UNIVERSITY OF COPENHAGEN DEPARTMENT OF PHARMACY



Master Thesis Catalogue 2024

Department of Pharmacy



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Preface

This thesis catalogue is intended to inspire you and help you complete the thesis that suits you best. In the next pages, you will find a description of each research group, together with examples of project titles and research areas. These descriptions should be viewed as tentative only, as future research results may alter the projects. Therefore, the final projects will be defined in agreement with the students immediately before the projects start.

What might not be written in the catalogue is that in addition to the projects performed in the facilities of the University of Copenhagen, most supervisors offer projects in collaboration with other institutions/industries in Denmark or abroad. Therefore, if you find an interesting project area, feel free ask for options as to where such a project can take place, also if you would like to know of options that are more theoretical e.g. projects that are not directly linked to practical laboratory work.

To make sure you have a positive experience, there might be expectations as to existing knowledge or grades, depending on the project placement, but please remember that grades are not everything, and that a good attitude will get you just as far as good grades.

NOTE: Groups do not all use the same procedure to recruit Master students. Look carefully at the section "Application procedure and dates" at the end of each group's presentation so as not to miss any deadline.

Good advice when contacting your potential thesis supervisor:

- 1. Study the research conducted in your potential supervisor's lab before you ask for a meeting
- 2. Don't send out generic emails tailor your emails for each potential supervisor you contact
- 3. Tell your potential future supervisor why you find their specific area of research interesting
- 4. Tell something about yourself in the email your academic background and your interests
- 5. Remember to be ready to answer questions about details about your study program, the timing of your thesis work, how many ECTS points, and remember to ask if the supervisor recommends any elective courses

Good luck and we hope to see many of you at the Department of Pharmacy in the near future.

CNS Drug Delivery and Barrier Modelling

www.pharmacy.ku.dk/research/cns-drug-delivery-barrier-modelling/



We investigate how we can overcome the barrier tissues in the body and deliver drug compounds at the site of action. The major focus is on transport of compounds through the blood-brain barrier or via the nose-to-brain pathway.

The practical work includes design of novel peptide drug compounds, physicochemical studies of drug compounds, prodrugs and model drug compounds, ADME studies in cell models and *in vivo* and characterization of relevant membrane transport proteins. Special focus is on peptides. A number of peptide drugs for the treatment of brain diseases are available. However, to reach their target site of action, they must pass the blood-brain barrier (BBB). The capillary endothelium comprises the major physical barrier of the BBB and allows only passive permeation of molecules <400 Da. Brain delivery of the larger biopdharmaceuticals, which today includes an increasing number of novel peptide-drug entities, is therefore restricted; both due to their large molecular size and hydrophilic nature. Thus, the development of peptide-drugs for the treatment of brain specific diseases requires a delivery strategy for overcoming the endothelial BBB in order to reach its final target within the brain. Alternatively, other pathways, such as the nose-to-brain pathway, may be exploited.

The group consists of one professor, one associate professor, one research scientist, as well as technicians, Postdocs, PhD-students, and Masters students. We work in a cross-disciplinary fashion; have a large international network and an exciting work environment.

Potential thesis supervisors

Mie Kristensen	Lasse Saaby
Associate Professor	Research Scientist (affiliated associate professor)
mie.kristensen@sund.ku.dk	lasse.saaby@sund.ku.dk
Researcher Profile	Researcher Profile
Birger Brodin	
Professor	
birger.brodin@sund.ku.dk	
Researcher Profile	

Examples of projects

Cell models for screening of CNS drug compounds

Industrial screening of CNS drug compound candidates involve the use of cell culture models. The project concerns characterization of drug transport in cell culture models developed by the group and investigation of their use in predicting blood-brain barrier permeability. The overall aim of the project is to generate predictive tools for CNS drug development.

Supervisors: Lasse Saaby & Birger Brodin. Max no of students: 3

Drug delivery across the blood-brain barrier using shuttle peptides

The shuttle peptides include cell-penetrating- and tight junction-modulating peptides. Subprojects count i) studies on the mechanism of barrier permeation at the cellular level, ii) effects of applying various labels to the shuttle peptide for detection and visualization purposes, and iii) pharmacokinetic evaluation in rodents including safety assessment.

Supervisors: Mie Kristensen. Max no of students: 2

Nose-to-brain as pathway for pharmacological treatment of stroke-triggered brain tissue damage

Subprojects count i) setting up and characterization of a state-of-the-art primary nasal epithelial cell culture model, ii) evaluate the potential of shuttle peptides to improve brain drug delivery *in vitro* and *in vivo*.

Supervisors: Mie Kristensen. Max no of students: 2

Application procedure and dates

If you are interested in writing your thesis with CNS Drug Delivery and Barrier Modelling, please write an email to one of the supervisors with more information about you. There is no deadline.

Copenhagen Centre for Regulatory Science

www.cors.ku.dk



Medicines are important for our society, both to improve public health, but also for economic growth. At the same time, medicines are one of the most regulated products in our society.

Regulation is set in place to protect public health, while still fostering innovation that ensures that Europe continues to benefit from new medicines. However, regulating medicines is an increasing complex issue. The structures of drug regulation that exist today have evolved over time, in an attempt to respond to an increasingly sophisticated pharmaceutical development, safety crises and needs and demands of the society.

The field of Regulatory Science seeks to study, evaluate and optimize drug regulatory systems in terms of their ability to ensure patient safety, enhance public health and stimulate innovation. This also includes the development of new methods, tools and instruments to assess the safety, effectiveness, quality, public health impact, or performance of medicines, thereby facilitating regulatory decision-making. Through improvement of the drug regulatory system, we aim to contribute to an improvement of the health of the society. Furthermore, we carry out research that produces evidence to be used in drug regulatory decision-making.



Potential thesis supervisor



Christine E. Hallgreen Associate professor cors@sund.ku.dk Researcher Profile

Examples of project topics

The Impact of Paediatric Regulations on Drug Development for Children

	In order to facilitate the development of medicine for children, regulations have been set in place in
	several regulatory regions. The European Paediatric Regulation came into force in 2007. In the US,
	Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA) were
	introduced in 2002 and 2003, respectively. Projects can relate to the evaluation and assessment of
	the paediatric regulations and their regulatory tools and processes, or the comparison of the
	paediatric regulations in different regions.
Use of real-wo	rld evidence to support regulatory decision-making
	Use of real-world evidence (RWE) to support regulatory and clinical decision-making is not new. In
	disease epidemiology and in post-marked safety evaluation RWE are already quite well established.
	Current both the FDA and EMA emphasize the potential of RWE to support approval of new
	medicinal products and new indications. Project within this topic could explore the acceptability
	and/or the request by regulatory agencies for RWE for example in connection to expedited pathways
	for MA or orphan drugs.
Evaluation of p	pharmacovigilance regulation
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You can find examples of previous Master thesis projects at CORS on our website: www.cors.ku.dk/education/

Application procedure and dates

If you are interested in writing your thesis with CORS, please write an email <u>christine.hallgreen@sund.ku.dk</u> with a short motivation (250 words) describing why you are interested in Regulatory Science (deadline December 2, 2022).

Drug Delivery and Biophysics of Biopharmaceuticals



www.pharmacy.ku.dk/research/drug-delivery-biophysics-biopharmaceuticals/

Our research focus is the design and development of optimal drug formulations with a focus on biopharmaceuticals, specifically peptides and proteins, used for e.g. metabolic diseases or infections. Our research spans from advanced physicochemical analysis of stability/aggregation of biomolecules, and biomembrane interactions via design of advanced drug delivery systems, to assessment of the efficacy in cell culture models and animals. We aim to gain detailed, fundamental, and mechanistic understanding of the challenges associated with these molecules when administered via injectable and non-injectable routes.

<u>Please note, that the below described projects serves as examples. We are always open for suggestions and discussions to design a project based on your scientific interests.</u>

Potential thesis supervisors



Hanne Mørck Nielsen Professor

hanne.morck@sund.ku.dk Researcher profile

Research focus: Drug delivery of peptides and proteins (biopharmaceuticals) and antimicrobial drugs. Oral peptide delivery, drug delivery systems, nanogels, cell-penetrating peptides, biomembrane interactions, mucus, cell uptake and cell transport, in vitro/ex vivo/in vivo assessment



Vito Foderà

Associate Professor vito.fodera@sund.ku.dk <u>Researcher profile</u> **Research focus**: Protein science; neurodegenerative diseases; nanomaterials for drug delivery; X-ray

and neutron science, microscopy and optical and IR spectroscopy; modelling of biological processes. If you want to look at my research focus, please visit: www.vitofodera.com/



Marco van de Weert Associate Professor marco.vandeweert@sund.ku.dk Researcher profile

Research focus: Peptide and protein formulation; biosimilars; analytical

chemistry; fluorescence spectroscopy; peptide and protein aggregation.

Examples of projects

Novel dosage forms with permeation enhancers for oral delivery of peptides and proteins



Holy Grail of drug delivery. In this project aims to design and investigate new approaches to enhance absorption of biopharmaceuticals across mucosa in the mouth, stomach or intestine by co-formulating the drug with permeation enhancers in novel solid dosage forms (e.g. mini-tablets, micro-containers, adhesive electrospun nanofiber patches, or expandable films). We investigate *in vitro* (cell culture models), *ex vivo* (excised tissue in Ussing chambers) and eventually *in vivo* how these approaches increase oral peptide delivery. Please note that projects with hands-on *in vivo* work requires 60 ETCS credits and elective course in Laboratory Animal Science.

Delivery of biopharmaceuticals after oral administration is considered the

Supervisors: Hanne Mørck Nielsen, PhD student and/or post doc. Collaboration with industrial partners possible.

Biobarrier interactions in drug delivery: Mechanism of action by functional excipients



When studying drug delivery across epithelial barriers, one of the key properties is the tightness of the epithelium comprising both epithelial cells as well as sealing tight junctions between cells. Epithelial integrity is crucial for the normal function of the tissue, and cannot be irreversibly disrupted. In this project, we investigate the mechanisms of how excipients and formulations act

on mucosa. Effects of specific junction-modulating compounds, permeation enhancers like cell-penetrating peptides or e.g. self-assembled nanosystems containing therapeutic peptides or proteins will be investigated in detail using *in vitro* cell culture models and *ex vivo* in Ussing chambers. Microscopy and histology of the tissue as well as integrity dynamics and peptide permeability should be assessed.

Supervisors: Hanne Mørck Nielsen and PhD student and/or postdoc

Hybrid drug delivery systems based on lipids and peptide/polymer self-assembled particles

Drug delivery systems based on well-characterized nanoparticles can be used to deliver various therapeutic compounds. In this project you will prepare and characterize nanoparticles and investigate their behavior *in vitro* using advanced characterization methods. Based on your interest, the project can be focused on the more fundamental biophysical characterization, on drug delivery system production methods, or the interaction of these systems with cells and mucus, as well as their performance in terms of release and drug activity.

Supervisors: Hanne Mørck Nielsen and PhD student

Ultrathin coats for efficient drug delivery into barrier-impaired skin

Applying conventional dosage forms, such as creams and ointments for cutaneous therapies requires physical contact that may disrupt the sensitive skin and cause discomfort for the patients. The proposal aims to design and investigate the potential of a new cutaneous formulations (based on e.g. lipid nanoparticles and/or thermoresponsive polymers) with anti-inflammatory and/or antimicrobial drugs for easy application onto dry, cracked, compromised skin that occurs in many inflammatory skin diseases including atopic dermatitis.

Supervisors: Hanne Mørck Nielsen and PhD student

Biopolymer composite hemostats for use on wounds

Hemostats are microporous sponges used to stop bleeding and to absorb wound fluids in e.g. surgery. In this project, you will prepare and characterize sponges prepared from selected biopolymers. Mechanical stability and a high fluid absorption capacity are critical parameters that will be influenced both by the material and the preparation procedures.

Supervisors: Hanne Mørck Nielsen and industrial collaborator

Characterizing ligand binding to proteins



The pharmacological effect of drugs usually depends on their binding to a target protein and to plasma proteins. Protein binding can also be used to stabilize therapeutic proteins. It is therefore important to characterize this so-called ligand binding to proteins using a set of analytical methods. To do this characterization properly can be a challenge, however. In this project you will use advanced analytical methods to characterize binding of model ligands to model proteins, and test different published approaches to analyze the data. You will thereby get an understanding of the advantages and limitations of various methods and learn how to critically assess the literature on this topic.

Supervisors: Marco van de Weert

Turning proteins into glass



Proteins are often much more stable in dried formulations, but then need to be rehydrated to allow injection. However, by producing these dry proteins as glassy microbeads, these formulations can be suspended in an oily phase and directly injected without the need for rehydration. This would simplify the administration of unstable proteins considerably. In this project you will prepare and characterize these protein-containing glassy microbeads in terms of size, protein structure, and suspendability in oily phases, using both advanced protein characterization methods and rheology.

