Master Thesis projects
2010
In this catalogue you can find small “appetizers” from each research area written by our staff. You can read about the purposes of the research projects and the methods that are being used. If these “appetizers” catches your interest, please contact the staff in question to learn more about the research.

The staff at this department collaborates with both Danish as well as foreign research environments. So if you are eager to write your thesis in environments like the industry, abroad or maybe you already have a thesis project ready but you need a thesis supervisor, please contact a member of the staff in that specific area or our Master thesis contact Lise Moesby. (lm@farma.ku.dk)

Department of Pharmacology and Pharmacotherapy Master Thesis information day will be, Friday 19. November, 12.30-16.30, her can you meet supervisors, and have a talk with them. The program will be announced.

Clinical Pharmacy

The Research Section Clinical Pharmacy conducts research within the areas:

Rational pharmacotherapy and clinical pharmacy
Pharmacokinetics
Immunopharmacology The research in the group is focused on optimising the individual treatment of patients with medicine. To optimise dosing the group is using population pharmacokinetics. In the future the group will focus on the implementation of pharmacodiagnostic tests to optimise dosing and prevent serious adverse reactions in specific patient groups. The research include all patients categories with speciel emphasis on CNS diseases and patients treated with immunsuppressant drugs e.g. cancer patients, transplant patients, patients with chronic infections. Other focus areas are treatment of pain, fatigue and emesis

Molecular and Cellular Pharmacology

The Molecular & Cellular Pharmacology Research Section is one of four research sections within the Department of Pharmacology and Pharmacotherapy. We are divided into seven individual Research Units which are described below. Each of these research units is investigating different aspects of biochemistry and pharmacology. Biochemistry is the study of the chemical processes in living organisms whereas pharmacology is the study the effects of drugs used to treat disease. Most of the research is focused on brain function. We employ a wide range of experimental methods from advanced techniques to study small molecules to behavioral studies on drug-treated rats.

Retrovirus assembly

Cellular stress, neurodegenerative diseases and biosensors
Ionotropic Glutamate Receptors
GABA Transporter Biology
Biochemical Pharmacology
Biomolecular Interaction Group (BIG)
NeuroMet
Social Pharmacy

The Section for Social Pharmacy performs research and teaching within social pharmacy. Social pharmacy may be defined as the discipline dealing with the role of medicines in society. Social pharmacy also embraces the role and activities of the pharmacy profession. Hence, social pharmacy spans a variety of themes from the experiences and perceptions of the medicine user to national and international drug policy. Within social pharmacy theories and methods from humanities, social science and natural science are applied in a cross-disciplinary manner.

The Section is divided into two teams: Medicine use Pharmacy practice

Systems Pharmacology

The research of the Systems Pharmacology Group comprises studies of functional aspects of pharmacology and the investigations target multiple levels of integration from individual cells across tissue sections and whole organ systems to intact animals. By performing pharmacological studies in a range of in vitro and in vivo preparations in addition to models of human diseases, we aim to comprehensively characterize suitable targets for pharmacological intervention in man, as well as predict the kinetics and dynamics of candidate therapeutic agents. The research efforts of the group, thus, encompass translational investigations and span the range from basic science to therapy. Moreover, we seek to enable pharmaceutical researchers and Pharmacists being trained within the group to bridge laboratory and clinical research.

In vitro and in vivo pharmacology

Cardiovascular and Muscle Pharmacology

The purpose of our research is to unravel the mechanisms that are responsible for changes in function and expression of relevant ion channels and receptors during various pathological conditions such as diabetes, hypertension, and metabolic disease. This information will increase our knowledge of the complex regulation and adaptation of vascular structure and function in health and disease and may lead to better pharmacotherapy of cardiovascular diseases.

Research questions
Mechanisms of (auto-) regulatory control and adaptation of vascular tone and morphology. Changes in receptor expression and intracellular signalling in healthy animals and animal models of disease (e.g. diabetes, heart failure, ischemia and reperfusion, preconditioning). Consequences of changes in free energy flux and metabolism on skeletal muscle, vascular smooth muscle and papillary muscle function under various patho-physiological circumstances or following pharmacotherapy. Neurohumoral regulation of blood vessels under various patho-physiological circumstances or following pharmacotherapy.

