OUR EXPERT TEAM

The **Laboratory of General Biochemistry and Physical Pharmacy** (Faculty of Pharmaceutical Sciences) is involved in mostly pre-clinical research on nanomedicines and physical delivery methods for improved targeted intracellular delivery of biopharmaceutics. Besides designing delivery materials, the laboratory focuses on how nanomedicines biophysically behave after administration, both in extracellular fluids and in the intracellular environment.

Prof. Stefaan De Smedt
Prof. Kevin Braeckmans
Prof. Katrien Remaut
Prof. Koen Raemdonck

The **Organic and Biomimetic Chemistry Research Group** (Faculty of Sciences) is specialized in the design and synthesis of modified peptides and nucleic acids, and methods for their conjugation and labeling. Specifically, major interests include the development of cross-linking of biomacromolecules, the design of novel reactive peptide- and oligonucleotide-based probes, and the construction of conformationally defined peptide architectures.

Prof. Annemieke Madder

The research of the **Supramolecular Chemistry Group** (Faculty of Sciences) focuses on the design of tailor-made polymer drug delivery vehicles to meet a wide range of requirements for delivery of small molecules, proteins and genes. The group explores the combination of well-defined "smart" polymer structures with supramolecular interactions as platform for the development of responsive and degradable delivery systems and hydrogels, functionalized with targeting or recognition units, if needed.

Prof. Richard Hoogenboom

The Nanobody Laboratory (Faculty of Medicine and Health Sciences) has key expertise in the implementation of the nanobody technology with a specific focus on 'antigens' (intracellular proteins) that play a role in cancer, inflammation and amyloid diseases. Single domain antibodies are used to temper *in vivo* functions of selected proteins without affecting their expression level. Biochemistry, protein chemistry, cell biology/molecular biology and proteome analysis are blended and integrated in a comprehensive approach.

Prof. Jan Gettemans

The **Biopharmaceutical Technology Unit** (Faculty of Pharmaceutical Sciences) operates at the interface between materials chemistry and immunology. The lab has top-notch expertise in synthesis, assembly, characterization and *in vitro/in vivo* evaluation of nanomedicines, with particular focus on immuno-oncology. Synthetic chemistry, often polymer-based, is developed and combined with nanotechnology to develop interactive biomaterials that can modulate the immune system.

Prof. Bruno De Geest

The **Laboratory of Barriers in Inflammation** (VIB-UGent Center for Inflammation Research) studies the physiological and pathological processes at the gut and brain barriers, and aims at identifying novel therapeutic targets to treat neuroinflammatory disorders and at developing novel strategies to deliver drugs to the central nervous system by targeting the blood-cerebrospinal fluid barrier epithelium.

Prof. Roosmarijn Vandenbroucke

The **Laboratory of Veterinary Immunology** (Faculty of Veterinary Medicine) specializes in the development of oral vaccines intended for human and veterinary medicine, and on the intestinal mucosal immune system in animals.

Prof. Eric Cox & Dr. Bert Devriendt

4Brain (Faculty of Medicine and Health Science) is specialized in *in vivo* preclinical and clinical research for neurological disorders, with a strong emphasis on the pathophysiology and treatment of epilepsy. Furthermore, 4Brain explores the possible ways in which local brain delivery itself may serve as a novel therapy.

Prof. Robrecht Raedt
Prof. Kristl Vonck
Prof. Paul Boon

The **Polymer Chemistry and Biomaterials Group** (Faculty of Sciences) focuses on the development, characterization and processing of cross-linkable polymer precursors and biopolymers, which can be processed into microparticles, nano/microfibers, porous scaffolds. Biofunctional polymers are used for biochemical applications, biomaterials, advanced drug/gene delivery systems and tissue engineering.

Prof. Sandra Van Vlierberghe
Prof. Peter Dubruel

The **Laboratory of Experimental Surgery** (Faculty of Medicine and Health Science) has a long-standing expertise in basic, translational, and clinical research in the field of intraperitoneal drug delivery for peritoneal cancers, with experimental focus on syngeneic and xenograft models of colon and ovarian cancer. An additional research focus is the study of biophysical properties of peritoneal tumours and how these affect drug penetration using advanced computational fluid dynamics.

Prof. Wim Ceelen

The **Nano-Biotechnology group** (Faculty of Bioscience Engineering) develops inorganic and polymeric nanoparticles and capsules targeting various applications, including those in nanomedicine. The group develops novel nanocarriers for drug delivery, particularly therapeutic enzymes and peptides for intracellular and in vivo delivery. These carriers are further characterized using fluorescence, infrared, Raman, and atomic force microscopy.

