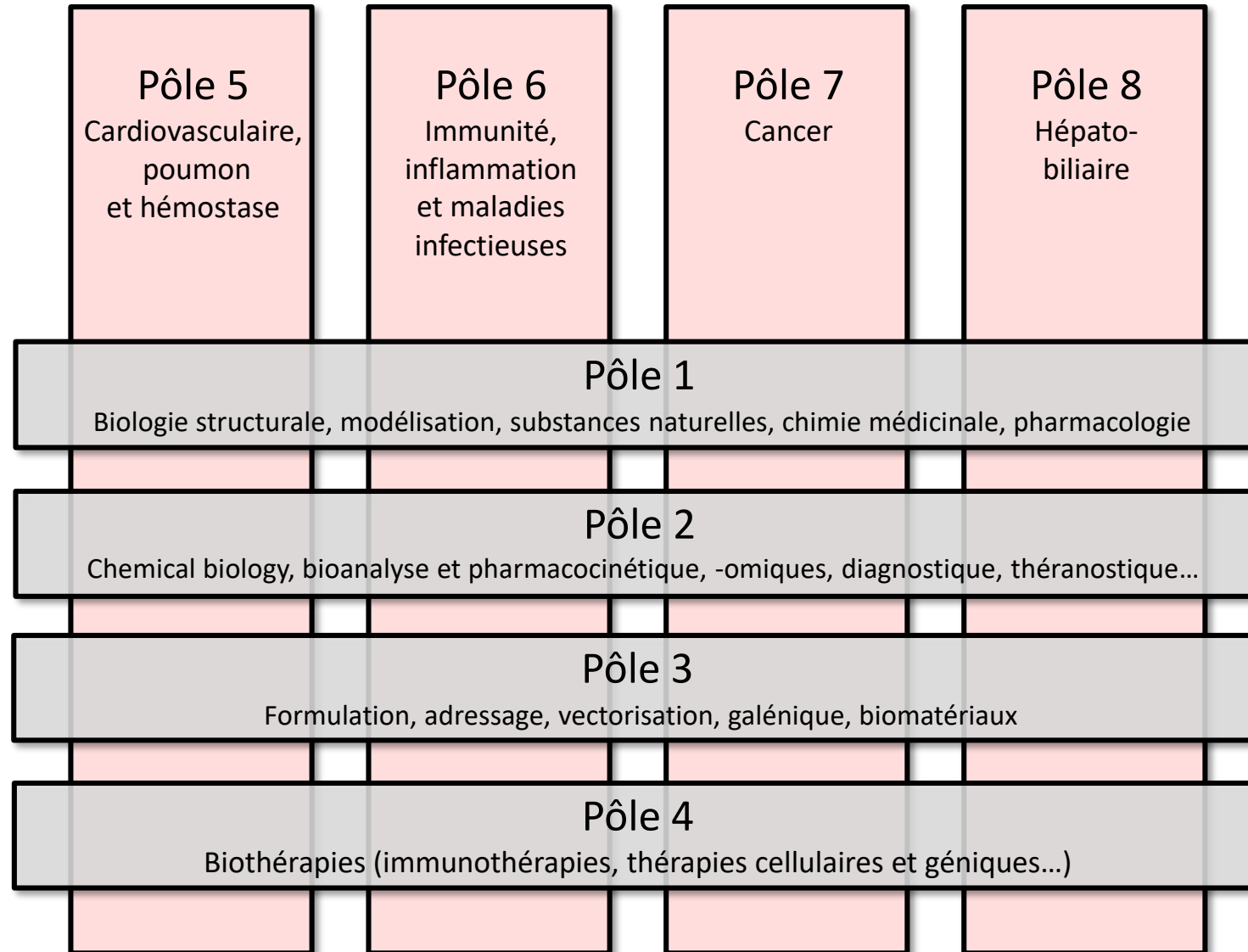
New therapeutics to combat 4 major classes of diseases

4 scientific axes	CARDIO-VASCULAR & THORAX	CANCER	IMMUNE-INFECTIOUS	HEPATOLOGY
TARGET & MOLECULE	Identifying and validating new therapeutic targets and designing molecules active on the targets; biologics; therapeutic antibodies			
RESISTANCE	Identifying new strategies to get around the reduction in effectiveness of a drug in curing a disease			
FORMULATION & DELIVERY	Vectorization; Galenic; Designing new delivery systems (nano/microtechnologies) to improve targeted drug delivery, protection against degradation, drug transport across biological barriers...			
DIAGNOSTIC & THERANOSTIC	Omics, imaging, labelling, probes, bioanalysis, pharmacokinetics, toxicology			

Vers un *Institut en Santé et Innovation Thérapeutique*



Institut Paris-Saclay en Santé et Innovation Thérapeutique



PARMA



UNIVERSITÀ DI PARMA

Department of Food and Drug Sciences



ULLA ExCo Meeting

Copenhagen November 16th, 2018

Food & Drug Department

- Est. in 2017.
- Study of **medicinal products and foods**, is based on the consideration that their scope of action is common: the health and well-being of humans and animals.
- The development of food and drugs the understanding of their mechanism of action and their formulation require an interdisciplinary approach that ultimately aims at the well-being of the person obtained through **balanced nutrition** with products that deliver vital substances to life, **nutraceutical products** that can prevent some pathologies, and **therapeutic treatments** that allow you to recover from a state of illness.

PHARMACY BUILDING

Parco Area delle Scienze 27/a - CAMPUS



Research Organisation (Pharma Side)

5 main areas

- Bio-organic Synthesis
- Medicinal Chemistry and Drug Design
- Drug Delivery and Pharmaceutical Technology
- Experimental Pharmacology
- Biochemistry and biotechnology

Bio-organic Synthesis group

Franca Zanardi (Associate Professor)

Lucia Battistini (Associate Professor)

Claudio Curti (Associate Professor)

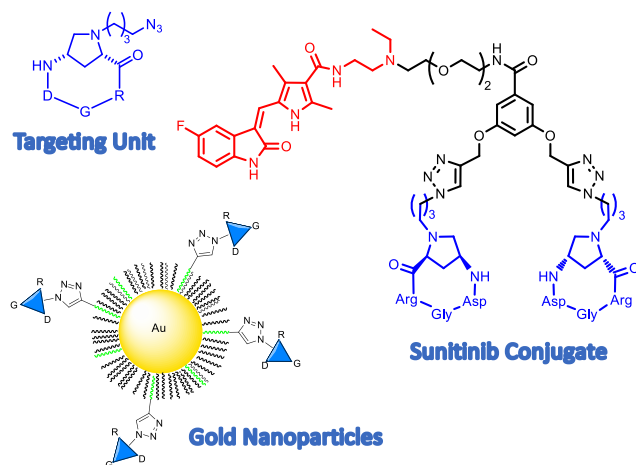
Andrea Sartori (Associate Professor)