Methods
Wire-myograph and pressurised myograph
Langendorff heart perfusion system
Organ bath
Measurement of physiological parameters (e.g. intracellular calcium, membrane potential, pH, oxygen concentration/gradient) using fluorescent microscopy
RT-PCR, Western blot, ELISA og immuno-histochemistry

Examples of Master theses
Pharmacological and molecular characterization of the KATP and BKCa-channels in porcine intracranial arteries: in relevance to pathophysiology of migraine, august 2007.
In-vitro study of the calcitonin gene-related peptide receptor in the Zucker Diabetic Fatty rats, may 2007.
Role of Na^+-K^-ATPase on glucose uptake in isolated working muscle.
Neurophysiological studies of CNS activity in stress-mediating nuclei

Repeated or prolonged stress can have serious consequences for the organism such as immunosuppression, cognitive impairment as well as compromised cardiovascular function. Moreover, maladaptive stress-responses have been linked to the etiology of several psychiatric ailments, including depression and post-traumatic stress disorder as well as to the development of addiction. Delineation of the CNS neurochemical signalling pathways that mediate stress responses, therefore, hold the potential of identifying targets for pharmacotherapy of stress.

The neural mechanisms that mediate the effect of stressors in eliciting stress-responses are, however, poorly understood. We aim to elucidate these mechanisms by initializing investigation of the in vivo activity of parvocellular neurons in the paraventricular hypothalamus, which activate the hormonal stress reponse.

Methods
In this context of these investigations, possible thesis research projects include:
Extracellular measurements of single neuron activity after stressor exposure, across circadian changes and during behavioural states (sleep-wakefulness).
Neuropharmacology of stress-mediating cell activity using intracellular and \textit{in vitro} recording methods.
Immunohistochemical analysis of the neurochemical content of parvocellular PVH cells.

Related areas of research in which thesis research may be conducted include:
In vitro investigation (patch clamp) of the neuropharmacology of cholinergic brain stem neurons involved in behavioural state regulation or addiction.

Neuropharmacological investigation of \textit{GABA}_A receptor ligands.

Research Area
GABA is the most important inhibitory neurotransmitter in the central nervous system, and disorders of the GABAAergic neurotransmission are presumably important in a number of neurological and psychiatric diseases. The \textit{GABA}_A receptor plays a central role in this context and is the target for several important drugs, among others the benzodiazepines, the use of which unfortunately is complicated by side effects. Several subtypes of \textit{GABA}_A receptors exist, some of which are placed inside and some outside of the synapses, and a number of investigations have shown that the in vivo pharmacological profile of a ligand depends on which subtypes the ligand affects. Thus, a more selective targeting at subtypes of \textit{GABA}_A receptors may improve the therapeutic outcome and perhaps open new indications for drugs acting at \textit{GABA}_A receptors.

Topics for investigation
Characterization of the subtype selectivity and mechanism of receptor activation of \textit{GABA}_A receptor ligands. Synaptic and extrasynaptic \textit{GABA}_A receptors as targets for new ligands aimed at treatment of neurological diseases, particularly epilepsy.

Methods
Electrophysiological investigations using recombinant receptors, neurons in primary culture and brain slices. If relevant, supplemented with fluorescence recordings. Computer modelling of ion channel function. In vivo epilepsy model.

Contact
Uffe Kristiansen (uk@farma.ku.dk)
Neurobiological control of sleep/wakefulness cycle and drug dependency

Research Interests:
My laboratory is interested in investigations of the neurobiological control of different states of arousal and motivated behaviors. Specifically, we are interested in control of the sleep/wakefulness state and drug dependency. While research on the mechanisms mediating addiction to drugs of abuse and mechanisms governing the sleep/wakefulness cycle may seem unrelated at first glance, control of these two processes of arousal share a common neuronal effector, the laterodorsal tegmental nucleus (LDT), a brainstem nucleus critically involved in the classical “ascending reticular activating system”. My studies focus on cellular actions of neuroactive chemicals relevant to control of sleep and addictive processes on this brainstem nucleus.

Technical Approach:
Questions of interest will be explored using in vitro patch clamp recordings from mouse brainslices. In some cases, concurrent, high-speed calcium imaging utilizing fluorescent markers will be conducted. Immunohistochemistry is also utilized to identify the signature neurotransmitters of neurons of interest.

Contact
Kristi A. Kohlmeier (kak1@farma.ku.dk)

Patho-physiology and treatment of chronic pain conditions

Research interests
The main focus of the research group is translational research into the patho-physiology, prevention and treatment of chronic pain conditions such as neuropathic pain, inflammatory pain, cancer pain and bone pain. Both animal studies (rats, wild type and knock-out mice) and clinical studies are conducted.