Supervisors: Marco van de Weert + possibly PhD student

Physical instability of peptides/proteins

Therapeutic peptides offer many advantages, but their instability is often a major formulation challenge. Many peptides tend to aggregate into long fibrillar structures. Preventing this fibrillation is a major challenge. Within this area you can go into some fundamental aspects of peptide (or protein) fibrillation, and study how the fibrillation process is changed e.g. by using heavy water (D₂O). In this project, you will use a panel of advanced analytical techniques to study the aggregation process.

Supervisors: Marco van de Weert + Vito Foderà and company supervisor

Formulation of injectable drug products

The subject of this project is the formulation of therapeutical relevant biomolecules intended for clinical testing. The formulation work of injectable drug product is often troublesome due to the unstable nature of peptides and proteins in solution. We are working with techniques to optimize the chemical and physical stability during thermal and physical stress conditions, and in order to do so we utilize several cutting-edge methods for analysis and characterization. This project will be conducted in collaboration with Department of Formulation Development at Novo Nordisk.

Supervisors: Marco van de Weert + Vito Foderà or company supervisor

Liquid-liquid phase separation in amyloid systems



Protein-protein interactions are regulated by the physicochemical properties of the solution. Cosolvents (e.g. alcohols), pH and mechanical stress strongly affect such interactions resulting in the modification of the stability of a protein solution. This generates phase separation and eventually aggregation. With this project, we want to investigate of the structure of surranglecular aggregates. There

the effect of different parameters on both the kinetics of formation and the structure of supramolecular aggregates. There is a possibility to perform part of the research abroad.

Supervisors: Vito Foderà + Postdoc

Amyloidogenic protein interaction with biological interfaces



Supervisor: Vito Foderà + Postdoc

Coding project: prediction of amyloid aggregate morphology via theoretical modelling

Protein-protein interactions are regulated by the physicochemical properties of the solution (pH salt, protein concentration, cosolvents) and determine the formation of different types of aggregates. With this project, we aim at simulating the different interactions between proteins and predicting the type of aggregates formed as a function of the initial conditions. A code in python is available and the student will vary the different parameters in the interactions, obtaining a large data set and creating a map of possible aggregates. Basic skills in coding would be preferable.

Supervisors: Vito Foderà + Postdoc

Enzyme-like activity of protein amyloid superstructures



Protein aggregation and fibrillation are associated with numerous neurodegenerative diseases such as Alzheimer's and Parkinson's. In addition to their pathological role, these amyloid materials have also been identified as functional biological materials *in vivo* and in many technological applications. Therefore, it is crucial to investigate the biological activities of amyloid materials. Aim of the project will be to study the enzyme activity in amyloid superstructures of the model proteins and investigate whether the morphology and conformation affect the antibacterial activity.

Supervisors: Marco van de Weert, Hanne Mørck Nielsen & Vito Foderà

Green and sustainable protein materials for drug delivery



A new frontier in protein self-assembly is represented by the analysis of protein structures in terms of their mechanical/structural properties. This is pivotal for the use of protein aggregates as sustainable materials for drug delivery. Aim of this project is to produce green protein nanoand micro- materials via electrospinning techniques, bulk methods and microfluidic chips and use them for the delivery of active compounds in *in vitro* and *in vivo* models.

Supervisors: Vito Foderà, Postdoc Mai Bay Stie and PhD student

Protein stability in pharmaceutical formulations



The presence of protein aggregates in protein drug products is a major concern in pharmaceutical industry. These particles may alter the efficacy of the product. Consequently, it is of great relevance to isolate and characterize each of these types of particles and evaluate their risk profile. Aim of this project is to produce and analyze homogeneous populations of protein aggregates, their features and stability.

Supervisor: Vito Foderà and Marco van de Weert + company supervisor or PhD student

Formulation of poorly soluble drugs



This industrial project will focus on the identification of critical process parameters for the manufacture of pharmaceutical formulations for poorly soluble drugs. These include solvent selection and spray drying conditions for solvent removal. We also aim at understanding external factors that impact drug solubilization and complex formation in solution. Specifically, we will investigate different stress factors such as, but not limited to, pH, temperature, salt concentration and competing solutes.

Supervisors: Vito Foderà and Korbinian Loebmann (Zerion Pharma)

Theoretical projects in the field of protein biophysics or protein delivery



We also offer the possibility to students interested in protein science and protein drug development, but not interested in doing experiments in the lab, to perform theoretical thesis in our group. We have a broad range of aspects that would be interesting to focus on, going from an in-depth literature review of emerging topics in the field, to the collection of already published data for further analysis. We can design the project based on the interests of the students.

Supervisors: Vito Foderà, Hanne Mørck Nielsen, Marco van de Weert

Projects in industry or at international universities

The group has many collaborations in industry (e.g. Ferring Pharmaceuticals, Novo Nordisk, Zealand Pharma, Leo Pharma) as well as abroad. Industrial collaborations will typically deal with peptide and protein stability and/or formulation and delivery, whereas at projects at other universities will depend on their focus of interest. Contact us for more details if interested. Be aware that these projects require an independent attitude and overall good grades.

Supervisors: Hanne Mørck Nielsen, Vito Foderà, Marco van de Weert

Application procedure

If you are interested in writing your thesis with Drug Delivery and Biophysics of Biopharmaceuticals, please contact us by e-mail for more details on our projects and possibilities. For projects in industry or with other external partners, be prepared to also include a CV and a grade list.

LEO Foundation Center for Cutaneous Drug Delivery

www.pharmacy.ku.dk/research/lfccdd/



The aim of the center is to contribute to an integrating knowledge on skin as a barrier for drug absorption, and key properties of drugs and excipients for cutaneous drug delivery. Based on a predominantly physicochemical approach, we aim to develop methods for the rational development of novel drug delivery systems for cutaneous and transcutaneous delivery of both small and large molecules, ranging from wounds to intact skin.

Potential thesis supervisors



Martin Malmsten Professor Martin.malmsten@sund.ku.dk

Researcher profile

Research focus: Microgels, nanoparticles for drug delivery, and host defence peptides for combatting infection and inflammation



Andrea Heinz Associate Professor Andrea.Heinz@sund.ku.dk Researcher profile

Research focus: Drug delivery, electrospinning, skin diseases



Mariena van der Plas Associate Professor mariena.van_der_plas@sund.ku.dk <u>Researcher profile</u>

Research focus: Skin and wound infections, inflammation, innate immunity, membrane vesicles, host defence peptides, peptide delivery systems, and



Stine Harloff-Helleberg Assistant Professor stine.harloff@sund.ku.dk Researcher profile

Research focus: Overcoming the skin barrier using delivery strategies such as deep eutectic solvents and surfactant based self-assembling systems with a focus on physicochemical characterization and structure-function relationship and skin barrier interactions

Examples of projects

Oxidative stress on lipid membranes as a new tool for developing new antimicrobial agents

UV irradiation time



Inorganic nanoparticles are very attractive as antimicrobial agents ('nanobiotics'), notably due to the increasing resistance development against conventional antibiotics. Apart from scalability and versatility, such materials offer advantages related to responsiveness of antimicrobial and anti-inflammatory effects and the possibility of controlling them by a range of triggering factors. For instance, oxidative stress is known to be behind the antimicrobial activities of TiO_2 nanoparticles when activated by UV light. However, studies on the mechanisms underlying these activities remain scarce. Based on

previous work done by our group on the oxidative destabilization of lipid membranes, and using different biophysical and surface-chemical techniques such as fluorescence spectroscopy, QCM-D, FTIR-ATR, and DLS, the present project will focus on the effects of TiO₂ nanoparticle-induced oxidation of lipid membranes, lipid degradation, and their consequences for membrane structure and stability. Any potential membrane selectivity that could allow more efficient antimicrobial activities along with reduced side effects will be also explored, for instance the combination with cationic peptide coatings. In a wider perspective, this project will contribute to the mechanistic foundation for the use of photocatalytic nanomaterials as triggerable antimicrobial agents.

Supervisor: Martin Malmsten

Electrospun skin patches for the treatment of psoriasis (Supervisor: Andrea Heinz)

Psoriasis is a chronic, inflammatory skin disease that occurs in episodes and affects 125 million people worldwide.



Patients are dependent on continuous treatment with cortisone, and compliance is often poor because creams and ointments have to be applied frequently and leave a greasy feeling on the skin. Treating the keratinized psoriasis plaques with a patch which continuously releases an anti-inflammatory agent would be beneficial.

The focus of this project is on the production of electrospun fibers consisting of a cortisone-containing core and a keratolytic-containing shell. After producing and optimizing the fibers (by using SEM as a control), you will characterize the fibers for their mechanical and solid-state properties (DSC, TGA, DMA, XRPD). Furthermore, you will investigate drug loading and release (HPLC for

quantification) and ensure the compatibility with skin cells by doing in vitro cell studies.

Phospholipase responsive drug delivery system for treatment of psoriasis (Supervisor: Andrea Heinz)

Psoriasis is a chronic skin disease affecting 2% of the world's population. The pathophysiology of psoriasis involves an upregulation of the enzyme phospho-lipase A2, which cleaves phospholipids, which is why a stimuli-responsive drug delivery system using phospholipase A2 as a stimulus is a promising novel approach to treat psoriasis.

The master project will work on developing a topical formulation relying on phospholipids to create a phospholipase A2responsive drug delivery system for the delivery of the anti-inflammatory drug tofacitinib. More in detail, incorporation of different phospholipids into cubosomes has proven to be a viable solution, and their potential as phospholipase A2-



responsive drug delivery system will be investigated.

The project covers the preparation of cubosomes, and their characterization by small-angle X-ray scattering, dynamic light scattering and cryo-transmission electron microscopy. Moreover, the drug release will be analyzed.

Pushing the boundary of transdermal delivery (Supervisor: Andrea Heinz)



Transdermal delivery is one the most beneficial administration routes of APIs, but it is restricted to a comparatively small number of molecules due to the skin properties. The goal of this project is to propose a systematic comparison of individual and combined strategies utilized in transdermal delivery, with a goal of establishing universal platforms for the delivery of drugs for both local and systemic treatments.

Terpene-based deep eutectic solvents (DESs) will be formed and their potential to solubilize model drugs will be assessed. Supersaturated state of the formulations will be triggered by heating and cooling method. Then,

DESs will be used to form microemulsions, nanoemulsions, and modified invasomes, which will be characterized in terms of their size, charge, and encapsulation efficiency. Finally, an effect of the formulations on transdermal delivery of the drugs will be investigated through permeation studies using the pig skin. Effect of the systems on the skin structure will be determined based on molecular and visual inspection.

2D and 3D skin models for atopic dermatitis

The goal of this project is to develop skin infection models for studying drug delivery systems in atopic dermatitis. The work will consist of techniques within the fields of immunology and microbiology (including cell and bacterial cultures, analysis of inflammatory markers and signalling pathways, cytotoxicity, and histology), as well as skin penetration studies of various drug delivery systems and penetration enhancers.

Supervisors: Mariena van der Plas

Membrane vesicles for targeted drug delivery



Supervisors: Mariena van der Plas

Antibiotic resistance development is one of the biggest challenges of our time. Antimicrobial host defence peptides are promising alternatives to antibiotics, as they kill a broad spectrum of microbes, including multi-resistant strains. As both human and microbial membrane vesicles play essential roles during infection, the purpose of this project is to investigate the potential of membrane vesicles as nanoparticles for targeted delivery of antimicrobial peptides. The work will include techniques within the fields of microbiology, cell biology, molecular biology, physical chemistry and drug formulation and characterization.

Peptide-based drug delivery systems for atopic dermatitis skin infections



Atopic dermatitis (AD) is a multifactorial relapsing inflammatory skin disease affecting 1 out of 5 Danish children. As decreased levels of antimicrobial peptides are a popular explanation for the increased susceptibility to infection in these patients, antimicrobial and immunosuppressing peptides have great therapeutic potential in AD.

The goal of this project is the development of potent and safe peptide delivery systems for treatment of AD lesions. The work will comprise optimisation and characterization of delivery systems, *in vitro* antimicrobial assays, biofilm assays and cell assays. Several students can work on this project independently.

Supervisor: Mariena van der Plas & Martin Malmsten

Deep eutectic solvents as transdermal delivery systems



Effective transdermal delivery of drugs across intact skin remains a challenging and complex goal, especially for large hydrophilic molecules. The skin's main barrier, the stratum corneum (SC), efficiently blocks mass transport due to the self-assembly of lipid multilayers. Therefore, to exploit the multiple advantages of topical delivery, new formulations are needed that overcome this barrier in a non-destructive manner, thereby improving the delivery of drugs through the skin. Recently, deep eutectic solvents (DESs) have shown great promise as solvents for topical delivery. In this project, we aim to understand the self-assembly of non-ionic surfactants in DESs. We will tune the physicochemical properties of the system to solubilise the maximum

amount of drug into the formulation, thereby ensuring rapid and efficient API delivery both into and through the SC. **Supervisor:** Postdoc, Stine Harloff-Helleberg & Martin Malmsten (minimum 45 ETCS)

How does formulation strategy impact skin permeation?