Research topics

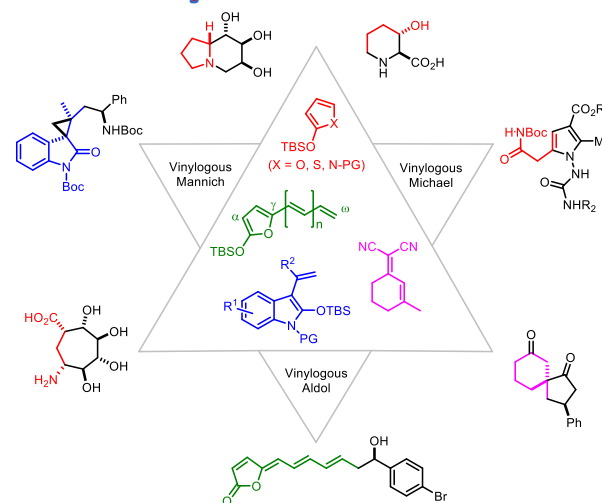
- Lab-scale asymmetric synthesis of chiral organic molecules
- Purification and analysis of enantiopure compounds
- In solution and solid-phase synthesis of small peptides, cyclopeptides and peptidomimetics
- Synthesis of covalent conjugates (peptide-small molecule drug ,peptide-lipide, peptide-fluorescent agent, peptide-chelating unit)
- Radiosynthesis (collaboration with Nuclear Medicine Unit, Parma Hospital)
- Fabrication and characterization of liposomes and gold nanoparticles
- Purification by chromatografic techniques (automated flash, HPLC)
- Spectroscopic characterization (1D and 2D-NMR, IR, CD, mass spectrometry)

Main Active Projects

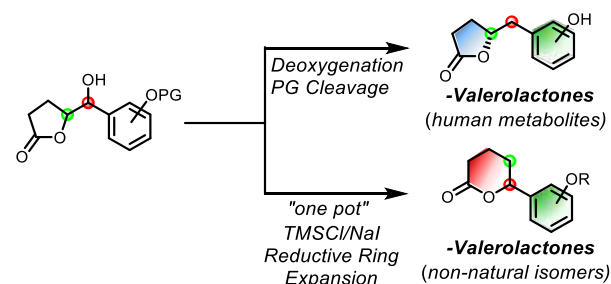
Synthesis of Multifunctional Peptidomimetics Targeting Integrins for Drug Delivery and Diagnosis



Introduction of Novel Chemical Methods in Asymmetric Synthesis to Selectively Access Molecular Diversity in the Domain of Medicinally-Relevant Small Molecules



Asymmetric Synthesis of Chiral Metabolites of Polyphenols and Liver Phase II-related Conjugates





Gabriele Costantino (Professor)

Marco Radi (Associate Professor)

Marco Pieroni (Assistant Professor)

Giannamaria Annunziato (Post doc)

Involved in developing novel small-molecule probes for a wide range of therapeutic targets by combining molecular modeling and combinatorial chemistry approaches.

Main therapeutic areas:

Anti-infectives

Anti tubercular agents

Nutraceuticals

Molecular modeling

Combinatorial chemistry

Main projects funded



INTEGRATE is a European Project aiming at the discovery of novel targets for the development of new antibacterial drugs.

The project is part of Marie-Curie actions of Horizon 2020 and is coordinated by prof. G. Costantino.

Main ongoing collaborations



Prof Miguel Viveiros



Prof William Bishai



Prof Martin Welch



Prof Caludiu Supuran



Dr. Antonio Felici



Dr Philip Gribbon

Drug Design & Discovery Group

Drug Design

Marco Mor (Professor)

Silvia Rivara (Associate Professor)

Alessio Lodola (Associate Professor)

Synthesis of Compounds

Riccardo Castelli (Assistant Professor)

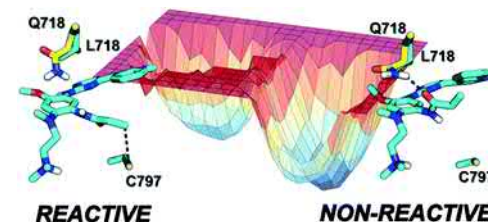
Pharmaceutical Analysis

Federica Vacondio (Associate Professor)

Claudia Silvia (Associate Professor)

Research areas

- **Modulators of the Endocannabinoid System**
 - Design and SAR analysis of Fatty Acid Amide Hydrolase (FAAH) inhibitors
 - Design and synthesis of N-acyl ethanolamine acid amidase (NAAA) inhibitors
 - Design and synthesis of Monoglyceride Lipase (MGL) inhibitors
 - Design and SAR analysis of NAPE-PLD inhibitors
- **GPCR ligands**
 - Design and QSAR analysis of MT₁ and MT₂ melatonin receptor ligands
- **Kinase inhibitors**
 - Design and synthesis of covalent inhibitors of EGFR
 - Design and synthesis of covalent inhibitors of FGFR
- **Protein-Protein Interaction Inhibitors**
 - Design and synthesis of small molecules acting as FGF traps
 - Design and synthesis of EphA2 antagonists

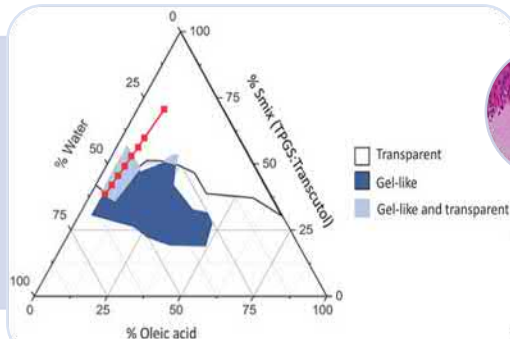


Skin, ocular and buccal drug delivery

- **Patrizia Santi (Professor)**
- Sara Nicoli (Associate Professor)
- Cristina Padula (Assistant Professor)
- Silvia Pescina (Assistant Professor)

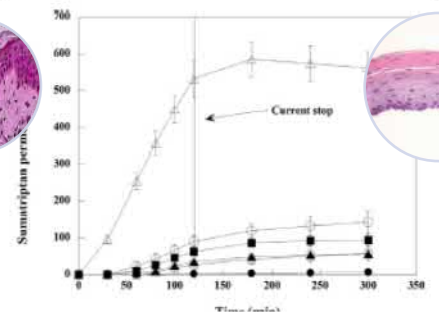
- International collaborations (5 y)
 - University of Helsinki, Finland
 - Universidade da Região da Campanha, URCAMP, Brazil
 - Universidade Federal do Rio de Janeiro (IMA/UFRJ), Brazil
 - Ege University, Izmir, Turkey
 - Universidade de Santiago de Compostela, Spain
 - Federal University of ABC, São Paulo, Brazil