Technical Approach
In vitro investigations of neurons and glial cells involving receptor-pharmacology, enzymatic activity, and signal transduction e.g. calcium response by FURA. Animal models (rats and mice) of acute pain; inflammatory pain; neuropathic pain; cancer pain and bone pain. In vivo imaging of tumour burden and bone degradation. The student will need to pass a course in laboratory animal science and will thereafter perform surgery in rats and mice, as well as observational studies and testing of nociceptive thresholds. Clinical investigations of new treatment paradigms in clinical pain testing and protocol design.

Previous projects

Contact
Ole J. Bjerrum (obj@farma.ku.dk) Anne-Marie Heegaard (amhe@farma.ku.dk)
Immunopharmacology

Innate immunity and pyrogens
Medicines intended for injection must be routinely tested for pyrogens. The rationale behind this is that pyrogen contaminated medicines can stimulate the immune defense. The best known response of an activated immune defense is fever. Pyrogens are microorganism or compounds secreted by microorganisms.

To ensure that medicines are pyrogen free, two assays are currently used: the Limulus Amebocyte Lysate (LAL) test and the Rabbit Pyrogen test. Both assays have been shown to be problematic. In our laboratory alternative cell based in-vitro test have been developed.

The principle of our new assay depends on human phagocytes. When these cells are exposed to pyrogens they get activated and this can be measured by immunoassays or by chemiluminescence.

Further we investigated the use of these cell based in-vitro test to identify and study immunomodulating substances and drugs.

Coming projects
Study of toxins and pyrogens from gram positive bacteria using the Mono Mac 6 (a Macrophage cell line).
Receptor expression on differentiated HL-60 cells (a granulocyte-like cell line).
Signaling pathways for antibodies and complement proteins in phagocytes.

Methods
Cell culturing, immunoassays (DELFIA, flow cytometric analyses, fluorescence microscopy), chemiluminescence.

Titles of projects already completed
- Comparison of HL-60 cells and human PMN regarding the generation of reactive oxygen species when challenged with pyrogens.
- Influence of the complement system on reactive oxygen species generation and phagocytic capabilities of ATRA differentiated HL-60 cells.
- Toll-like receptor signaling and production of IL-6 and CXCL8 in Mono Mac 6 cells.

Contact
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Biochemical Pharmacology

Bioactive lipids
Homepage: http://www.farma.ku.dk/index.php/Biochemical-Pharmacology/8235/0/

Problemstillinger
Vi arbejder med at forstå de fysiologiske og patofysiologiske funktioner af endocannabinoider og acylethanolamider. Hvor, hvorledes og hvornår dannes de, og hvad gør de godt for? Endocannabinoiderne, anandamide og 2-arachidonoylglycerol, vides at aktivere cannabinoid receptorer, og de er derigennem med til at regulere så forskellige biologiske processer som hukommelse, smerte, cellevækst, muskelkoordination, appetit og energistofskifte. Acylethanolamiderne omfatter bl.a. anandamide, oleoylthanolamide og palmitoylthanolamide hvoraf oleoylthanolamide er med til at regulere fødeindtagelsen og lipolyse i fedtvæv via PPARα og/eller GPR119, og palmitoylthanolamide er anti-inflammatorisk.

Metoder
Enzymmålinger med radioaktive substrater, massespektrometri til bestemmelse af vævsniveauer af bioaktive lipider, fodoringsforsøg med dyr.

Kontakt
Harald S. Hansen (hsh@farma.ku.dk)

Molecular Neuropharmacology

Molecular Neuropharmacology - Molecular pharmacology of ionotropic glutamate receptors and drug development
My research is focused on the study of the AMPA/kainate ionotropic glutamate receptors (iGluRs) and we are employing several different approaches to examine the functional and physiological role of iGluRs. Binding of (S)-glutamate to iGluRs is a key step in rapid excitatory synaptic transmission among nerve cells within the mammalian central nervous system (CNS). iGluRs are important in the development and function of the CNS and are implicated in learning and memory. Furthermore, iGluRs also seem to be associated with certain neurological and psychiatric diseases (e.g. epilepsy, Alzheimer’s, depression) and are therefore considered as potential drug targets. Recombinant receptors are pharmacologically characterized by expression in *X. lævis* oocytes using TEVC electrophysiology as well as by radioligand binding assays. These pharmacological and functional studies on iGluRs are complemented by biostuctural analyses, within FARMA’s GluTarget project (www.glutarget.ku.dk), using X-ray crystallographic investigations of the binding of ligands to receptor binding site(s). Selected compounds from *in vitro* studies are screened for activity in various behavioural models *in vivo*.