With this project, we will evaluate the impact of drug carrier on drug permeability. First, selected cutaneous delivery systems will be prepared and structurally characterized using orthogonal biophysical techniques. Second, the interaction and solubilization effect on the skin barrier will be evaluated using in vitro and eventually ex vivo techniques.

Supervisor: PhD student & Stine Harloff-Helleberg (minimum 45 ETCS)

Application procedure and dates

If you are interested in writing your thesis with the LEO Foundation Center for Cutaneous Drug Delivery, please write an email to one of the supervisors with more information about you. There is no deadline.

Manufacturing and Materials

www.pharmacy.ku.dk/research/manufacturing-materials/



The Manufacturing and Materials group is focusing on processing and material sciences around solid state and semisolid pharmaceuticals. This international group has over 20 PhD students, postdocs and associate professors. The section is aiming for understanding the chemical and physical properties of the active pharmaceutical ingredients, both small molecules and bio-macromolecules, and excipients in relation to their processing behaviour. Further, the group aims to optimize stability and bioavailability of the final dosage form. The research is focusing on facilitating the future implementation of Quality by Design (QbD) principles for drug development processes, as well as implementation of process analytical technologies (PAT) for industrially relevant applications.

We focus on processing of small-molecule and protein/peptide-based medicinal products. Our goal is to understand the properties of active pharmaceutical ingredients and excipients in relation to their processing behaviour, and further, in relation to the optimal bioavailability of the final dosage form.

Potential thesis supervisors



Lene Jørgensen Associate Professor lene.jorgensen@sund.ku.dk Researcher Profile

Research focus: Protein stability, protein formulation, adsorption to surfaces, manufacturing and processing of protein pharmaceuticals, excipients design and requirements, quality of pharmaceutical products, regulatory aspects of manufacturing pharmaceuticals.



Natalja Genina Associate Professor natalja.genina@sund.ku.dk Researcher Profile

Research focus: 2D printing/inkjet printing, 3D printing/additive manufacturing, personalized medicine, physicochemical characterization of innovative product, innovative manufacturing, spectroscopy.

of



analysis,

data analysis.

Johan Peter Bøtker Associate Professor johan.botker@sund.ku.dk Researcher Profile

Research focus: Computational simulations, image

pharmaceuticals, solid state characterisation, multivariate

and

processing

manufacturing

Mingshi Yang

Associate Professor

Research focus: Pharmaceutical article engineering,

pulmonary drug delivery, and tissue engineering.

mingshi.yang@sund.ku.dk



Jukka Rantanen Professor jukka.rantanen@sund.ku.dk <u>Researcher Profile</u>

Research focus: Process analytical technologies, pharmaceutical materials science, bulk powder analysis, spectroscopy, computational pharmaceutics



Anders Østergaard Madsen Associate Professor a.madsen@sund.ku.dk Researcher Profile

Research focus: Crystallography, pharmaceutical materials science, synchrotron-based techniques, computational pharmaceutics.

Examples of projects

Hot melt processing of biopharmaceuticals



In this project, the amorphous environment created by various polymers in a hot melt process will be studied to see whether it is sufficient to prevent the degradation caused by heat, and therefore would enable protein formulations to be produced by hot melt processing. This will be investigated by monitoring structural changes in both the solid and the liquid state. Several process and formulation variables form a good basis for the application of Design of experiments (DoE).

Supervisors: Lene Jørgensen and Johan Peter Bøtker

Processing and physical stability of proteins



formulation and manufacturing, since the biological activity may otherwise be reduced. We will expose a protein to various types of stresses, formulation components, processing and use advanced techniques to characterize the changes that we observed. In this project, you will gain knowledge of basic protein formulation, effect from various types processing and excipients and you will get experience with techniques to study protein stability and structure.

Maintaining the physical stability of proteins is crucial in both

Supervisor: Lene Jørgensen

Master project in industry or abroad

You could also do your project in the pharmaceutical industry, Medico industry or at a University abroad (e.g. University of Otago, School of Pharmacy, Dunedin, New Zealand). This requires planning, so short notice project are often not possible. You need to plan 6 months-1 year ahead. You will be asked to supply a copy of your grades, as you will need to work independently. The projects topics in industry are typically defined in detail 2-3 months before the actual start of the project.

Supervisor: Lene Jørgensen

Information-rich pharmaceutical products



Data-enriched edible pharmaceuticals (DEEP) enable encapsulation of both the drug and the sensitive information in a single dosage unit. This can pave the way against counterfeiting of medicine. The goal of the project is to explore the further possibilities of efficient and secure data storage within edible drug-containing dosage unit, and fully characterize the obtained dosage forms by employing the up to date analytical tools and the standard pharmacopeia methods.

Supervisors: Natalja Genina and External from the Department of Computer Sciences or PhD student Ilari Ahola.

Feasibility of printed medicine



Currently, there is only one commercially available 3D printed medicine, and one is on the way. If the needs of the patients are identified, the situation can be different in the near future with more printed drugs coming to the market to provide more exact pharmaceutical treatment in society. The aim of the project is to explore the patients' attitude towards the idea of getting personalized digital drug product by conducting interviews and showing the possibilities of 3D printing.

Supervisors: Natalja Genina and Sofia K. Sporrong

Development of personalized medicine by 2D and 3D printing



Delivering an accurate dose of active pharmaceutical ingredients (API) and tailoring their release profile are the key factors to produce efficient pharmacotherapy, including the fixed dose combination drug products. With current dosage forms, tunable dosing and tailoring multidrug products' properties are difficult and perilous. The evident flexibility of the printing technology allows commercial on-demand fabrication of individualized dosage forms. The overall goal is to produce novel solid dosage forms with easily adjustable doses and release profiles.

Supervisors: Natalja Genina and Johan Bøtker



Image analysis of pharmaceuticals

In this project, image analysis of e.g. the tablet coating quality is investigated using MATLAB programming. The project will revolve around creating MATLAB scripts for segmenting objects in images and constructing and operating analytical scripts as well as artificial neural networks for classification purposes. This project will thus focus on optimizing both the process of obtaining the images and the programming needed to analyse the images.

Supervisor: Johan Peter Bøtker

Optimization of bulk properties of pharmaceuticals



Particle properties determine the successful manufacturing of solid dosage forms. Shape and size distributions are critical parameters affecting flow ability of materials. However, it is a huge scientific challenge to translate these particle characteristics into optimal final formulation. There are several new innovative approaches to investigate powder rheology together with solid form analysis, making a huge impact in commercial scale process and product optimization. This project will investigate powder rheology as a part

of solid dosage form development, as well as implementation of process analytical technologies (PAT) in an industrial setting. The projects topics in industry are typically finalized in detail 2-3 months before the actual start of the project. This project can also be performed as an industrial project at AstraZeneca, LEO Pharma, Lundbeck or Novo Nordisk. **Internal supervisors:** Jukka Rantanen

External supervisors: AstraZeneca, LEO Pharma, Lundbeck or Novo Nordisk

Pulmonary drug delivery

Lung diseases including chronic obstructive pulmonary disease (COPD), respiratory infections and lung cancer are leading cause of death world-wide. Inhaled drugs can directly reach the sites of the diseases, lower side effect, and improve pharmacological effect. The aim of this project is to utilize particle engineering technology to improve the efficacy of inhaled products by improve lung deposition, modulating dissolution rates and absorption of inhaled drugs. This project can be carried out at University of Sydney or Shenyang Pharmaceutical University, China.

Supervisor: Mingshi Yang

Spray-dried protein formulations



The spray-drying process may be less expensive, but more efficient to process proteins or peptides as compared to other drying techniques. This technique has additional potentials in not only stabilization of the proteins but also engineering the protein formulations into dry particles for various pharmaceutical applications, e.g. inhalable, injectables, and oral administration. This project is intended to investigate the influence of formulation and process variables in the spray-drying process on particle characteristics and physicochemical stability of the protein formulations. This project can be carried out at Novo Nordisk.

Supervisor: Mingshi Yang

Electrospraying/Electrospinning in pharmaceutical application



Electrospraying/Electrospinning are emerging technologies in the pharmaceutical filed to fabricate micro/nano-structured materials for drug delivery and tissue engineering. This project aim to explore the application of this technology and investigating to promote this technology in the pharmaceutical field for producing orodispersible films, wound dressing, and injectable depot microparticles.

Supervisor: Mingshi Yang

Anhydrate-hydrate systems in pharmaceutical products



During production and storage of solid state dosage forms the role of hydrate formation cannot be underestimated. The transformation between hydrates and anhydrates occurs as a function of temperature and humidity, and severely affects the properties of the crystals. The aim of this project is to understand how the water activity level

and the temperature can influence the ratio of the anhydrate and hydrate forms of different model compounds, and how the properties of the bulk material changes as a consequence of these transformations.

Supervisors: Anders Ø. Madsen, Jukka Rantanen

Crystal growth and dissolution - simulation, observation and analysis



Crystalline drugs and excipients are the main components of solid state dosage forms. Their growth and dissolution behaviour are crucial for both tablet production and oral drug delivery. In this project, we observe the growth and dissolution of crystals in different conditions using visual microscopy in combination with X-ray diffraction techniques and correlate these observations with computer simulations. Depending on your skills and interests, the project can be laboratory based or involve Monte Carlo simulations of crystal growth, python programming to develop machine-learning approaches to automate analysis of microscopy images and videos.

Application procedure and dates

If you are interested in writing your thesis with the Manufacturing and Materials group, please write an email to one of the supervisors with more information about you. There is no deadline.

Microscale Analytical Systems

www.pharmacy.ku.dk/research/microscale-analytical-systems/

Our research group develops analytical chemical tools for tackling many challenges in pharmaceutical and medical research, especially in situations where sample size is limited, where the molecules of interest are only present in small concentrations, or where a large number of samples needs to be processed in a short time frame. To enable this cutting-edge analysis we develop and apply technologies such as micro-nano engineering, microfluidics, and polymer science for next generation high-throughput workflows, e.g., in protein characterization, peptide analysis, drug transport studies, and drug delivery.





Main focal areas of the group are modern separation techniques (e.g. LC, CE) coupled to mass spectrometry, advanced sample preparation methods (e.g., μ SPE, μ EME), traditional spectroscopic techniques (e.g., NMR, IR, Raman) and a range of microfluidics-driven techniques (e.g., droplets, micro-nano particle fabrication); furthermore, we apply ex vivo models and develop microphysiological *in vitro* models (i.e., organ-on-a-chip) that are all intended to understand drug-target interactions, investigate drug metabolism, and getting insight into disease progression and therapeutic efficacies.

Potential thesis supervisor



Jörg P. Kutter Professor jorg.kutter@sund.ku.dk Researcher profile

Research focus: Microfluidic devices for bioanalytical challenges in pharmaceutical and related life sciences.



Nickolaj J. Petersen Associate Professor nickolaj.petersen@sund.ku.dk Researcher profile

Research focus: Miniaturized analytical techniques, in particular separation methods coupled to mass spectrometry, for pharmaceutical analysis



Claus Cornett Associate Professor claus.cornett@sund.ku.dk Researcher profile

Research focus: Quantitative analysis of pharmaceutical compounds from plants; human metabolism and drug validation.



Stig Pedersen-Bjergaard Professor stig.pedersen-bjergaard@farmasi.uio.no

Researcher profile

Examples of projects

Lab-on-a-Chip for next-generation sample separation and analysis



The analysis of complex protein mixtures is of tremendous importance for pharmaceutical drug discovery. To identify potential drug targets, complex mixtures such as blood, cell cytoplasm or secretome have to be screened.

High-throughput screenings involve large numbers of samples and compounds, which are, however, only available in small amounts. Therefore, the sample preparation has to be miniaturized, integrated and automated. Ideal platforms to meet these requirements are microfluidic devices, which allow the precise control of chemical reactions and the integration of other functional elements (so-called

lab-on-a-chip). For instance, microchip liquid chromatography provides high separation efficiency, resolution, and sensitivity. During such a project, a microscale device capable of chromatographic separation will be further developed to enable direct coupling to highly sensitive analytical methods, such as mass spectrometry (MS). **Supervisors:** Jörg P. Kutter, Nickolaj J. Petersen; No of students: 1-2

Advanced sample preparation methods on microfluidic chips



Analysis from complicated matrices (i.e., cell cultures) requires advanced sample preparation tools. This is particularly challenging when small sample volumes are involved. Here, we develop techniques such as electro-membrane extraction to, e.g., monitor drug transport through cell-based models of natural barriers (socalled organ-on-a-chip systems).