Main research subjects



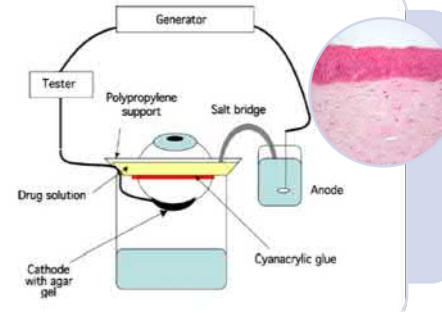
Dermal and Transdermal Delivery Main model: Porcine ear skin

- Ex1. microemulsions for imiquimod dermal delivery
- Ex2. transdermal iontophoresis for enhanced drug delivery
- Ex3. bioadhesive patch for dermal and transdermal delivery



Buccal Delivery Main model: Porcine esophageal epithelium

- Ex1. sumatriptan succinate buccal iontophoresis
- Ex2. microemulsions for triamcinolone acetonide delivery



Ocular Delivery for anterior and posterior segment Main model: Porcine eye

- Ex1. influence of the vehicle on stability and transcorneal diffusion of cysteamine
- Ex2. iontoporetic transcleral delivery of mAb and oligonucleotides

Drug Delivery and pharmaceutical technology

Ruggero Bettini, Professor

Lisa Elviri, Associate Professor

Fabio Sonvico, Associate Professor

Francesca Buttini, Associate Professor

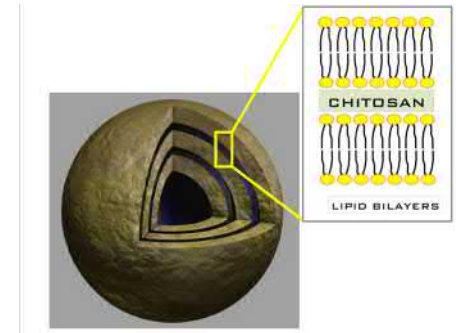
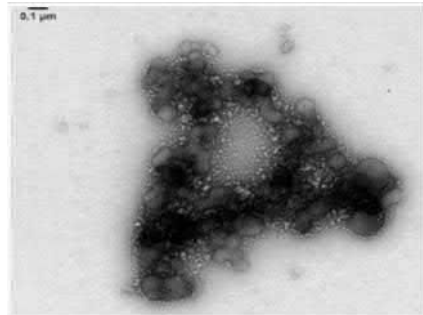
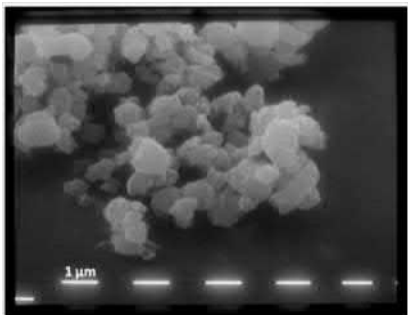
Alessandra Rossi, Assistant Professor

Post doc

Annalisa Bianchera

Adryana Rocha Clementino

Irene Rossi

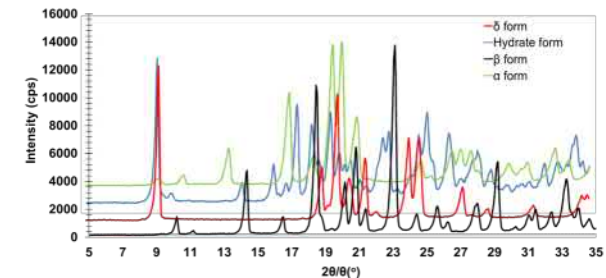


Research topics

Nasal and pulmonary drug delivery (small molecules peptides and proteins)

Oral controlled drug delivery (poorly absorbed compounds, local delivery)

Nose to brain delivery



Approaches

Solid state manipulation

Nanoparticulate systems

Nonosystems



free flowing powders

COMBINATION of 3D TECHNOLOGY and BIOMATERIAL to DEVELOP MEDICAL DEVICES for TISSUE REGENERATION

DIFFERENT COMPOSITION

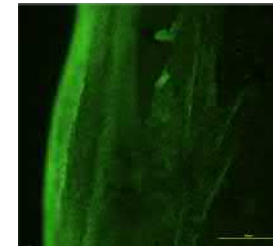
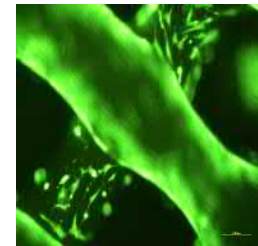
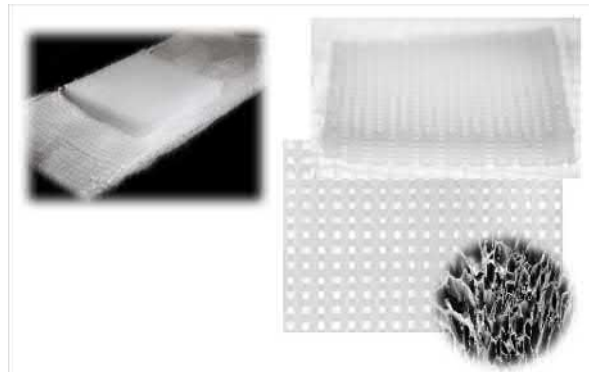
3D printing of a wide range of natural and synthetic polymers
(i.e. hyaluronic acid, alginate, collagen, fibroin..)

ACTIVE COMPOUNDS

Inclusion of a variety natural active compounds
(i.e. antioxidants, lipids, oils, vitamins etc.)