**Methods:** molecular biology, electrophysiology, receptor binding, Western immunoblotting, cell and virus culture, *in vivo* behavioural pharmacology

**Previous speciale titles:**
- Arylalkysulfonamides: Pharmacological characterization of a novel series of AMPA-R potentiators.
- Structural and pharmacological study of the partial selective agonist CPW-399.
- Effekt af en dimer positiv AMPA receptor modulator på indlæring og hukommelse.
- A pharmacokinetic and behavioral study of the AMPA-receptor modulator (R,R)-PIMSD.

**Contact:** Darryl Pickering (picker@farma.ku.dk)

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**Neurometabolism**

**Neurometabolism Research Unit**

The research in NeuroMet is focused on energy and amino acid metabolism in the mammalian brain. Primary mouse cell culture systems of neurons and astrocytes from cerebral cortex or cerebellum are extensively employed. In addition, acutely isolated cortical prisms, isolated mitochondria and cell lines are applied as model systems. An array of 3H, 15N and 13C isotopes is utilized in the mapping of metabolic pathways and their regulation. HPLC and mass spectrometry are key analytical tools combined with biochemical assays, protein biochemistry, molecular biology and fluorescence-based assays and imaging techniques.

**Examples of Master of Science projects:**

**Cerebral ischemia**

Mitochondria play a vital role in cellular bioenergetics. Thus, any condition that affects mitochondrial function such as a stroke will have severe consequences. In this project, we are mapping changes in mitochondrial function during global ischemia in rat brain in search of new potential drug targets to treat the detrimental effects of a stroke.

Cerebral energy metabolism: roles of glucose and lactate as neuronal energy substrates

The brain utilizes glucose as an energy substrate; however, at the cellular level lactate produced by other cell types may play a role as an energy substrate for neurons. This is of course interesting for pure scientific reasons; however the extent to which neurons utilize lactate produced by other cell types has implications for how we interpret functional brain imaging signals. Furthermore, cerebral energy metabolism is compromised in a number of neurological diseases. In this project, we are investigating neuronal bioenergetics with a focus on the role of intracellular Ca2+ for regulating energy metabolism.

**Hepatic encephalopathy**

Cerebral hyperammonemia is believed to play a pivotal role in the development of hepatic encephalopathy, a debilitating condition arising due to acute or chronic liver disease. In the brain, ammonia is thought to be detoxified via the activity of glutamine synthetase, an astrocytic enzyme. Moreover, it has been suggested that cerebral tricarboxylic acid cycle metabolism is inhibited and glycolysis enhanced during hyperammonemia. In this project, we are investigating the ammonia-detoxifying mechanisms as well as the effects of ammonia on energy-generating metabolic pathways in both in vitro and in vivo-based systems.

Role of the enzyme glutamate dehydrogenase in glutamatergic signaling

Glutamate neurotransmitter homeostasis is pivotal for brain function. Deregulation of glutamate homeostasis is linked to a number of brain diseases including ischemia, neurodegenerative diseases and schizophrenia. One of the key enzymes involved is glutamate dehydrogenase (GDH) of which two isoforms exists, namely GDH1 and GDH2. Interestingly, mice only express
GDH1 whereas humans express both GDH1 and 2. In this project, we are pursuing several lines of investigation such as delineating the roles of GDH1 vs. GDH2 in synaptic glutamate homeostasis and how this links to energy metabolism.

Recent titles of M.Sc. projects:
Mitochondrial heterogeneity in the brain
Pathophysiology of hepatic encephalopathy
Involvement of uncoupling in the effect of an elevated ammonia level in the brain
Studying the basic properties of intermolecular glycogenesis and glycogenolysis in the brain
Importance of GDH in neurons and astrocytes for maintenance of ammonia homeostasis

Contact information
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The mechanism behind treatment of epilepsy with a ketogenic diet.

Epilepsy is a common disease which affects 0.5-0.7 % of all children. Antiepileptic treatment has many side effects and some epileptic patients are resistant to drug therapy. The ketogenic diet (KD) is a high fat, sufficient protein and low carbohydrate diet, which has shown remarkable efficacy in the treatment of drug-resistant childhood epilepsy. Our understanding of how the KD produces its anticonvulsant and anti-epileptogenic effects remains incomplete. Several hypotheses focus on ketone bodies, fuel molecules that circulate at millimolar concentrations in the blood of patients on a KD, as causative agents. In our group we work on two of these hypothesis one of them involving a possible role for altered glycolysis and consequent activation of a class of potassium channels called KATP channels, the other one focusing on purinergic receptors.