Supervisors: Jörg P. Kutter, Nickolaj J. Petersen, Stig Pedersen-Bjergaard; No of students: 1-2

Quality assurance and development of Plant medicine



Focus will be on characterizing plant based raw materials. Earlier and ongoing projects have been centered around Cannabis and Quinine, a current project (funded by DANIDA) is studying *Synadenium glaucescens* from Tanzania, and profiling industrial hemp, primarily via terpene profiles.

BYOP (Bring Your Own Plant...), if You have a special interest in a plant medicine, and access to plant material, let's negotiate.

Analytical methods used: HPLC-UV, HPLC-MS, GC-MS and NMR.

Supervisors: Nickolaj Petersen and Claus Cornett; No of students: 1-2

Streamlining the grasshopper in vitro model



Finding human drug metabolizing enzymes in other species, such as insects, can reduce the number of animal experiments in pre-clinical trials in drug discovery and development. Within this project, you will work with the grasshopper Schistocerca gregaria, to find relevant drug metabolizing enzymes in the grasshopper's "blood" – the hemolymph. You will learn, how to inject drug compounds into the grasshopper and how to collect samples, and how to set up and run enzyme assays, and how to prepare these samples for instrumental analysis with LC-MS or UV detection. Finally, you will be able to evaluate drug metabolism in the grasshopper's hemolymph and

conclude on the relevance of your findings for the grasshopper model in early drug discovery and development. Analytical methods used: HPLC-UV, HPLC-MS, GC-MS and NMR.

Supervisors: Nickolaj Petersen and Claus Cornett; No of students: 1-2

Grasshopper model for drug permeation and metabolisation studies in brain



Small animal models are a tool in early drug discovery to predict drug uptake and metabolism. Recently, the grasshopper Schistocerca gregaria has been introduced as a model to investigate drug uptake and metabolism in the grasshopper brain. In order to optimize throughput we will investigate the feasibility of using frozen grasshopper brains, as the excision of the brains is time consuming, so the possibility of using previously frozen brains would enable well-plate methods or microanalytical methods.

Analytical methods used: HPLC-UV, HPLC-MS

Supervisors: Nickolaj Petersen and Claus Cornett; No of students: 1-2

Capillary electrophoresis coupled to MS



Capillary electrophoresis (CE) provides great potential for a wide range of molecular formats, from small peptides to proteins, DNA and nucleotides. With CE-MS analysis, information about the degradation pathways, post-translational modifications and process-related impurities could be acquired which would otherwise be difficult to obtain with LC-MS.

Samples from Novo Nordisk that have been stress tested for stability will be investigated to compare advantages and limitations compared to traditional LC-MS.

Analytical methods used: CE-MS, HPLC-MS

Supervisors: Nickolaj Petersen; No of students: 1



Tailor-made projects in collaboration with industrial partners

Supervisors: Jörg P. Kutter and colleagues; No of students: 1-2

Application procedure and dates

If you are interested in writing your thesis with Microscale Analytical Systems, please write an email to one of the supervisors with more information about you. There is no deadline.

Pharmaceutical Physical and Analytical Chemistry

www.pharmacy.ku.dk/research/pharmaceutical-physical-analytical-chemistry/



The main purpose of the Pharmaceutical Physical and Analytical Chemistry (PPAC) Group is to develop novel approaches for physical chemical characterization of drugs and delivery systems. The work paves the way for design of effective novel medicines and a better understanding of the fate of drug substances and delivery systems through application of quantitative analytical methods.

The PPAC group applies physical chemical approaches in combination with advanced analytical techniques (ICP-MS, SAXS, UV-Imaging and Taylor dispersion analysis) to advance understanding of fundamental processes in drug design, development and characterization. Common to the activities is a focus on the interplay between basic physical

chemical properties of drug substances and excipients, kinetics and transport processes in relation to both drug delivery and analytical methods.

Keywords: analytical chemistry, cubosomes/hexosomes, drug delivery, excipients, injectables, *in vitro* release, LC-ICP-MS, metallo-drugs, nanoparticles, preformulation, SAXS, Taylor dispersion analysis.

Potential thesis supervisor



Jesper Østergaard Professor jesper.ostergaard@sund.ku.dk Researcher Profile

Research focus: Physical chemical characterization of drug substances and delivery systems.

Development of methods for physical chemical characterization, transport studies, *in vitro* release and dissolution testing (e.g., UV imaging, capillary electrophoresis (CE), Taylor dispersion analysis (TDA)). Molecular interactions. Study of non-covalent interactions of drugs substances and development of affinity methods based on affinity CE and TDA. Development of parenteral depot formulation principles (intra-articular and subcutaneous administration). Kinetics. In relation to drug transport processes as well as chemical kinetics and stability testing. Design of prodrugs.



Stefan Stürup

Associate Professor stefan.sturup@sund.ku.dk Researcher Profile

Research focus: Our general research interest is to develop and apply advanced analytical techniques for exploration of novel drug delivery systems and gain knowledge of the uptake, distribution, and metabolism of inorganic and bioinorganic molecules and drugs in biological systems. To pursue this interest we apply LC-ICPMS, CE, and LCMS.



Anan Yaghmur Associate Professor anan.yaghmur@sund.ku.dk Researcher Profile

Research focus: 1) Design of soft drug nanocarriers based on cubosomes, hexosomes, and other related nanodispersions. 2) In situ formation of parenteral dosage forms with tunable liquid crystalline nanostructures. 3) Cancer cubosomal and hexosomal nanomedicines. It is also of my interest to design theranostic cubosomal and hexosomal nanomedicines. Development of methods for physical chemical characterization, transport studies, *in vitro* release and dissolution testing (e.g., UV imaging, capillary electrophoresis (CE), Taylor dispersion analysis (TDA)). Molecular interactions. Study of non-covalent interactions of drugs substances and development of affinity methods based on affinity CE and TDA. Development of parenteral depot formulation principles (intra-articular and subcutaneous administration). Kinetics. In relation to drug transport processes as well as chemical kinetics and stability testing. Design of prodrugs.



Susan Weng Larsen

Associate Professor susan.larsen@sund.ku.dk Researcher Profile

Research focus: Investigation and application of physicochemical approaches to improve understanding of processes in drug delivery including parenteral depot design, profiling of drugs and analytical approaches for *in vitro* release testing. Research projects are related to i) development of parenteral sustained release drug delivery systems including in situ suspension-forming injectables, in situ formed liquid crystalline nanostructures and prodrug approaches and ii) development and utility of *in vitro* release methods to predict *in vivo* performance of depot formulations for the subcutaneous and intra-articular route of administration.



Huiling Mu Associate Professor huiling.mu@sund.ku.dk Researcher Profile

Research focus: Our research aims at exploring the application potentials of functional excipients based on a better understanding of excipient effects on drug release and absorption, as well as interactions between excipients and drug molecules. We use both lipids and polymeric excipients, and are especially interested in lipid excipients due to their versatility and stability, as well as the potential in controlling drug release. The main research activities include designing and characterizing drug carriers such as microparticles, films and foams, optimizing formulations for specific applications, and developing *in vitro* models to evaluate formulations with sustained drug release properties.



Bente Gammelgaard

Professor bente.gammelgaard@sund.ku.dk Researcher Profile

Research focus: Analytical chemistry. Our general research interest is to develop and apply advanced analytical techniques for exploration of novel drug delivery systems and gain knowledge of the uptake, distribution, and metabolism of metal-based drugs, trace elements, peptides and proteins, and nanoparticles in biological systems. Selenium metabolism is a special interest. To pursue this interest we apply LC-ICPMS, CE- ICPMS, and LCMS.

Examples of projects

Characterization of nanoparticulate drug delivery systems

This project focuses on the development of new methods to characterize nanoparticulate drug delivery systems, e.g., liposomes, cubosomes, nanocrystals. New methods based on capillary electrophoresis, Taylor dispersion analysis and UV imaging will be developed. It is important that the methods require limited amount of sample as nanoparticulate drug delivery systems are usually only produced in small quantities. The methods will allow us to address critical parameters such as incorporation efficiency, release, non-covalent interactions, aggregation and adsorption.

Supervisors: Jesper Østergaard, Henrik Jensen and Bente Gammelgaard

Novel in vitro drug release models for predicting in vivo performance of injectables

The aim of the project is to develop novel *in vitro* release testing methods suited for predicting the *in vivo* fate of injectables. Such methods are of importance in the development of future drugs for subcutaneous, intramuscular or intra-articular injection. We intend to combine a understanding of the transport processes occurring at the injection site with efficient characterizing techniques for unravelling release mechanisms and predicting the biological fate. The ultimate validation will be establishment of an IVIVC.

Supervisors: Jesper Østergaard and Susan Weng Larsen

Compound screening in early drug development using real-time surface dissolution imaging

Surface dissolution imaging provides new opportunities for visualization and study of drug dissolution mechanisms. The aim of the project is to identify and establish best practices in UV imaging-based dissolution testing. The work will involve development of new methods for selected test compounds.

Supervisors: Jesper Østergaard (project may involve an internship at external partner)

Characterization of monoclonal antibodies (mAbs) by Flow Induced Dispersion Analysis

Characterization of therapeutic mAbs with respect to structure, aggregation and antigen binding using FIDA. Investigation of sensitivity to stress conditions (temperature and chemical denaturation). **Supervisor**: Jesper Østergaard

Supervisor. Jesper Distergaard

Thesis projects on pharmaceutical analysis with pharma industry or hospital pharmacy

Characterization of therapeutic mAbs. Raman spectroscopy. Drug stability.

Ask for current possibilities.

Supervisor: Jesper Østergaard

Cancer cubosomal and hexosomal nanomedicines

Formation, characterization, and uses of cubosomal and hexosomal nanomedicines for delivery of anticancer drugs.

Supervisor: Anan Yaghmur



Cubosomes & hexosomes as versatile nanocarriers for biofilm lung infection treatment

Development of nanomedicines for treatment of biofilm lung infections. The project involves biophysical characterization studies with relevant biological evaluations.

Supervisors: Anan Yaghmur, PhD student H. Jan, and co-supervisor NN

Design of sustained release injectable liquid crystalline formulations



In situ formation of liquid crystalline depots with sustained drug release properties. Combination of biophysical investigations with drug release studies.

Supervisors: Anan Yaghmur & Susan Weng Larsen

BRAIN-PENetrating cubosomal and hexosomal NANOcarriers for glioma-targeting delivery Image: Supervisor: Anan Yaghmur This project focuses on the formulation of nanocarriers for drug delivery to cancerous brain tumors.

Local and sustained co-delivery of drugs to improve outcomes following joint replacement

To improve pain management and prevent infections related to joint replacement surgery, there is a need for efficient drug delivery systems (DDSs) that can maintain and sustain an optimal therapeutic level of multiple drugs at the surgical site. The current project focuses on rational design of parenteral *in situ* forming DDS based on lyotropic non-lamellar liquid crystalline phases for co-delivery of drugs. The drug substances are incorporated in lipids, which self-assemble upon contact with the tissue fluid to form well-ordered inverted type nanostructures (bi-continuous cubic and hexagonal phases). The aims of the project are to i) study incorporation of model drugs with different physicochemical properties in these systems and ii) investigate drug release characteristics from *in situ* formed liquid crystalline phases. Various *in vitro* release methods as well as the presence of biologically relevant fluid will be used to characterize events influencing the sustained release properties.

Supervisors: Susan Weng Larsen, Anan Yaghmur and Jesper Østergaard

A novel prodrug principle to achieve localized and sustained NSAID action after joint injection



Orally administered NSAIDs are intensively used in the treatment of osteoarthritis for pain management and reduction of inflammation. However, oral NSAIDs may evoke severe side effects even after short term use which constitutes impediments to their use. Following direct injection into the injured joint, a high therapeutic NSAID concentration can be accomplished while minimizing systemic adverse effects. As NSAIDs disappear rapidly from the synovial space (half-lives of 0.5-6 h), depot strategies are needed. In the current project, a prodrug-based *in situ* suspension-forming system intended for localized and sustained NSAID action upon intra-

articular injection will be investigated. The project relates to characterization of synthesized NSAID prodrugs and will include: (i) solubility in aqueous buffers and in synovial fluid, (ii) pH dependent stability, (iii) sensitivity to enzymatic cleavage (plasma and synovial fluid), (iv) affinity to proteins and (v) rate of NSAID release from prodrugs using an *in vitro* release model simulating the joint environment.