DRUG DELIVERY SYSTEMS

Development of localized controlled drug delivery systems



Experimental pharmacology

Elisabetta Barocelli (Professor)

Vigilio Ballabeni (Associate Professor)

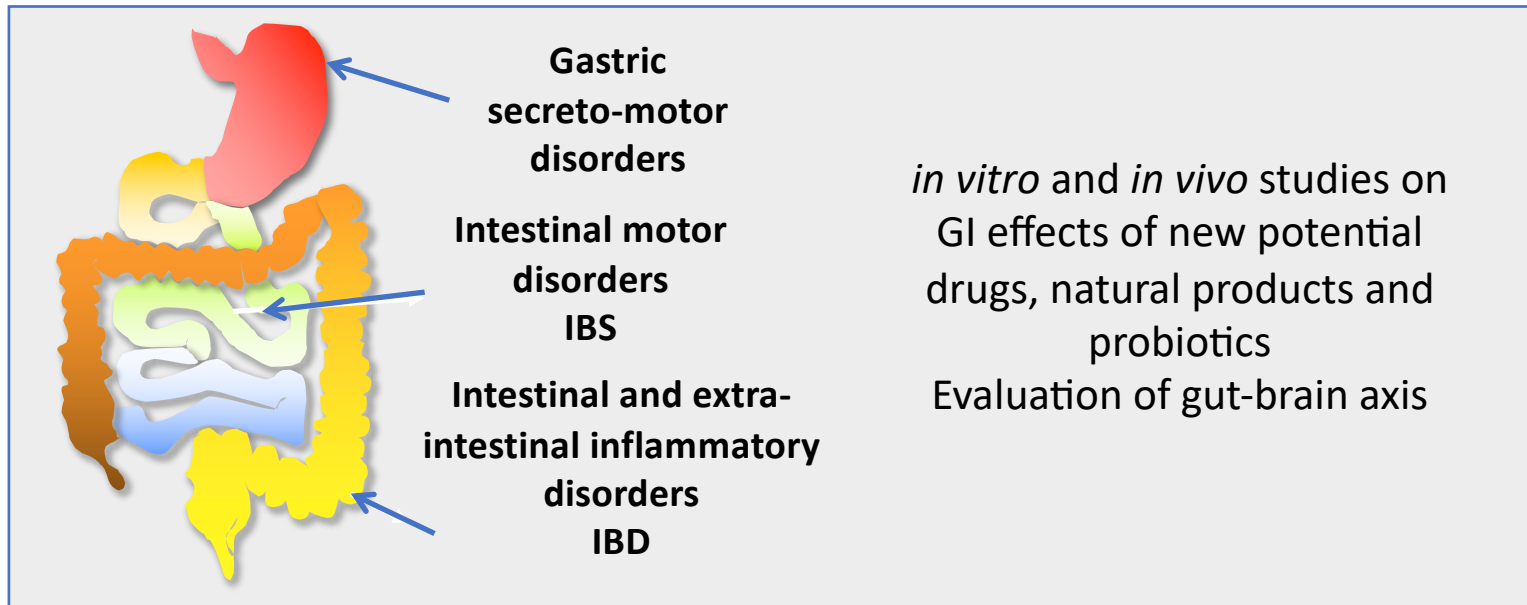
Massimiliano Tognolini (Associate Professor)

Simona Bertoni (Assistant Professor)

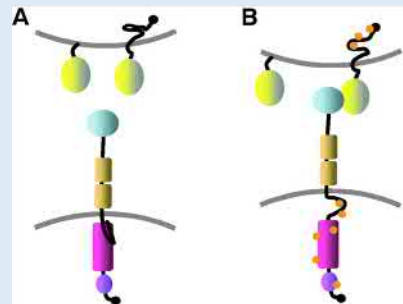
Research Topics

- Study of the local and systemic effects of drugs delivered by pulmonary inhalation
- Pharmacokinetics and safety pharmacology studies of new potential drugs and formulations

Main research



Discovery and development of new protein-protein Inhibitors of Eph-ephrin interaction



- ✓ Binding assay
- ✓ In vitro studies on cell cycle, signal transduction, cell proliferation and migration, angiogenesis
- ✓ In vivo studies in models of cancer, diabetes, pain, blood clotting disorders

Lipid pharmacology

Lipid metabolism as a pharmacological/nutraceutical target for the treatment of cardiovascular, autoimmune, pulmonary and neurodegenerative diseases

Pleiotropic effects of PCSK9

Association of HDL functionality with atherosclerosis and Alzheimer

Role of diet/microbiota in health and disease

Pharmacological/Nutraceutical modulation of cholesterol metabolism

- **Franco Bernini, Professor**
- Nicoletta Ronda, Assistant Professor
- Ilaria Zanotti, Assistant Professor
- Francesca Zimetti, Assistant Professor
- Maria Pia Adorni, Post-doc

In vitro studies (cell cultures)

- Intracellular cholesterol metabolism and trafficking
- Expression of lipid transporters
- Cellular pro-inflammatory responses

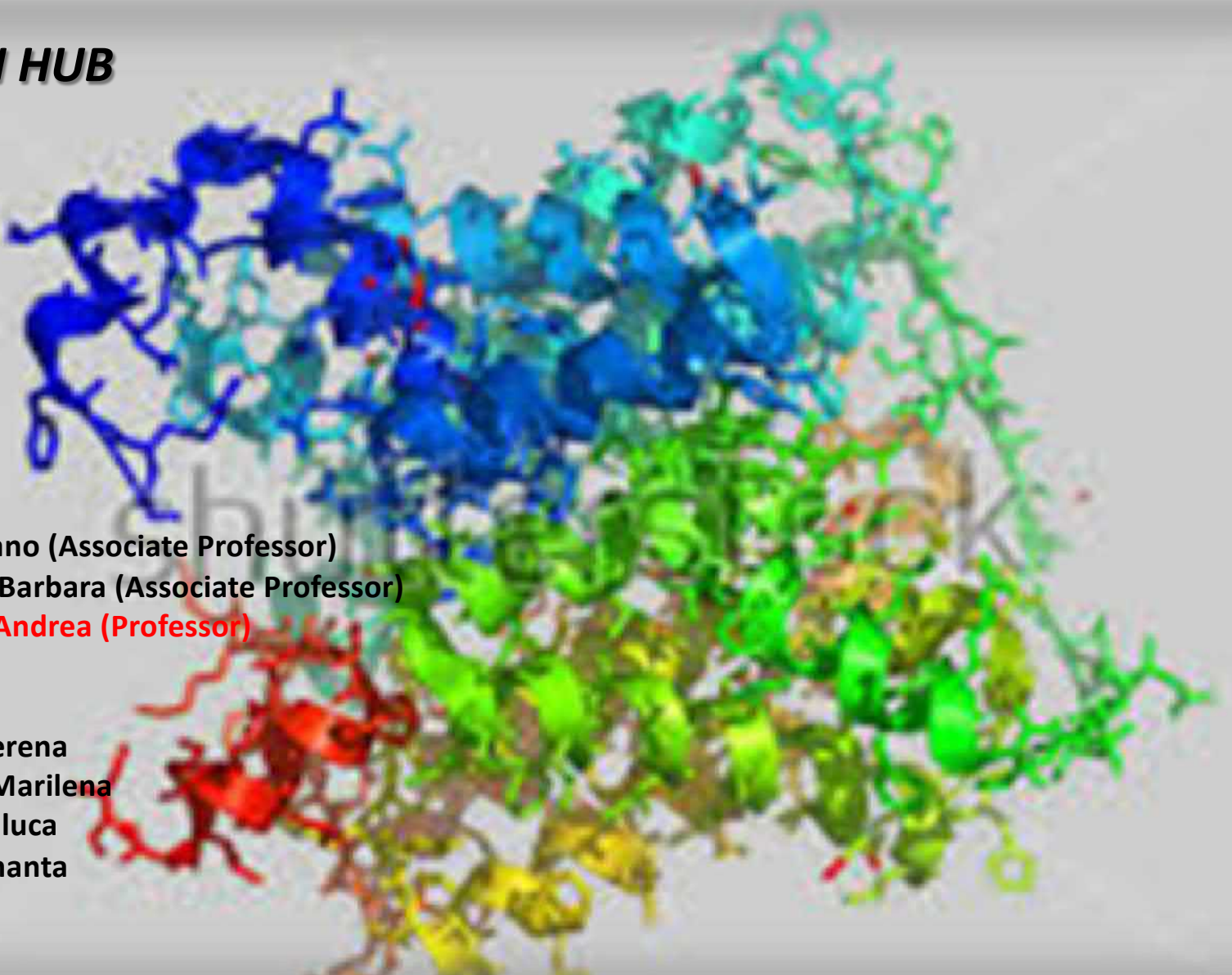
In vivo studies (rodents)