Aim:
Our aim is to obtain an understanding of the mechanism behind treatment of epilepsy with KD. Hopefully this will enable us to improve treatment for epileptic patients and pinpoint new targets for antiepileptic drugs.

Methods:
We utilize cultured neurons, calcium imaging, neurotransmitter release and biochemical methods for studying the hypothesis.

Project titles in 2010:
The involvement of KATP channels in neurotransmitter release from murine neuron cultures
Effect of ketone bodies on the neurotransmitter release from cerebellar neurons and involvement of ATP-sensitive potassium channels

Contact:
Trine Meldgaard Lund (tml@farma.ku.dk) or Majid Sheykhzade (mash@farma.ku.dk)

Molecular & Cellular Pharmacology

Genetic engineered antibodies and identification of antigens
We have developed plasmids for genetic engineering of antibodies. We have cloned antibodies against glutamate receptors (in collaboration with people from Dep. of Medicinal chemistry), antibodies involved in blood cancer, antibodies for use in investigation of multiple scleroses and allergy antibodies. We have lately made a library of antibodies from camels, called nanobodies, and we have identified nanobodies against glutamate receptors and against bacteria involved in dental paradentosis

Within our different research we can offer projects using the technologies: genetic engineering, PCR, gelelectrophoresis, DNA sequencing, protein expression and purification and handling of prokaryotic and eukaryotic cells.
We also have a collaboration with “Seruminstituttet” whereto we send students to work with antibiotic treatment of intestine pathogenic E.coli and Clostridium difficile.

Examples of master projects:
Development of antibody fragments as subtype specific binders of the GluA4 receptor.
Toxin producing Clostridium difficile

Contact: Erik Riise (esr@farma.ku.dk)

Control and assembly of HIV and other retrovirus

Retrovirus are assembled from two central structural proteins: the core protein GAG and the surface protein ENV. The GAG protein attaches the viral RNA and controls the budding where the ENV proteins in the cell membrane are collected. Later the virus particle is matured by a cleavage of the GAG protein.

In the virus assembly and during infection of cells, the virus proteins bind to a number of cell proteins, which are important for the virus life cycle. It is therefore interesting to examine protein-protein interactions.

HIV

In the HIV project we are looking for peptide sequences, which bind to HIV proteins. An important protein is the GAG protein p6. It acts as an control protein, namely: It binds to cell proteins, which are important for the budding of new virus particles. It also binds to the HIV protein Vpr, which is important for reverse transcription and integration of the formed virus DNA into the cell DNA.

In former thesis projects (see below), binding sequences are found, which could belong to regulative proteins.

Methods: Phage display, sequencing, Gene technology, ELISA

Thesis work from the last year:
Jacob Wolfgang (2009) "Binding of peptides to the C-terminal end of HIV gag p6"
Michael V Overgaard (2010) "Peptides binding to the C-terminal end of HIV gag p6"

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Pathways to chronic inflammatory diseases – defining drug target by studying candidate genes

Chronic inflammatory diseases, like Multiple Sclerosis (MS) and Rheumatoid Arthritis (RA) are caused by genetic and environmental factors. In order to understand the underlying genetic factors, we have identified candidate genes that possibly predispose to disease development. We are now studying proteins encoded by these genes and how they are involved in the pathology of disease development.

We use two different experimental mouse models for MS and RA, Experimental Autoimmune Encephalomyelitis (EAE) and Collagen Induced Arthritis (CIA), respectively. EAE is induced by immunization with myelin basic protein (MBP) peptide and CIA is induced by immunization with type II collagen. Studies of specific genes are done by DNA sequencing and by expression studies with real time PCR. For the studies of specific genes on the protein level we use flow cytometry, cellular assays, and additional assays of protein phenotype and function. In addition, we use bioinformatics to find information about candidate genes; their interactions with other genes; and for comparative studies of human genes and other species.