Supervisors: Susan Weng Larsen and Jesper Østergaard

Design of in vitro drug release models for predicting in vivo performance of depot injectables

Development of *in vitro* release models for quality control as well as formulation design purposes is a critical activity in the characterization of parenteral depot formulations. Ideally, an *in vitro-in vivo* correlation should be established, however, it requires that the drug release mechanism is the same *in vitro* and *in vivo*. The project focuses on characterizing drug release from sustained release formulations for subcutaneous and/or intra-articular administration. The aim of the project is to develop *in vitro* release models to achieve in depth understanding of how formulation designs as well as physiological parameters influence drug release mechanism and rate and drug transport the blood capillaries. **Supervisors**: Susan Weng Larsen and Jesper Østergaard

Functional excipients and drug delivery



Excipients play an essential role in drug delivery. Lipid-based formulations can increase the bioavailability of lipophilic drugs by improving drug dissolution and permeation. Both solid lipid particles and polymeric particles are good carriers for sustained drug delivery, but the mechanism of drug release from those particles are different. Hybrid polymer-lipid particles provide better effect in sustained delivery of drugs due to synergistic effect of polymer and lipids. The project aims at evaluating effect of excipients and particle preparation methods on drug release kinetics in order to design efficient drug carriers for specific applications via different administration route.

Supervisor: Huiling Mu

In vitro models to evaluate formulations for sustained drug delivery

Understanding the release kinetics of drugs from particles is a fundamental prerequisite for efficient design of drug carriers for drug delivery. However, there is no suitable method available to assess formulations with sustained drug release properties *in vitro*. The project aims at establishing bio-relevant *in vitro* models addressing *in vivo* conditions including pH, temperature, and matrix composition.

Supervisor: Huiling Mu

Bioadhesive formulations for local mucosal drug delivery

Solid lipid formulations can be used for sustained drug delivery. Incorporation of functional excipients in the formulations may create extra application potentials and be used to improve local therapeutic effect by adhesion to the mucosal surfaces (e.g. mouth, eye). The project aims at investigating the potential of combining bioadhesive excipients in formulations and validating the bioadhesive *in vitro*. Nanoparticles, prepared by hot melting and probe sonication method, will be incorporated into thin films or hydrogels, drug encapsulation efficiency and drug release, as well as bioadhesion properties will be evaluated.

Supervisor: Huiling Mu

Projects at Department of Forensic Medicine (External projects) – Two students per project is preferred

Suggestions for projects - the final project can be discussed based on skills and interest:



investigations – e.g. qualitative or quantitative analysis of new psychoactive substances (NPD) or pharmaceuticals

✓ Application of automated pipetting robots in analysis of biological samples from forensic

✓ Analysis of drugs and drugs of abuse in alternative matrix, such as hair, nails etc.

✓ Use of informatics and statistical methods for optimization and quality control in forensic chemistry

Supervisor: Bente Gammelgaard + external supervisor

Projects at the National Research Center for the of Working Environment (External projects)

 \checkmark Method development of 2D-LC-MS-MS method for metabolites of organophosphate esters in urine

- ✓ Dermal uptake of PCBs using an ex vivo skin model and GC-MS-MS analysis (collaboration w. SDU)
 - ✓Method validation and analysis of pesticides on silicone wristbands from farmers in Uganda using GC-MS-MS

Supervisor: Bente Gammelgaard + external supervisor

Determination of trace element impurities in drug products (External project)

This project entails development and validation of new ICP-OES based analytical methods to comply with Pharmacopeia requirements for elemental impurities. The project is a collaboration with Lundbeck Pharma A/S.

Supervisors: Stefan Stürup

UHPLC-ESI-MS/MS for quantification of isotope labeled metabolites

Development and validation of a UHPLC-ESI-MS/MS method for quantifying of isotope labelled glucose metabolites such as citrate, succinate, glutamate and glutamine. The final method will be applied for determination of isotopologues in cell samples.

Supervisors: Stefan Stürup, Laura McNair (ILF), Blanca Garcia (ILF)

Stability assessment of protein based drugs

In this project, the FIDA methodology is utilized for stability assessment of protein based drugs. While protein based drugs have proven efficient for the treatment of a range of serious diseases, a number of challenges remains in developing and formulating these drug compounds. Notably, they are known to be structurally labile and efficient methods for assessing stability are currently suboptimal. In this project we take advantage of the fact that structural changes can be monitored as size changes, change in optical properties and altered function (binding ability).

Supervisors: Jesper Østergaard

Application procedure and dates

If you are interested in writing your thesis with Pharmaceutical Physical and Analytical Chemistry, please write an email to one of the supervisors with more information about you. There is no deadline.

Physiological Pharmaceutics

www.pharmacy.ku.dk/research/physiological-pharmaceutics/



In the Physiological Pharmaceutics group (PhysioPharm) we work with oral and mucosal drug delivery. We develop novel drug delivery systems (DDS) to improve drug bioavailability and/or to ensure the maximal therapeutic effect with fewest possible side-effects. We work with both poorly soluble drugs and peptides, and focus on lipid-based DDS and customized release. We develop DDS for special populations (e.g. children; the elderly and patients with hypochloridia or inflammatory bowel disease). We use *in vitro* models of the mouth, eye and the gastro-intestinal (GI) tract that we are continuously improving in order to make them as physiologically relevant, and predictive for bioadhesion, dissolution, release and permeation, as possible. In addition, we also use and develop in silico models to further understand the absorption and metabolism of the drug.

Note 1: As a general rule, a co-supervisor will be allocated to each master student, often a PhD student from the PhysioPharm Group, or a person from the industry or from other institutions.

Note 2: All of us have close contact to the industry and other universities – so come talk with us if you desire a master project in the industry – or abroad.

Potential thesis supervisors



Jette Jacobsen Associate Professor jette.jacobsen@sund.ku.dk Researcher profile

Research focus: Mucosal drug delivery, oromucosal (buccal, sublingual), ocular, bioadhesion, ex vivo permeation, liquid-semi solid- solid formulations, xerostomia.



Daniel Bar-Shalom Associate Professor daniel.barshalom@sund.ku.dk Researcher profile

Research focus: Pediatric and geriatric formulations. Functional excipients. Implementing learnings from food science and material science into pharmaceutical science.



Anette Müllertz Professor anette.mullertz@sund.ku.dk Researcher profile

Research focus: Development of predictive *in vitro* models, based on human or rat gastro-intestinal physiology. Lipid-based drug delivery systems. Small-scale methods to evaluate solubility, dissolution and supersaturation propensity of drugs. Application and development of in silico PBPK models to evaluate release effect on pharmacokinetics.

Examples of projects

In vitro in vivo correlation of oromucosal lubrication and bioadhesivness



- of selected polymers with different physico-chemical properties (charge, molecular size, chemical structure, HLB) aiming at a platform for screening of oromucosal bioadhesiveness. Today, human *in vivo* studies of oromucosal bioadhesion are sparse. Examples of qualitative and quantitative *in vitro* bioadhesion methods to be validated in this project: Zeta potential, tissue-based tensile strength, rheology, tissue-based retention model, turbidity, contact angle. Initially, an application to authorities for study of human *in vivo* oromucosal bioadhesiveness must be written.

Supervisor: Jette Jacobsen

Safety and enhancement of oromucosal drug permeability

These projects aim at evaluating excipients (e.g. absorption enhancers, bioadhesive polymer, co-solvents, buffering pH, surface active preservatives, flavours ect.) to gain a mechanistic knowledge of *in vitro* mucosal permeability of drugs with different physico-chemcial properties by employing physiological relevant transport studies with cell cultures or ex vivo animal mucosa in side-by-side diffusion cells (e.g. sublingual or buccal mucosa). Potential formulations are liquids (e.g. original product and generics), drugs printed on bioadhesive films (for individualized personal medicine) or solids. The projects may be planned in collaboration with pharmaceutical industrial partner and Chr. Janfelt to perform high-resolution MALDI mass spectrometry imaging of drugs and excipients.

Supervisors: Jette Jacobsen, Miriam Kolko (ILF), Susan Weng Larsen, Natalja Genina, Christian Janfelt

Bioadhesive formulations for alleviation of xerostomia

Xerostomia (dry mouth) can be a very disabling state of health. Xerostomia can be due to e.g. use of medicine or illness (Sjögrens syndrome, radiation therapy in cancer). We hypothesize that each, salivary proteins and lipids, contribute to maintain functions of saliva in bulk and at the mucosal surface. The projects will focus on formulation of a physiological relevant composition for daily care and as a drug delivery system. The work may comprise preparation and characterization of semisolid or liquid bioadhesive formulations with and without drugs, development of *in vitro* cell culture based methods for oromucosal spreadability/wettability (i.e. measurement of single-sided contact angle and surface tension) or friction of formulations, characterization of bioadhesiveness (retention time and force), and mucosal hydration rate. The projects are in collaboration with an external clinical specialist in oromucosal medicine and pathology.

There are different scenarios requiring different solutions: (a) Individual, single dose commercial products to be produced by the industry, (b) Vehicles to be added to magisterial compounded products at the hospital or community pharmacy and (c) Vehicles for mass treatment in the developing world where a whole village is treated at once (for example, with anti-parasitic combinations) etc. The projects are usually carried out in collaboration with interested parties (pharmaceutical and food industry, raw materials suppliers, analytical instrumentation producers and academic partners. Many

Supervisors: Jette Jacobsen, Huiling Mu and Daniel Bar-Shalom

Development of "instant pudding" vehicles



Supervisors: Daniel Bar-Shalom

Paediatric/Geriatric drug delivery

Children and the elderly are special population groups from the oral drug delivery perspective. Their swallowing (in)abilities are different from those of the "average population" (those able to swallow tablets and capsules). The elderly and chronically sick children tend to take multiple drugs, thereby complicating the treatment.

of those abroad)

Our approach is to individually microencapsulate the drugs to eliminate the (bad) taste problem, to prevent unfortunate interactions between the drugs when in combination and to provide controlled release, if possible. The microencapsulates are mixed with dry, "instant pudding" formulations, and just before administration water is added, resulting in a pleasant, easy to swallow pudding/applesauce mass.

Supervisor: Daniel Bar-Shalom

Development of the dispensing systems for Microencapsulate/Pudding products

It is not sufficient to have the components of the product, a dispensing strategy and device are needed too. Project in this part involve collaboration with design experts.

Supervisor: Daniel Bar-Shalom

Simulating food effect on poorly soluble drugs



Many poorly soluble drugs have positive food effect; they have a better bioavailability in the fed state. This is a problem for the reproducibility of the therapeutic effect and it is therefore desired to develop DDS that abolish the food effect. The aim is to develop *in vitro* models, simulating the fed state GI tract, and by use of this to develop formulations without food effect.

Supervisor: Anette Müllertz

Development of microencapsulated particles for children and elderly

Different applications require different solutions. The drugs used at the hospital are a very heterogeneous group, those given in anti-parasitic treatments are notoriously water insoluble, in single doses and long-term stability is expected. **Supervisor:** Daniel Bar-Shalom

Oral controlled release of high dose, highly soluble drugs

The problem of insoluble drugs is much researched all over the world, including people in our own department. The opposite problem has been largely ignored, but it is there and represents an interesting "niche". **Supervisor:** Daniel Bar-Shalom

Probiotics as therapeutic agents

Our GastroIntestinal Tract, GIT is the home of a rich population of microorganisms, in fact, there are more microorganisms there than cells in the entire human body. The focus has been on the delivery of selected microorganisms to the lower GIT and on "fecal transplantation" (transferring feces from a healthy patient to another suffering from certain diseases. Getting the bacteria - alive! - to the target is a tricky problem, far from satisfactorily solved. Other areas, nose, mouth (which might or might not be considered a part of the GIT), vagina and skin are other areas where "flora manipulation" is being explored.

Supervisor: Daniel Bar-Shalom, Anette Müllertz

Development a combined gastrointestinal digestion and permeation in vitro model.



In order to achieve a systemic response following oral administration, a given drug needs to dissolve (or be solubilized) in the gastrointestinal (GI) fluids and permeate the intestinal mucosa to reach the systemic circulation. As many poorly water soluble drugs are affected by the co-administration of food, or formulated in a lipid based drug delivery system to ensure GI drug solubilization, the GI digestion processes will affect the drug absorption. Therefore, two key parameters to evaluate in order to predict the *in vivo* performance of orally administrated poorly water soluble drugs are the drug solubilization during GI digestion and the permeation across

the intestinal mucosa. As these two processes affect each other, a predictive *in vitro* model needs to mimic both processes simultaneously. The purpose of the present master's thesis project is to develop and evaluate a combined GI digestion and permeation *in vitro* model.

Supervisors: Mette Klitgaard (phd student) and Anette Müllertz

Is intestinal mucus an important factor in solubilization and absorption of poorly soluble drugs?