Prof. Andre Skirtach

CONTACT INFORMATION

The Nanodelivery cluster is supported by the business units ChemTech, DiscoverE and Biomarked.
They are the focal point for industrial collaborations.

The business units facilitate and coordinate a set of industrial projects and manage a strategic IP portfolio and its licensing opportunities.

The business developers of ChemTech, DiscoverE an Biomarked are supported by a project manager, and they are at your disposal:

Dr. An Van Den Bulcke
ChemTech Technologies
for Life Science

Krijgslaan 281, S4
B-9000 Gent – Belgium

An.Vandenbulcke@UGent.be
www.chemtech.ugent.be
T +32 9 264 44 62
M +32 474 81 23 81

Dr. Dominic De Groote
DiscoverE
Academic drug discovery

Ottergemsesteenweg 460
B-9000 Gent – Belgium

Dominic.Degroote@UGent.be
www.discovere.ugent.be
M +32 478 56 87 29

Dr. Daisy Flamez
Biomarked
Biomarkers for diagnostics and targeted therapies

Coupure Links 653
B-9000 Gent – Belgium

Daisy.Flamez@UGent.be
T +32 9 264 99 12
M +32 477 44 71 10

Dr. Cristina Pintucci
Cancer Research Institute Ghent
CRIG

Coupure Links 653
B-9000 Gent – Belgium

Cristina.Pintucci@UGent.be
T +32 9 264 99 12

GHENT
UNIVERSITY

EXPERTISE AT UGENT

Nanodelivery

GHENT
UNIVERSITY

OUR OFFER

Chemical design and synthesis of polymeric delivery systems

UGent has extensive know-how in the design and chemical synthesis of novel polymers and their assembly into functional (nano)materials that can respond to specific intracellular stimuli such as pH, oxidation/reduction and enzymatic hydrolysis. These materials are used to formulate small molecules and macromolecular (peptide, protein, RNA) drugs. The polymer composition and the degree of bioconjugation as well as the cleavable can be modulated for tuning the release rate of incorporated drugs and nanoparticles. Specific knowledge is also in the synthesis of self-assembling polymers as basis for polymer therapeutics, micellization of amphiphilic polymers, and biodegradable thermoplastics such as polyesters. A strong know-how is also the synthesis of peptides and nucleic acids for the design of novel reactive peptide- and oligonucleotide-based probes with applications in antisense and antigen strategies, protein and miRNA/lncRNA target identification and receptor pulldown.

Cell transfection and gene delivery vehicles

Cell transfection for the development of biopharmaceuticals is a key expertise of UGent, with a strong know-how on nanoscopic carriers' improvement for targeted intracellular delivery of nucleic acids (siRNA, miRNA, ASO, sgRNA, mRNA, pDNA). Transfection through physical delivery methods is also a strong competency, with the strong focus on the use of ultrasound and light triggers for both *in vivo* and *in vitro* delivery of macromolecules in cells. Furthermore, UGent designs novel drug delivery nanocarriers, including excipients for polyplexes and liponanocarriers for improved gene delivery.

Novel hydrogel carriers

We have extended know-how in the field of hydrogels and a very large portfolio on mostly proprietary biomaterials for hydrogel development. Hydrogels can be constructed from functionalized biopolymers (gelatines, alginates, etc.) or from synthetic (biodegradable or non-degradable) polymers (PCL, PLA, PLGA, PEG, etc.). A variety of unique hydrogels can be based on our novel hydrogel precursors that cross-link in solid state (AUP platform), our highly versatile poly(2-oxazoline) platform or on polyacrylamide pre-polymers. Injectable hydrogels can be designed based on responsive polymers or based on our proprietary self-assembling peptide hydrogelator platform. We have full control over the hydrogel structure and can tailor the properties in function of the required release profiles.

Delivery adjuvant

We explore novel bio-inspired approaches for the delivery of macromolecular drugs (e.g. RNA drugs) across intra-and extracellular barriers by evaluating distinct biomaterials (e.g. polysaccharide hydrogels, pulmonary surfactants) and cellular pathways to make nanomedicine-mediated delivery of RNA more efficient. Top expertise is created by, e.g. repurposing two distinct cationic amphiphiles (low molecular weight cationic amphiphilic drugs, CADs) as well as the endogenous lung-related surfactant protein B (SP-B) to improve cellular delivery of small RNA therapeutics.