- Lipidemia and functional serum lipid profile
- Inflammatory markers
- Atherosclerotic lesions

Clinical studies

- Serum cholesterol efflux capacity
- Serum cholesterol loading capacity

PROTEIN HUB



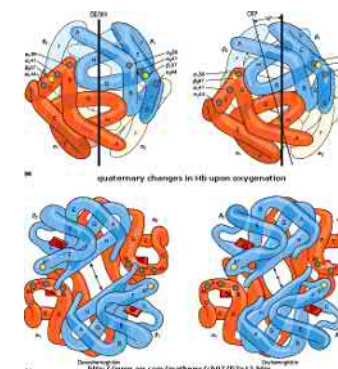
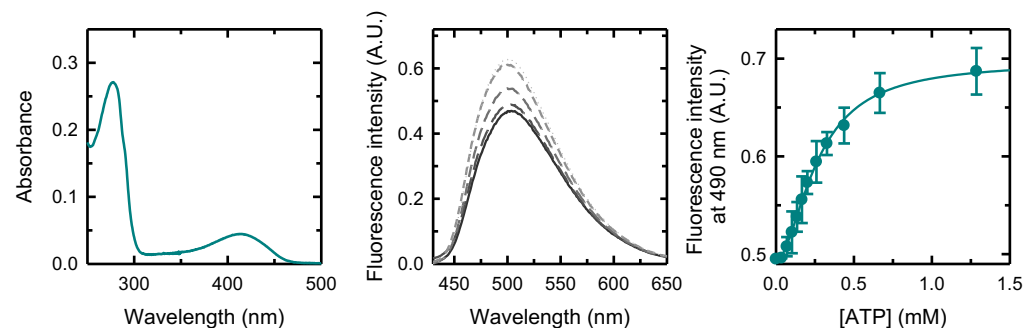
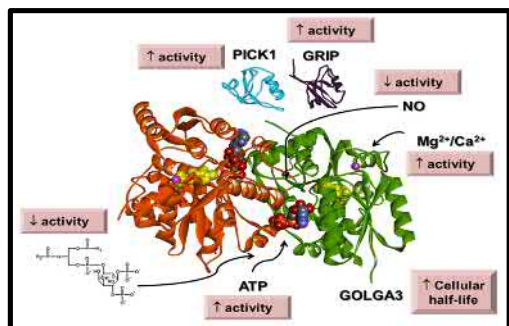
Bruno Stefano (Associate Professor)
Campanini Barbara (Associate Professor)
Mozzarelli Andrea (Professor)

Postdocs

Faggiano Serena
Margiotta Marilena
Paredi Gianluca
Raboni Samanta

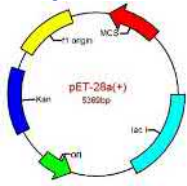
Protein Expression, Purification and Characterization of structure, dynamics, function and regulation

- PLP-dependent enzymes
 - serine racemase - target for neuropathologies
 - O-acetylserine sulfhydrylase – target for adjuvant of antibiotics
 - methionine gamma lyase – biologics for cancer
- Other enzymes
 - serine acetyltransferase –target for adjuvant of antibiotics
 - glyceraldehyde-3-phosphate dehydrogenase – target for malaria and cancer
- Other proteins
 - alpha-1-antitrypsin – biologics for pulmonary diseases
 - Hemoglobins and pegylated hemoglobin – biologics for oxygenation therapy



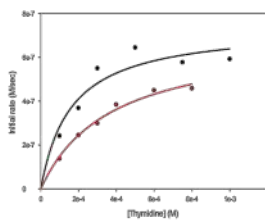
Methods and Instrumentation

Protein engineering and production



Fermentor

Enzyme assay development, determination of inhibition mechanisms and K_i , rapid scanning stopped-flow



Inhibition profile

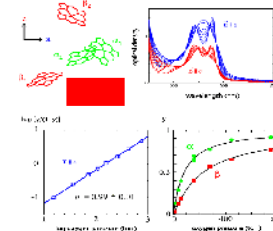


Stopped-flow

Spectroscopy and ligand binding of protein in single crystals and encapsulated in silica gels



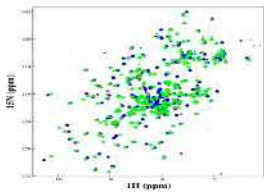
Microspectrophotometer



Protein chemical modification

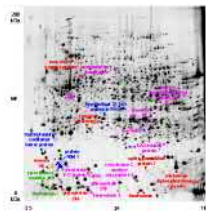


Protein NMR, STD-NMR

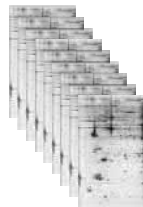


Jeol 600 MHz

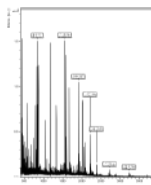
Gel-free and gel-based Proteomics



Gel spot cutter

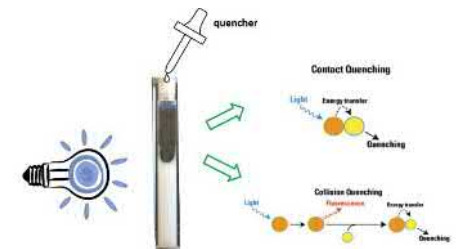
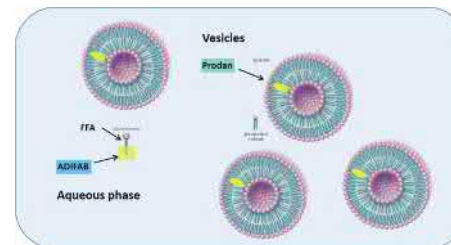