Efficient oral therapy is dependent on a good and reproducible drug absorption. However, many active drug candidates suffer from poor water solubility, which makes it difficult to formulate them into delivery systems with high and reproducible bioavailability. One important factor influencing this, is the poor understanding of the actual conditions in the gastrointestinal tract, and the factors that are limiting for the drug absorption. Therefore, the tools that are used in the development process are in many cases not predictive for the *in vivo* situation. One example is the media that are used for predicting the drug dissolution in the intestine, which often underestimates the *in vivo* dissolution. We hypothetize that the intestinal mucus layer has a larger solubilization capacity than the intestinal fluids and is therefore a major player in the absorption mechanism for poorly water soluble drugs. Thus, the mucus layer need to be included in *in vitro* models simulating drug dissolution and absorption.

This project aims to elucidate the impact of the intestinal mucus layer in dissolution, solubilization, diffusion and absorption of poorly water soluble drugs. The project will be directly linked with the current PhD project of Mette Klitgaard.

Supervisors: Mette Klitgaard (PhD student), Anette Müllertz, Jette Jacobsen

Development of a targeted drug delivery system by use of micro-containers



Inflammatory bowel disease (IBD) affects more than 50,000 people in Denmark. Current treatment options are not effective and are often associated with severe side effects due to systemic uptake of the drug. The aim is to develop a DDS that targets only inflamed areas of the gastrointestinal tract in IBD patients. This can be achieved e.g. by functionalizing the surface of the DDS. Newly developed DDS will be tested *in vitro*, and the promising DDS will be investigated *in vivo* in a preclinical IBD rodent model.

Supervisors: Anette Müllertz, Thomas Rades & Maja Nørgaard Kristensen (PhD student)

The effect of gastric transfer rate on supersaturation and precipitation of poorly water soluble weak bases



A large solubility difference in the low pH stomach and neutral pH small intestine is a challenge for many new drugs. This solubility difference can lead to supersaturation and subsequent precipitation in the small intestine, This can lead to a large variability in pharmacokinetic studies. Supersaturation is an unstable system, where the concentration of a compound exceeds the (thermodynamic) solubility and over time will precipitate. The aim is to establish a novel two-step dissolution model with a gastric and an intestinal compartment to investigate the effect of gastric transfer rate on small intestinal supersaturation and precipitation of formulations of poorly water soluble weak bases.

Supervisors: Anette Müllertz & Jakob Plum (Post doc, Leo Pharma)

Functionalized self-emulsifying DDS (f-SEDDS) for oral delivery of peptides or proteins



Self-emulsifying drug delivery systems (SEDDS) are solutions of oil, surfactant and co-surfactant spontaneously forming an oil/water emulsion upon mixing with an aqueous medium. SEDDS have shown great potential to improve the bioavailability of peptides by the advantages of mild preparation conditions, protection against enzymatic hydrolysis and build-in permeation enhancement. We will develop functionalized SEDDS (f-SEDDS) with e.g. mucoadhesive properties. F-SEDDS will be characterized by particle size, zeta-potential and *in vitro* digestion. The performance of the developed f-SEDDS will be evaluated by *in vitro* cell culture study and *in vivo* animal models.

Supervisor: Anette Müllertz

Assessing the relation between release profile and pharmacokinetics using PBPK models

Physiologically based pharmacokinetic (PBPK) modelling is important in the drug development process to understand the relation between drug release, absorption and plasma profile. However, there is still shortcomings in the input (absorption) profiles in the PBPK models, e.g. the entire drug solubility profile in the GI tract is not considered. We want to apply PBPK models to different solubility and dissolution profiles, from selected formulations. We will use the softwares GastroPlus and SimCyp.

Supervisors: Anette Müllertz, Jakob Plum (Post doc, Leo Pharma)

Development of a predictive in vitro dissolution-, permeation model for evaluating amorphous solid dispersions



Many drug molecules suffer from low aqueous solubility, which results in low oral bioavailability. Some of these drug molecules can benefit from the formulation principle of amorphous solid dispersion (ASD), in which the drug is molecularly dispersed in a polymer matrix. Dissolution of ASDs might result in a supersaturated solution of the drug, thereby increasing the absorbable drug amount in the gastrointestinal fluids. The aim of this project is to develop an in vitro model, predicting the in vivo performance of such ASD formulations.

Supervisors: Anette Müllertz & Jacob Rune Jørgensen (Postdoc)

Application procedure and dates

If you are interested in writing your thesis with Physiological Pharmaceutics, please write an email to one of the supervisors with more information about you. There is no deadline.

Protein Analysis Group

www.pharmacy.ku.dk/research/protein-analysis-group/



The vast majority of drugs work by binding to and changing the function of proteins in the human body. Furthermore, many new drugs are themselves protein-based (so-called biopharmaceuticals) and these complex drugs account for the most rapidly growing drug in the pharmaceutical industry. Analysis of proteins is therefore at the core of pharmaceutical research.



Our research focus on the use of mass spectrometry (MS) to provide the critical information concerning quality, structure and interactions of proteins - which is needed to guide and develop new and improved drugs. In particular, we have world-leading expertise with the **HDX-MS technique**, an incredibly sensitive method for studying the conformation, dynamics and interactions of proteins. Furthermore, the lab is also equipped with instrumentation to perform cross-linking mass spectrometry (XL-MS) whereby we provide structural constraints for structural models of proteins and protein complexes.

Examples of our publications involving past master thesis projects: <u>Møller et al. 2019</u>; <u>Svejdal et al. 2019</u>; <u>Trabjerg et al. 2017</u>; <u>Trabjerg et al. 2015</u>; <u>Qiu et al. 2016</u>; <u>Jensen et al. 2016</u>; <u>Hongjian et al. 2014</u>

Through the thesis projects below, you can get hands-on laboratory experience of how to perform analytical chemistry of proteins and learn state-of-the-art LC-MS techniques for detailed structure analysis and characterization of proteins, protein-drug targets and biopharmaceuticals (keywords: protein chemistry, protein structure and dynamics, liquid chromatography and mass spectrometry e.g. LC-MS).

Potential thesis supervisors



Kasper D. Rand Professor kasper.rand@sund.ku.dk <u>Researcher Profile</u>

Research focus: Protein Analytical Chemistry, HDX-MS (& see above)

Examples of projects

Analysis of the structure and dynamics of biopharmaceuticals



Analysis of the primary and higher-order structure of protein-based drugs is critical for both understanding molecular action as well as monitoring and comparing drug product quality. In this suite of projects, you will apply a new powerful analytical technology that uses mass spectrometry to measure the hydrogen/deuterium exchange of proteins in solution (HDX-MS). By HDX-MS, we can obtain detailed information on the structure and dynamics of biopharmaceuticals. You will use this technique to analyze and compare the structural properties of new potential protein drugs in development and thus help to achieve a molecular understanding of their pharmaceutical

Esben Trabjerg Assistant Professor

Researcher Profile

Research focus: Protein cross-linking mass

spectrometry (XL-MS), HDX-MS

esben.trabjerg@sund.ku.dk

properties and function in the human body. Work will be done in close collaboration with researchers at UCPH or industrial collaborators such as Biogen Idec (USA), Roche (Germany) and Novo Nordisk (Denmark), depending on the project. There is typically also the possibility to perform parts of the project at the industrial collaborator. **No. of students: 1-2**

Understanding the binding of drugs to target proteins of the human body



No. of students: 1-2

-y-

Drug Ligand

Coupling microfluidics and mass spectrometry for improved analysis of proteins



MS analysis of proteins requires specialized sample treatment and advanced analytical techniques as they are large and complex and often contain modifications (e.g. glycosylations, disulfide bonds). We are exploring the use of microfluidic chips to perform rapid and automated preparation of protein samples for MS analysis. You will learn how to implement protein chemistry and sample processing on a microfluidic chip coupled to MS. The project is supported by a large grant to the group from the EU (ERC Consolidator Grant) and has the potential to be extended into a PhD project.

No. of students: 1-2



Studying the structure and dynamics of the TCR-CD3 signalling complex

The T-cell receptor (TCR) signalling complex (TCR-CD3) on the surface of T-cells is essential for the human immune system. The complex allows T-cells to discriminate between healthy and malignant cells via the ability of TCR to bind peptide antigens presented on the surface of target cells by the major histocompatibility complex (MHC). Binding leads to T-cell activation and elimination of the target cell. However, the activation mechanism of the TCR-CD3 complex is not fully understood. In this project you will use HDX-MS and XL-MS to investigate the structure and dynamics of the complex, in a quest to

elucidate the activation mechanism. The project is supported by a grant to the group from the NovoFonden. No. of students: 1-2

Application procedure and dates

If you are interested in writing your thesis with the Protein Analysis Group, please write an email to <u>kasper.rand@sund.ku.dk</u> with more information about you. There is no deadline.

Social and Clinical Pharmacy Group

www.pharmacy.ku.dk/research/social-clinical-pharmacy/



Social pharmacy seeks to have the broad view of medicines in society and focuses on how medicines are perceived, used, and managed by different stakeholders. Clinical pharmacy seeks to ensure the optimal and rational use of medicines for the benefit of patients and society through collaboration between pharmacists, other health professionals, and the patient. SCP's research ultimately seeks to ensure the benefit of medicines for users, organizations, and society. SCP's research is concerned with the three levels (the user, organization and society) and how they interact to ensure the optimal use of medicines.

Potential	thesis	supervisors	

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Anna Birna Almarsdóttir	Lourdes Cantarero-Arévalo
Professor	Associate Professor
Researcher Profile	Researcher Profile
Lotte Stig Nørgaard	Susanne Kaae
Associate Professor	Associate Professor
Researcher Profile	Researcher Profile
Charlotte Vermehren	Ramune Jacobsen
Associate Professor	Associate Professor
Researcher Profile	Researcher Profile

In addition to these supervisors, SCP has contact to researchers off campus who are willing and able to supervise, e.g. at hospital pharmacies, Pharmakon, Medicinrådet, regional research centers, etc. Each of these come with ideas that are important to them and can be used as basis for a master project under their supervision, but in close collaboration with the SCP supervisors.

Project ideas

Master thesis projects may be connected to existing research projects in the SCP Group, but other relevant ideas for master thesis projects within social and clinical pharmacy are also welcome. If you wish to know more about us and what kind of research we do you can have a look at <u>our website</u> and at our <u>WHO collaborating center</u>. Alternatively, you can use the "<u>Find a Researcher</u>" option for members of the research group on the website of the University of Copenhagen.

We expect that projects by master students can be within already established areas such as polypharmacy, communication over the counter, medicines use among adolescents, mental health issues among young people and vulnerable population, ethical dilemmas in medicine use among others.

The SCP master thesis system

We have a coordinated master thesis student system. We first accept students for the entire group, and we then allocate a supervisor to each student. The contacts regarding master theses are lou.cantarero@sund.ku.dk and anna.birna@sund.ku.dk. Please do not write to others in the SCP group with questions about thesis projects. The deadline is 15 December, 2021.

On **28th of October from 1 pm-4pm**, we arrange our own Open House in the SCP group **(temporary address: Building 17, 5.floor**). You will be able to discuss with us about possibilities for master theses and our process for selecting students. Note that we do not arrange individual meetings with students. Therefore, if you want to know more, please join us on 24 November 2021. Students selected for master thesis writing in 2023 in our group will be notified in week 51.

The following project is an example of cross-research group collaboration:

Sustainable Pharmacy with focus on Antimicrobial Resistance as a global public health threat



The 17 United Nations Sustainable Development Goals (SDGs) are a collection of independent but interconnected goals carefully designed to give all of us a better future on our planet. From design, all the way to access and use, pharmaceuticals affect the SDGs directly and indirectly. Sometimes in a positive way (SDG3 'Good health and well-being'), sometimes negatively (environmentrelated SDGs).

In order to optimize the positive effects and mitigate the negative ones, we need to develop innovative and sustainable ways to develop and deliver

pharmaceuticals. Students interested in working on the development of solutions that can contribute to human and planetary sustainability will first identify challenges, and will thereafter

receive guidance and support on how to contribute practically to its solutions.

Supervisor: Lou Cantarero and Holger Grohganz

Solid State Pharmaceutics

www.pharmacy.ku.dk/research/solid-state-pharmaceutics/

The scientific staff consists currently of the two scientists Thomas Rades and Holger Grohganz, and a varying number of PhD students.

We develop drug delivery systems based on high-energy solids. The aims are improved stability of the formulations, and solubility enhancement of poorly water-soluble drugs. We furthermore aim to obtain a deeper understanding of the underlying mechanisms for amorphous stability and have a keen interest in novel formulations approaches and novel excipients. In future, sustainable techniques will play a more important role in pharmaceutical development and it is thus of importance to also focus on this area.