Tissue- and cell-specific targeting

Targeted delivery is realised by bioconjugation and labelling of biomacromolecules (i.e. peptides, proteins and oligonucleotides) as well as design of nanoparticles. UGent develops novel bioconjugation methodologies like site-selective furan-oxidation, novel click chemistries or stable alternatives to maleimide-based conjugation. Nanocarriers that target specific tissues and/or microenvironments are developed for, e.g. immune system engineering. This is accomplished via functionalization of polymer- and lipid-based nanomaterials which can modulate the pharmacokinetic and pharmacodynamic profile of immuno-modulatory stimuli and antigens. Target specificity is also obtained by cloning and expressing recombinant proteins or protein fragments in bacteria or mammalian cells. Furthermore, nanobody derivatization is done via incorporation of, i.e. non-canonical amino acids, which allow drugs as well as other substances to be linked to nanobodies without losing activity as the coupling is done in a site-specific manner. Vaccines are also used as strategy for targeting specific tissues for human and veterinary medicine.

Characterization of delivery vehicles

Fluorescence, transmission and label-free microscopy are offered to characterize new or existing drug delivery carriers. Infrared and Raman microscopy can be used for characterizing the composition, while atomic force microscopy is offered to probe mechanical, rheological properties as well as the strength of interaction with cells and tissues. Fluorescence Correlation Spectroscopy and Single Particle Tracking are offered to follow up drug loading and release of cargo from delivery carriers, and to determine their behaviour (mobility, aggregation, stability) in biological environments (e.g. blood, serum, intraperitoneal fluid, vitreous, intracellular environment).

OUR OFFER

Chemical design and synthesis of polymeric delivery systems

Cell transfection and gene delivery vehicles

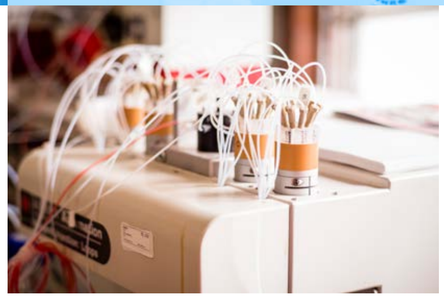
Novel Hydrogel Carriers

Delivery adjuvant

Tissue- and cell-specific targeting

Characterization of delivery vehicles

OUR TOOLBOX



Delivery of oligonucleotides and macromolecules

- Introduction of non-canonical amino acids in nanobody's primary sequence
- Click chemistry
- Site-specific coupling of e.g. fluorophores, gold particles and pharmaceutical compounds to nanobodies

Enhanced intracellular delivery

- Antigen-specific nanobodies for expression in the cytoplasm of mammalian cells (intrabodies)
- Laser-induced photoporation for enhanced transfection of cells *in vivo* and *in vitro*
- Low molecular weight cationic amphiphilic drugs (CADs) for cellular delivery of siRNA
- Cationic polymers for polyplex formation

Intraperitoneal delivery systems

- Intraoperative hyperthermic perfusion (HIPEC) with closed or open abdomen
- Prolonged intraperitoneal drug delivery (IPDD) with or without catheter/pump implantation
- Isolated peritoneal tumor for studying drug penetration after intraperitoneal drug delivery

Ocular drug delivery

- *Ex vivo* retinal explants
- Study of vitreal mobility
- Study of the internal limiting membrane (ILM) barrier function
- Subretinal (SR) and intravitreal (IVT) injections

Immunotherapy

- Immune innate activation engineering
- Cancer vaccines
- T cells engineering

Tissue-specific delivery: lung, nervous system, brain, lymph node, intestine

- Delivery to lung:
  - Use of endogenous lung-related surfactant protein B (SP-B) to improve cellular delivery of small RNA therapeutics
- Delivery to the nervous system:
- Transduction of cells of the nervous system using *in vivo* injection of viral vector (AAV, CAV)
- Delivery to the brain
  - Optogenetics/Chemogenetics – Use of viral vector-based gene therapy to render brain cells sensitive to light/designer drugs. These approaches can be used to modulate neurons with unprecedented temporal, spation and cellular specificity.
  - Photopharmacology - Administration of photo-caged and photo-switchable compounds, and local activation of the compound in the brain via administration of light to the brain
  - Drug delivery across the blood-CSF barrier via receptor-mediated transcytosis (Trojan horse technology)
- Delivery to lymph node:
  - Via nanogels, block polymer amphiphiles, solid lipid nanoparticles
  - Via small molecule immune-modulators (TRL and STING agonists, chemotherapeutics)
  - Via peptide antigens and RNA-based therapies
- Delivery to intestine:
- Vaccine antigens and microparticles targeted to the entry portals of the small intestinal epithelium in *in vivo* models

Biophysical characterisation of nanomedicines

- Advanced microscopy techniques (Fluorescence Correlation Spectroscopy, Single Particle Tracking) for studying the biophysical behaviour of nanomedicines in the relevant biological environment, and investigating their intracellular processing
- Raman and IR microscopy to characterize capsules, proteins, cells
- Atomic force microscopy