Protein digester



Mass spectrometer
MALDI TOF-TOF

Structure and stability of formulation by fluorescent solvatochromic probes



The city



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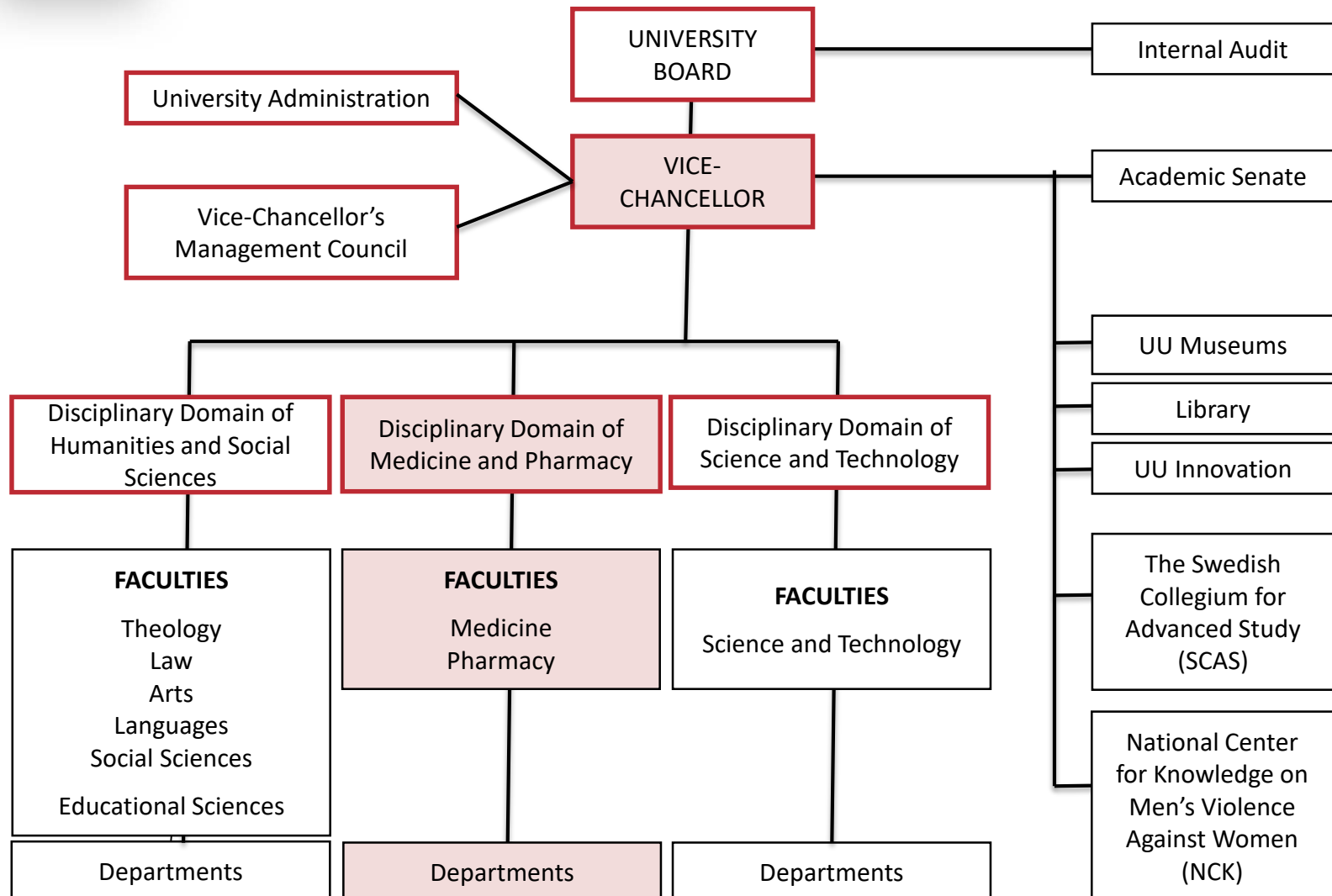
Margareta Hammarlund-Udenaes, Dean of the Faculty of Pharmacy
mhu@farmbio.uu.se

Anders Backlund, Vice-dean of research training at the DOmaine of Medicine & Pharmacy
& Vice-chancellor special advisor on internationalisation
anders.backlund@fkog.uu.se



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Organization





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Medicine and Pharmacy

Disciplinary domaine management

Stellan Sandler, Vice-Rector
professor in medical cell biology

Mats Larhed, Deputy Vice-Rector,
professor in organic pharmaceutical chemistry

Margareta Hammarlund-Udenaes, Dean of the Faculty of Pharmacy
professor in pharmacokinetics

Eva Tiensu-Janson, Dean of the Faculty of Medicine,
professor in endocrin oncology



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The Faculty of Pharmacy



- Organized in three departments covering chemical, biological and pharmaceutical aspects on drugs and medicines
- Focus on the sciences underpinning the discovery, development and use and abuse of medicines
- Generic as well as focused on therapeutic areas

“With its three departments, the Faculty constitutes a dynamic centre for everything relating to pharmaceuticals” / Research Assessment Exercise Q&R 2011