Low solubility is the major challenge for many small-molecule drugs. By stabilizing a poorly water-soluble drug in its amorphous form, its bioavailability can be increased, due to a higher dissolution rate and apparent solubility. Understanding molecular interactions and thereby overcoming the inherent instability of amorphous drugs is one solution to the solubility problem. The amorphous drug can be stabilized with both polymers and small molecules. The amorphous formulation is characterized by a wide range of advanced analytical state-of-the-art methods.





CRYSTALLINE drug poor solubility



AMORPHOUS drug

For the production of amorphous formulations of both, small molecules and biomacromolecules, various production techniques, such as ball milling, spray-drying, freeze-drying, microwaves and hot melt processing are applied. Understanding the influence of process and formulation parameters on the solid state of both excipient and drug enables a rational choice of formulation.

Potential thesis supervisors



Holger Grohganz Associate professor holger.grohganz@sund.ku.dk Researcher Profile

Research focus: Development of solid dosage forms, including preformulation, formulation, processing and manufacturing together with the relevant solid-state characterization and multivariate analysis. This includes in particular the development co-amorphous systems as well as a deeper understanding of freeze-drying as production technique.



Thomas Rades Professor thomas.rades@sund.ku.dk <u>Researcher Profile</u>

Research focus: Development of solid oral dosage forms, including preformulation, formulation, processing and manufacturing together with the relevant solid-state characterization and quality control. This includes in particular the development of amorphous and co-amorphous systems as well as amorphous solid dispersions.

Examples of projects

Down-stream processing of co-amorphous formulations



In this project, co-amorphous systems intend to be moved from the powder formulation state towards a more applicable state, i.e. downstream-processing towards a final dosage form. In this regard especially granulation and compaction are relevant unit operations to investigate. The influence of critical processing and formulation parameters on the pharmaceutical performance, as well as the influence of amorphous versus crystalline form with regard to downstream processing needs to be investigated. The effect of various excipients on compactability and compressibility of co-amorphous systems will be connected with the results of pharmaceutical quality testing.

Supervisors: Holger Grohganz and Thomas Rades (co-operation with Manufacturing and Materials possible)

Evaluation of preparation methods for co-amorphous formulations



Low drug solubility is the major challenge for future small molecule drugs. In order to overcome the problematic solubility of BCS class 2 drugs, small excipients are investigated to form co-amorphous formulations. Due to the low solubility, ball milling is used as preferred production process. Due to the low capacity of ball mills, other production procedures, such as freeze-drying, spray-drying and hot-melt processing should be evaluated.

Supervisors: Holger Grohganz and Thomas Rades

Sustainable Pharmacy with focus on Antimicrobial Resistance as a global public health threat



The 17 United Nations Sustainable Development Goals (SDGs) are a collection of independent but interconnected goals carefully designed to give all of us a better future on our planet. From design, all the way to access and use, pharmaceuticals affect the SDGs directly and indirectly. Sometimes in a positive way (SDG3 'Good health and well-being'), sometimes negatively (environment-related SDGs).

In order to optimize the positive effects and mitigate the negative ones, we need to develop innovative and sustainable ways to develop and deliver

pharmaceuticals. Students interested in working on the development of solutions that can contribute to human and planetary sustainability will first identify challenges, and will thereafter

receive guidance and support on how to practically contribute to its solutions.

Supervisor: Holger Grohganz and Lou Cantarero

Quality by design (QbD) in the processing of biomacromolecules



The quality by design (QbD) principle can be expected to influence pharmaceutical processing in the years to come towards the development of more rational processes. Although, freeze-drying and spray-drying are widely used in peptide and protein formulation, the interaction between various excipients and proteins is not fully understood. This project aims to obtain a deeper understanding of the influence of various composition and process parameters on the solid state form of both novel and established the excipients, and the macromolecule. Analytical techniques may include X-Ray powder diffraction, dynamic mechanical analysis, NIR

and Raman spectroscopy as well as the application of multivariate data analysis.

Supervisor: Holger Grohganz

On the role of water in amorphous systems



Water is generally seen as detrimental for the stability of amorphous drugs and solid dispersions. However, initial in-house work has shown that this may not necessarily be true for all systems especially at low water concentrations. The aim of this Masters project is to determine the water absorption and stability of a range of amorphous systems (pure drugs, amorphous solid dispersions with polymers and co-amorphous systems with amino acids) in the presence of different amounts of water. The student will learn preparative techniques, including ball milling and quench cooling as well as using a wide range of analytical techniques, water determination and dissolution techniques.

Supervisors: Thomas Rades and Holger Grohganz

Electrospun amorphous solid dispersions of poorly water-soluble drugs.



The development of oral dosage forms from poorly water-soluble active pharmaceutical ingredients (APIs) remains a major challenge for the pharmaceutical industry. Preparing amorphous solid dispersions (ASDs) allows increasing the solubility and dissolution rate of an API, hence, increasing its bioavailability. The application of electrical energy during electrospinning can generate ASD nanofibers from drug-loaded solutions and melts. This project focuses on the development of an electrospinning method to produce ASDs. The electrospun fibers will be comprehensively characterized by a range of analytical techniques, including scanning

electron microscopy, X-ray powder diffraction, differential scanning calorimetry and dynamic mechanical analysis. The dissolution rate advantage will also be determined.

Supervisor: Thomas Rades and Andrea Heinz



Supervisor: Thomas Rades

Development of novel Dispersome® formulations



The novel solubility enhancing Dispersomes® technology is based on the use of whey protein isolate as excipient for amorphous stabilization and solubility enhancement and is the basis of the KU spin-out company ZERION Pharma A/S. The projects aim is to further understand the mechanisms behind the amorphous stabilization and solubility enhancement of a given drug when formulated as Dispersomes®. In addition, downstream processes of the Dispersome® formulations into final dosage forms such as

tablets or capsules will be investigated. The projects will be an industry based project at the lab facilities of ZERION Pharma A/S at Symbion and are co-supervised by Zerion scientists.

Supervisor: Several projects are available in co-operation with Assoc. Prof. Holger Grohganz and Prof. Thomas Rades as well as the scientists Søren Søgaard and Korbinian Löbmann @Zerion Pharma ApS

Application procedure and dates

If you are interested in writing your thesis with Solid State Pharmaceutics, please write an email to one of the supervisors with more information about you. There is no deadline.

Structured Biointerfaces

https://pharmacy.ku.dk/research/structured-biointerfaces/



Potential thesis supervisors



Ben Boyd Professor ben.boyd@sund.ku.dk Researcher Profile

Application procedure and dates

If you are interested in writing your thesis with the Structure Biointerfaces Group, please write an email to one of the supervisors with more information about you. There is no deadline.

Surface and Colloid Chemistry Group

www.pharmacy.ku.dk/research/surface-colloid-chemistry/



The goals of the Surface and Colloid Chemistry Group are to advance the knowledge regarding the membrane interactions of antimicrobial peptides and different nanomaterials, particularly inorganic nanoparticles with potent antimicrobial activities or used as carriers for antimicrobial and anti-inflammatory agents. Both state-of-the-art techniques and innovative approaches are used in the group to evaluate the interactions between these agents and membrane components of cells and bacteria, including for instance fluorescence spectroscopy, DLS, QCM-D, FTIR-ATR, neutron and X-ray scattering. The overarching aim is to take fundamental research about

physicochemical properties and mechanisms to a stage where it can be translated to further therapeutic development.

Potential thesis supervisors



Martin Malmsten Professor Martin.malmsten@sund.ku.dk

Researcher Profile

Research focus: Microgels, nanoparticles for drug delivery, and host defence peptides for combatting infection and inflammation



Elisa Parra Ortiz Assistant Professor elisa.parra@sund.ku.dk <u>Researcher Profile</u>

Research focus: Lipid membranes, lipid peroxidation, nanoparticles for drug delivery

Examples of projects

Membrane interactions of structured silica nanoparticles as antimicrobial agents



In the wake of increasing bacterial resistance against conventional antibiotics, there is a growing interest in alternative approaches for reaching antimicrobial effects. Among those, nanoparticles are attracting considerable current interest due to the comparatively low cost, good scalability, and broad versatility of such materials, but also due to presently undeveloped bacterial resistance. Here, various nanomaterials offer opportunities for triggered functionalities to combat challenging infections. Although the performance in these diverse applications is governed by a complex interplay between the nanomaterial, the properties of included drugs (if any), and the

biological system, nanoparticle-membrane interactions constitute a key initial step and play a key role for the subsequent biological response. Clarifying key factors controlling membrane binding and destabilization of nanoparticles is therefore key for the successful development of the latter towards therapeutics.

In the present project, membrane interactions will be investigated for mesoporous silica nanoparticles, which offer opportunities in combating challenging infections. For example, both low molecular weight and biomacromolecular drugs can be readily incorporated into such nanoparticles, allowing large drug loads due to their large specific surface area. In addition, silica nanoparticles can be designed to display needle-like surfaces, which may be used to effectively

"puncture" bacterial membranes by "needle-like" actions. Within the project, factors determining membrane interactions of "spiky" mesoporous silica nanoparticles will therefore be investigated by previously developed model lipid membranes, in combination with various biophysical techniques, such as QCM-D, FTIR-ATR, and DLS. Results from such biophysical studies, e.g., on effects of membrane composition, structure and charge of the silica nanoparticles, and effects of co-administration of such particles with other potent antimicrobial agents, notably antimicrobial peptides, will be correlated to biological results on antimicrobial effects and cell toxicity for selected systems.

Supervisor: Martin Malmsten & Elisa Parra-Ortiz. Number of students: 1

Application of oxidative stress on lipid membranes as a new tool for developing new antimicrobial agents

UV irradiation time



Inorganic nanoparticles are very attractive as antimicrobial agents ('nanobiotics'), notably due to the increasing resistance development against conventional antibiotics. Apart from scalability and versatility, such materials offer advantages related to responsiveness of antimicrobial and anti-inflammatory effects and the possibility of controlling them by a range of triggering factors. For instance, oxidative stress is known to be behind the antimicrobial activities of TiO₂ nanoparticles when activated by UV light. However, studies on the mechanisms underlying these activities remain scarce. Based on previous work done by our group on the oxidative destabilization of

lipid membranes, and using different biophysical and surface-chemical techniques such as fluorescence spectroscopy, QCM-D, FTIR-ATR, and DLS, the present project will focus on the effects of TiO_2 nanoparticle-induced oxidation of lipid membranes, lipid degradation, and their consequences for membrane structure and stability. Any potential membrane selectivity that could allow more efficient antimicrobial activities along with reduced side effects will be also explored, for instance the combination with cationic peptide coatings. In a wider perspective, this project will contribute to the mechanistic foundation for the use of photocatalytic nanomaterials as triggerable antimicrobial agents.

Supervisor: Martin Malmsten & Elisa Parra-Ortiz. Number of students: 1

Application procedure and dates

If you are interested in writing your thesis with the Surface and Colloid Chemistry Group, please write an email to one of the supervisors with more information about you. There is no deadline.

Toxicology and Drug Metabolism

www.pharmacy.ku.dk/research/toxicology-drug-metabolism/



We perform experimental research revealing the occurrence, fate, and toxicological and endocrine effects of xenobiotics, especially pharmaceuticals, with the aim of assessing their risks to humans and biota. We apply various *in vitro*, ex vivo and *in vivo* assays and advanced analytical techniques, such as LC-MS and mass spectrometry imaging.

Potential thesis supervisors

Bjarne Styrishave Associate Professor bjarne.styrishave@sund.ku.dk Researcher Profile



Christian Janfelt Associate Professor christian.janfelt@sund.ku.dk Researcher Profile







Examples of projects

Endocrine disrupting pharmaceuticals



Public awareness concerning endocrine disrupting drugs has increased the last few years, as these are presumed to affect reproductive ability and to increase the occurrence of hormonedependent cancers. Endocrine disrupting drugs are, however, generally much less potent than physiological hormones, and therefore there is doubt as to whether or not these substances can affect humans.

Recent research indicate that simultaneous exposure to a cocktail of endocrine disrupting drugs, each at a concentration below the effect level, might result in a significant additive or synergistic effect. The

present project wishes to uncover interactions between selected hormone-disturbing substances in various *in vitro* test systems and/or animal experiments with selected endpoints, including hormonal activity, changes in aromatase activity and the impacts of endocrine disrupting drugs on endogenous hormone metabolism. **Supervisor:** Bjarne Styrishave, No of students: 2-3

Endocrine toxicity of drug enantiomers and metabolites



Increasing evidence exists that certain pharmaceuticals disturb the human hormone system and may contribute to endocrine related diseases like infertility, obesity and different types of cancers. It is well known that enantiomers of drugs can differ strongly in their biological activity. Furthermore, drug metabolites formed in the body can be active and possess higher activity than the parent compound. Very little is known about how toxic effects on the hormone system depend on the enantiomeric form and the metabolic products of a drug. The focus of this project are chiral drugs like azole fungicides, which are used for the treatment of severe systemic and superficial

fungal infections. The goal is to elucidate the endocrine toxicity of azole enantiomers and metabolites through pharmacokinetic and –dynamic studies. The practical work includes enzyme and cell based *in vitro* assays as well as *in vivo* experiments. A large part of the project is the development of analytical chemical methods for the identification and quantification of enantiomers and metabolites in different biological matrices with enantioselective HPLC-MS/MS. **Supervisors:** Bjarne Styrishave, Claus Cornett. No. of students: 1-2

Development of a microfluidic assay for testing the endocrine disrupting potential of pharmaceuticals



Currently, the pharmaceutical industry loses more than 80% of their drug candidates during drug development, since existing in vitro and animal tests are too time- and cost-intense and do not predict adverse effects of drugs in humans with sufficient accuracy. The goal of this project is the development of a microfluidic toxicological in vitro assay, which can assess the toxicity of drugs in a fast, cheap and more human relevant manner. Within this project a miniaturized cell-based in vitro assay will be established on a microchip (endocrine gland on-a-chip) and applied for the testing of adverse effects of drugs on the human steroid hormone system. Work

students will perform includes cell culturing, design/ fabrication of microchips, in vitro toxicity tests as well as analytical chemical measurements.

Supervisors: Bjarne Styrishave. No. of students: 1-2

Pancreatic infections: Local and systemic antibiotics in infected walled-off pancreatic necrosis.



Severe acute pancreatitis is characterized by organ dysfunction and necrosis of the pancreas. Mortality is high, up to 20%. Infection in the pancreas is a serious complication and is associated with high mortality, up to 20%. After 3-4 weeks the necrosis becomes encapsulated a so-called walled-off necrosis (WON). The primary treatment is systemic antibiotics. However, little is known about the penetration of antibiotics into the necrosis and the ability of

antibiotics to stop the infection. Several factors may influence the activity of the antibiotics, such as the fibrous capsule surrounding the necrosis, the size and the physic-chemical milieu of the necrosis. Using 2D-DESI-imaging and LCMS/MS, this project aims to investigate the distribution of the most commonly used antibiotics in pancreatic necrosis. The purpose is to identify the most effective treatment, thereby decreasing mortality and morbidity in patients suffering from pancreatic necrosis.

Supervisors: Bjarne Styrishave, Christian Janfelt. No. of students: 1-2.

Danida project: Green Resource Innovations For Livelihood Improvement (GRILI)



traditional medicine in Tanzania, and are key components for primary health care and livelihoods of more than 50% of the inhabitants. Unfortunately, many herbal products are adulterated with drugs, such as antibiotics, antimalarials and mild analgesics. The present study aims to investigate the adulteration of herbal drugs from Tanzania, by analysing the presence of different drug classes in herbal medicines collected from markets and health providers in Tanzania. Samples will be collected and extracted in Tanzania and transported to Denmark, where the samples will be analysed. The project included approximately 3 months of field work in Tanzania.

Medicinal plants as green resource products (GRPs) are used as

Supervisors: Bjarne Styrishave. No. of students: 1-2.

Mass spectrometry imaging of drugs in tissue sections from mice and rats

How does the drug distribute in the organism? Which metabolites are formed, and where and when are they formed. Does the drug reach the target, or is it actually a metabolite, which has the pharmacological effect (as in a pro-drug)?



These are some of the questions, which Mass spectrometry imaging (MSI) can provide the answers to. MSI is a way to do MS analysis direct from a surface, e.g. a tissue section from an animal. From thousands of mass spectra recorded throughout the sample, images can be created for every detected compound, including drugs, metabolites and endogenous compounds. In this project, MSI in the form of DESI-MSI will be used to study the distribution of a drug in mice or rats. For both animals, cryo-

sections are made of different organs of interest, which are subsequently imaged, and for mice it is even possible to do whole-body cryosection to get the full overview of the drug in the organism. The project will be planned in collaboration with pharmacologists or medicinal chemists.

Supervisors: Christian Janfelt. No. of students: 1 or 2

Mass spectrometry imaging in studies of plant material



Plants constitute an important source for new and existing medicinal products, both because they through millions of years of evolution provide inspiration for new pharmaceutical compounds and their derivatives, but also because they through biosynthesis provide elegant products of complex compound which cannot readily be produced by chemical synthsis. Mass spectrometry imaging (MSI) of specialized plant metabolites provides information about where is the plant pharmaceutical compounds of interest are synthesized, but also distributions of the different precursors of the compound which provide information about the biosynthesis of the compounds. It may

also provide information about the plant's protection and response to herbivore attacks and knowledge, which can contribute to more efficient production of pharmaceuticals or other products from plants. In this project, a plant will be characterized though MSI with regards to its production of specialized metabolites or their significance for the function of the plant. The project will be planned with a research group or a company working in the field of plant biology. **Supervisors:** Christian Janfelt. No of students: 1

High-resolution MALDI mass spectrometry imaging for studies in drug delivery



Where are the barriers for a drug to absorbed in the organism? How may drug excipients improve the absorption of a drug through the skin or other barriers? Which drug has not only the best pharmacological effect but also the best properties for reaching the target?

Mass spectrometry imaging (MSI) by MALDI-MSI can produce images with microscopic details showing the drug and the drug excipients together with endogenous molecules, which can be used as tissue markers. The tissue markers reveal the different layers in the tissue like epidermis, mucosa, glands or connective tissue. In this

way the mechanisms of drug absorption can be studied in high detail in biological systems like skin, buccal mucosa (inside of cheek), intestine and lung tissue. The samples can be from in-vitro diffusion experiments on excised tissue (e.g. human skin or pig skin) or from animal experiments where e.g. intestine or lungs are studied by MSI at different post-dose times. The project will be planned in collaboration with groups working with drug delivery. **Supervisors:** Christian Janfelt. No of students: 1 or 2



The capabilities of DESI and MALDI MSI to
 image the distribution of endogenous
 compounds together with a drug and its
 metabolites make them ideal in the study of skin
 penetration of drugs. This project takes place in
 collaboration with Department of Dermatology,
 Bispebjerg Hospital, which develops new
 treatments for skin cancer. One approach is to

ablate channels in the skin in order to be able to perform local, topical chemotherapy of skin cancer. In this project MALDI imaging and LC-MS will be used to optimize the delivery of one or more chemotherapy agents by imaging of tissue sections from difference depths in the treated skin.

Supervisors: Christian Janfelt and Catharina Lerche. No of students: 1 or 2

DNA damage in the urine after UVR-exposure



Thymine dimer is the major form of DNA damage that happens when ultraviolet radiation penetrates the skin. Nucleotide excision repair (NER) is the main pathway for the repair of thymine dimers. The importance of this process is illustrated by the very high risk of developing skin cancer in individuals with disorders in which NER is defective. NER removes thymine dimers from DNA and subsequently they are excreted in the urine. The aim of this study is to investigate the effect of irradiation dose, exposed skin area, and skin type on the amount of excreted thymine dimers. The study involves irradiation of healthy volunteers, collection of urine samples and LC-MS. The study is part of SCIN-CAG (read more).

Supervisors: Catharina Lerche. No. of students: 1

Pharmacological photoprotection



Sun exposure is the primary risk factor for keratinocyte cancer and despite massive prevention efforts, Danish incidences have risen to an estimated 38,500 per year. Pharmacological photoprotection is the concept of using pharmacological compounds before or after exposure to environmental carcinogens e.g. ultraviolet radiation. There is increasing evidence that compounds (e.g. nicotinamide and NSAIDS and less known plant- and marine- derived compounds), may be useful in keratinocyte cancer prophylaxis. The aim is to discover that reduce compounds delay or even photocarcinogenesis. Pharmacological compounds will be tested in

well-established UVR-induced murine models. Laboratory Animal Science certificate is needed for this master project (FELASA A/B/D). The study is part of SCIN-CAG (read more). **Supervisors:** Catharina Lerche. No. of students: 1

Vitamin D-metabolite distribution in the skin analyzed by mass spectrometry imaging



Vitamin D plays a key role in the maintenance of calcium/phosphate homeostasis and elicits biological effects that are relevant to immune function and metabolism. It is predominantly formed through UVB exposure in the skin by conversion of 7-dehydrocholsterol (7-DHC). Melanin in the skin absorbs UVB irradiation and plays a major role in the protection against skin cancer, higher concentrations of melanin gives a better protection. Vitamin D is formed in all skin types, so the distribution of 7-DHC must be closer to the skin surface than melanin. Mass spectrometry imaging (MSI) enables the ability to gain spatial information of various molecules with spectra being mapped to individual pixels.

The aim of this study is to investigate the vitamin D-metabolite distribution in the skin using high mass resolution instrumentation and relate the findings to melanin in the skin.

Supervisors: Catharina Lerche and Christian Janfelt. No. of students: 1

Application procedure and dates

If you are interested in writing your thesis in toxicology and drug metabolism, please write an email to one of the supervisors with more information about you. There is no deadline.

Vaccine Design and Delivery

www.pharmacy.ku.dk/research/vaccine-design-delivery/



The research focus of the Vaccine Design and Delivery Group is advanced drug delivery. The group uses *in vivo* imaging (e.g., NIR, MRI and SPECT/CT) to guide and optimize the design of new nanoparticle-based delivery systems for vaccines and nucleic acid-based therapeutics to improve therapy. The research in the group is highly interdisciplinary. The team comprises international researchers of various backgrounds, including pharmacists, biologists, biochemists, physicists and biotechnologists. "Biopharmaceuticals like vaccines and nucleic acid-based therapeutics are challenging from a pharmaceutical perspective, because they are highly complex products, which can only be understood via solid fundamental science. Using systematic knowledge-based quality-by-design approaches, combined with advanced physicochemical and biopharmaceutical assessment, and molecular imaging, we design new delivery systems for biopharmaceuticals to optimize their stability, efficacy and safety" says Professor and Group Leader, Camilla Foged. The overall research goal is to improve disease prevention and treatment in the fields of infectious and inflammatory diseases, and cancer. The group is addressing drug delivery challenges from bench-to-bedside, via international collaborations, using state-of-the-art technologies. This has fostered innovative solutions and high-impact publications in drug delivery.



Potential thesis supervisors



Camilla Foged Professor camilla.foged@sund.ku.dk <u>Researcher Profile</u>

One of the primary goals of the Vaccine Design and Delivery Group is to gain new fundamental knowledge that can facilitate the design, optimization and development of novel delivery systems capable of delivering loaded biopharmaceuticals to the intended target site(s). The Vaccine Design and Delivery Group addresses the complex challenges associated with the formulation and targeted delivery of vaccines and nucleic acid-based therapeutics.

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Examples of projects

Microfluidics-assisted design of next-generation mRNA vaccines - a novel tool for fighting cancers and challenging infectious diseases



There is an unmet medical need to develop novel vaccines against the so-called "difficult targets" such as AIDS, TB and cancer. One promising strategy is the use of vaccines based on mRNA that encode antigenic proteins from pathogens or tumor cells. Using microfluidics, we will develop multifunctional nanoparticle-based vaccine that both delivers mRNA encoding antigen and induces CTL responses. The efficacy and safety of the mRNA vaccines will be tested in animal models of infection and cancer.

Supervisors: Camilla Foged and Abhijeet Lokras

Design and investigation of nanoparticles for targeted delivery of small interfering RNA (siRNA)

	Small interfering RNA (siRNA) holds a promising therapeutic potential for treating a variety
	of diseases via gene silencing. However, the physicochemical properties of siRNA often limit
	its therapeutic efficacy rendering it unfavourable for efficient intracellular delivery. We have
	developed lipidoid-polymer hybrid nanoparticles (LPNs) and demonstrated safe and efficient
LPNs	intracellular delivery of siRNA. In this project, new generation of lipidoid-based LPNs will be
	evaluated for their transfection efficiency, safety, and therapeutic effect in animal models of
	acute inflammation.

Supervisors: Camilla Foged and You Xu

Design of inhalable mRNA vaccines for mucosal vaccination

The ability to induce airway mucosal immunity is an essential property of mRNA vaccines because several pathogens, *e.g.*, respiratory viruses, enter into the human body *via* the airways. It is well known that protection against these pathogens requires activation of the mucosal immune system, which can only be primed *via* mucosal vaccine administration. However, little is known about how to design safe nanoparticle-based mRNA vaccines optimal for the induction of airway mucosal immunity. In this project, design criteria and immune signatures of inhalable mRNA vaccines for inducing protective CD8⁺ T cell immunity in the airways will be evaluated in epithelial cell and animal models of infection.

Supervisor: Camilla Foged and Melike Ongun

Application procedure and dates

If you are interested in writing your thesis with the Vaccine Design and Delivery group, please write an email to <u>camilla.foged@sund.ku.dk</u> with more information about you. Places are given on a first come, first served basis.