● Pharmaceutical cell biology -Steroid biochemistry

 Drug Safety and Toxicology

Pharmaceutical bioinformatics

Pharmaceutical cell biology -Söderberg

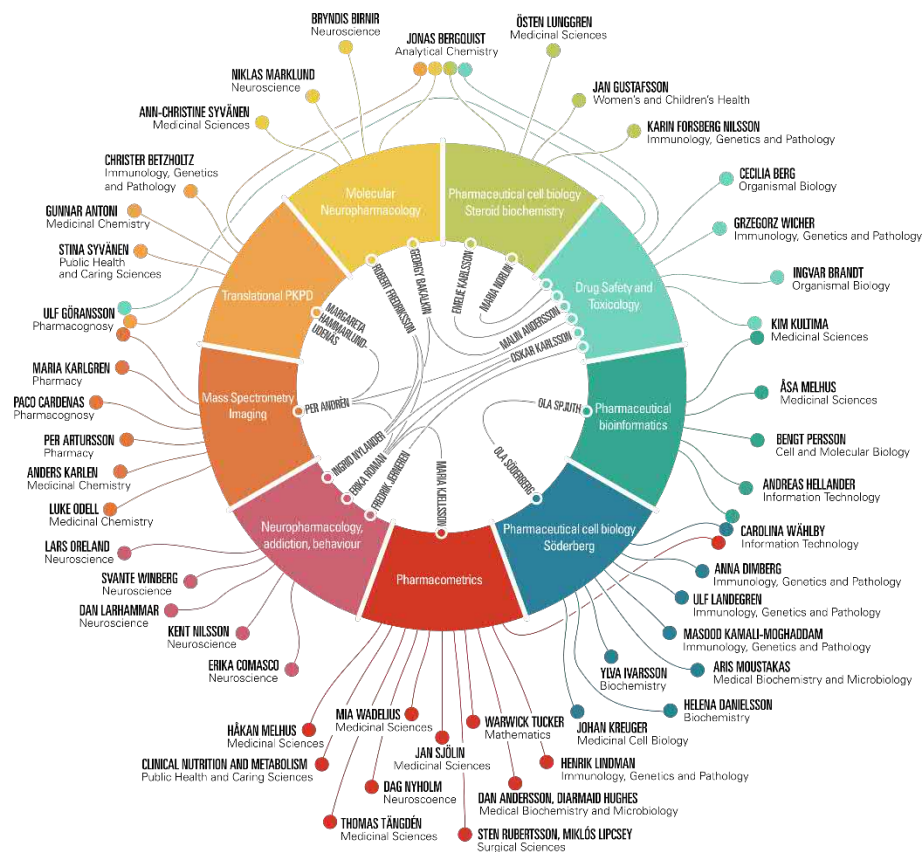


Pharmacometrics

● Neuropharmacology, addiction, behaviour

 Mass Spectrometry Imaging Translational PKPD

 Molecular Neuropharmacology





Pharmacometrics Group

Mats O. Karlsson

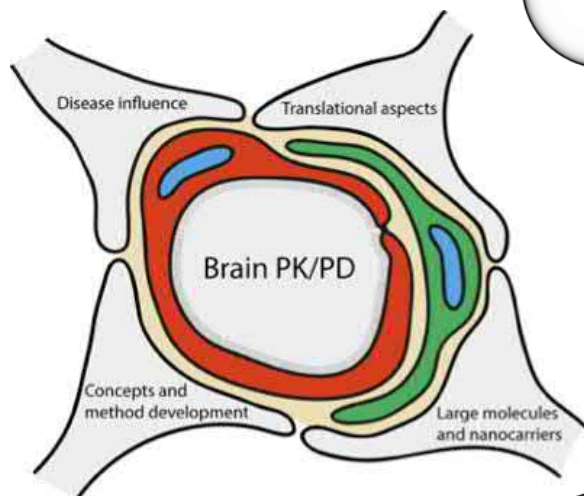
- Developing and using mathematical models to understand drug and disease mechanisms, and optimizing drug development and therapy





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Translational PKPD Group



Quantitative brain drug delivery - concepts and method development

Translational aspects of brain drug distribution in health and disease

The role of pericytes in brain drug distribution

Biomolecular drugs (peptides) and nanocarriers

Pharmaceutical Cell Biology Group

Ola Söderberg, Sara Mangsbo, Greta Hultqvist

- Strategic employments on immunology and large molecule research



Professor
Protein
interactions in
disease



Associate
senior lecturer
Immuno
oncology



Associate
senior lecturer
Protein drug
design



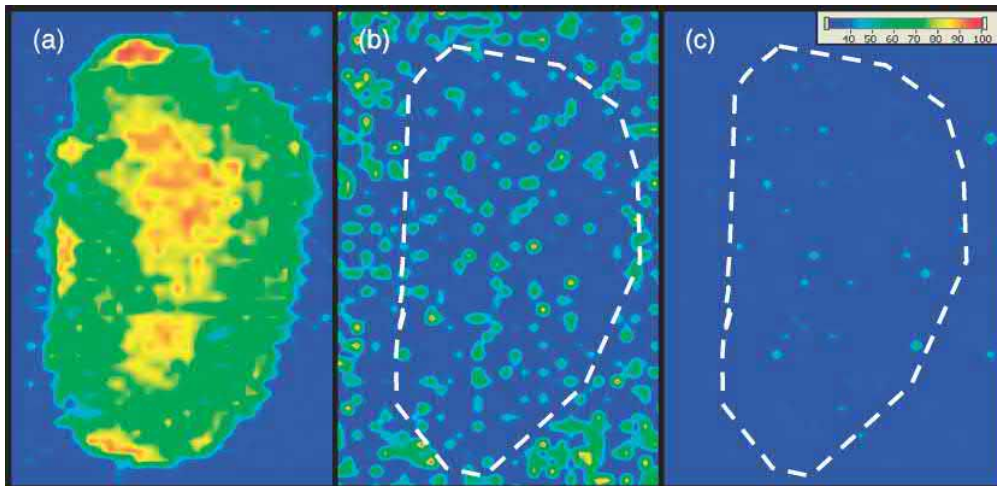
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Mass Spectrometry Imaging

Per Andrén



- MALDI/IMS method development and tissue distribution of drugs and endogenous compounds





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Department of Medicinal Chemistry



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Pharmacognosy

Ulf Göransson

What can we learn from the chemistry in nature?



Extracting sponge DNA with magnetic beads

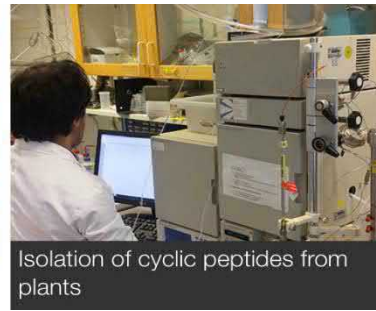
Sponge natural products →



Exploring the chemical space to select and predict new drug leads



Fieldwork: truffle hunting



Isolation of cyclic peptides from plants



Fieldwork: sponge collecting



A deep-sea sponge crude extract with some antibacterial activity



Extracting RNA from marine worms for transcriptomics



Growing and collecting violet leaves for peptide extractions



Setting up a Leishmania assay



Designing grafted peptides as new drug leads



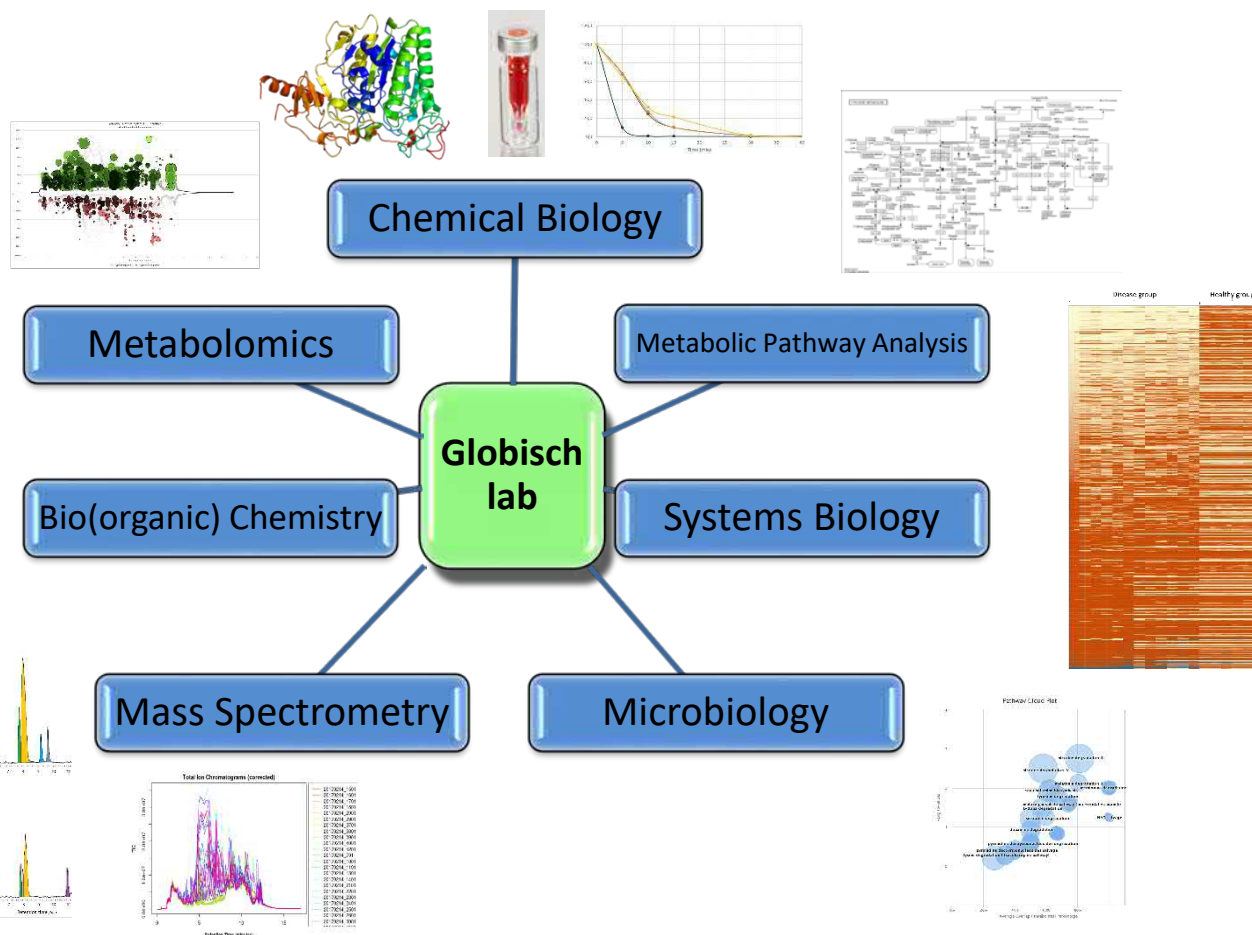
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Chemical biology for biomarker discovery

Daniel Globisch



SciLifeLab





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Drug design and discovery

Anders Karlén



We perform basic research in both experimental and computational medicinal chemistry. New strategies are developed for both design and synthesis of small drug-like molecules.

The division is host for a number of research initiatives, including the SciLifeLab DDD Medicinal Chemistry – Lead Identification Facility, the IMI antibiotic development project ENABLE and the Medicinal Chemistry Node of The Beijer Laboratory for Drug Discovery.



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Preparative Medicinal Chemistry

Mats Larhed



The research interests encompass a range of protein targets of pharmaceutical relevance, including proteases and G-protein coupled receptors (GPCRs). Lead compounds are preferentially synthesized using new efficient transition metal-catalyzed reactions developed in our laboratory. Considerable efforts have in particular been devoted to the development of new robust and useful palladium-catalyzed C-C bond forming reactions and novel equipment for microwave and/or flow synthesis.

Research is conducted to identify novel ligands that interfere with proteins in the renin/angiotensin system. The first drug-like selective and potent angiotensin II, type II receptor (AT2R) agonist (M24/C21) was discovered in our laboratory.



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Department of Pharmacy



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Drug delivery group

Per Artursson &
Christel Bergström



- A number of experimental models for measuring properties of importance for drug delivery (dissolution, solubility, transport across cells, formulate-ability).
- First world-wide to introduce computational modelling to identify successful drug-specific formulation pathways.

In 2014 Christel Bergström received the European Research Council Starting Grant



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Pharmaceutics

Göran Alderborn



The study of solid systems, their formulation and manufacturing (solid dosage form technology), with the overall aim to develop new and improved methods and strategies to predict and manipulate the properties of particles and particle systems.

In addition, the group conduct research on new drug delivery solutions for controlled drug release, currently focused on topical drug delivery systems



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UAC – Uppsala Antibiotic Centre



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**Uppsala
Antibiotic Center**

PhD school



Dan Andersson

Director,
Spec. in development of
Bacterial Antibiotic Resistance



Anders Karlén

Medicinal Chemistry



Åsa Melhus

MedFarm



Staffan Svärd

(SciTech)



Francesco Ciabuschi

(HumSam)





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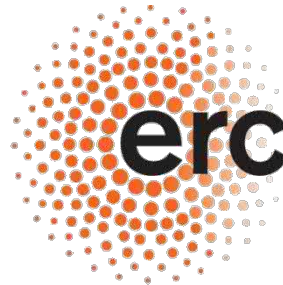
Developing collaborations





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Some supportive organizations



European Research Council
Established by the European Commission



SciLifeLab



Innovative Medicines Initiative

PET-MR

U-CAN



Biobank Sweden

U-CARE



Vetenskapsrådet



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See more information on specific research projects at:

- Department of Pharmaceutical Biosciences
 - <http://www.farmbio.uu.se/research/?languageId=1>
- Department of Pharmacy
 - http://www.farmfak.uu.se/farm/research_en.shtml
- Department of Medicinal Chemistry
 - <http://www.ilkk.uu.se/research/>