Titles of recent "specialerapporter":
"Identification of Novel Molecular Disease Factors in Two Experimental Autoimmune Diseases"
"Structural and functional investigations of a candidate gene in the Eae27 locus"
"Investigations into the role of March6 in Collagen-Induced Arthritis; an animal model for Rheumatoid Arthritis"

Contact: Åsa Andersson (aaa@farma.ku.dk)
Farmakokinetik och -dynamik

Forskningsområde:
Per Hartvig Honoré är professor i Farmakokinetik vid Farma, KU. Han har tidigare erfarenhet inom klinisk farmakologi och gjort studier av farmakokinetisk koppling till läkemedels effekt hos patienter med främst sjukdomar in CNS, men också vid smärtlindring, inom onkologi och mot infektioner.
Forskningen avser att, tillsammans med kontakter inom sjukvården utveckla klinisk farmakokinetik och klinisk farmakologi.
Studierna görs med populationsbaserade metoder där information från en större grupp patienter senare kan användas hos enskilda patienter för att förbättra dosering av läkemedel från farmakokinetisk-effekt dokumentation Ett intresse är onkologisk farmaci som önskas vidareutvecklas och nedan några följer projekt inom området. Möjligt kan finnas för att deltaga i andra liknande projekt men också i projekt för att öka kunskap inom klinisk farmakoterapin.

Farmakokinetisk-farmakodynamisk optimering av
cystatikida dos med populationskinetiskt stöd och
försök med ”dose-banding”

Problemstillinger
Cytostatika doseras vanligt mot kroppsyta. Den kliniska rationalen för denna
doserings påljudik dokumenterad i randomiserade kontrollerade kliniska försök. Det
saknas studier som klarlägger sambandet mellan cytostatika farmakokinetik relaterat
till farmodynamik effektparametrar med hänsyn tagen till njurfunktion,
farmakogenetik och ålder mm. värderade i populations studier.

Metoder
Studierna utförs hos patienter med cancer. Farmakokinetik studeras hos utvalda
cystatikida bland annat antracykliner och relateras en objektivt kvantifierbar mätbar effekt vid olika typ cancer. En PK-PD
model utformas som utnyttjas i en populations studie med många patienter vars demografiska data tillsammans med övrig
klinisk information utnyttjas för att bättre prediktera individuell dos hos enskilda patienter.

Delstudier i projektet bearbetar den kliniska effekten av metaboliter till de cytostatika som ges och resultaten värderas med
populationsbaserad PK-PD.

Kontaktperson: Per Hartvig Honoré, peh@farma.ku.dk tel 35336575, rum 202b,

Understödsterapi hos cancerpatienter,

Problemstillinger
Patienter med cancer har ofta biverkningar inte bara på grund av läkemedel utan
också beroende av den underliggande sjukdomen. Tidigare har smärta och illamående varit vanliga orsaker till patientens
lidande. Bättre behandling av dessa gör nu att svår trötthet är minst lika vanligt. Andra svåra biverkningar hos patienter med
cancer är också mucosit, härawfall, diarré, förstopning, kakexi och frekventa
infektioner. Förebyggande behandling skall finnas till hands och skall inkluderas i en
behandlingsplan för varje enskild patient.

Metoder
Farmakologisk smärtbehandling med alternativa medel prövas hos patienter med olika typer av smärta förutom cancerrelaterad,
i populationsbaserade studier (Se ovan: Smerteprojekt).
Biokemiska metoder utnyttjas för att bestämma transmittorer och markörer för svår trötthet kantiteras hos patienter med
tumör före, under och efter pågående cytostatika behandling. BDNF och ett antal cytokiner som bidrager vio av trötthet
kaviteras i CSF och relateras ett score, Fatigue Score Index.
Cancersjukdomens inverkan på patientens dagliga liv och förändringar inom familj, arbete och välbefinnande kommer studeras
i olika etniska grupper och stödbehandling försökes

Studier inom andra terapiområden utöver cancer kan erbjudas, liksom studier av kvalitetsäkring av patientmedicinering
(klinisk farmaci).

Kontaktperson(er). Per Hartvig Honoré, peh@farma.ku.dk

Speciale 2010
Fatigue relaterat till cytokinfrisättning i olika faser av cytostatika kur
Farmakokinetik och effekt av cytarabine och aktiv metabolit vid AML
Farmakokinetik värdering av njurdialys vid överdos av läkemedel
Farmakokinetik och effekt av daunorubicin och aktiv metabolit
Smärtlindrande effekt av betalaktam antibiotika hos rätt och patient

Klinisk Farmaci og Farmakoterapi


Udbuddet af opgaver indenfor Klinisk Farmaci og Farmakoterapi tager udgangspunkt i projekter med fokus på lægemiddelanvendelse indenfor hospitalssektoren og sektor overgange.

Projekter 2012

Der vil i 2012 være mulighed for at udarbejde speciale projekter indenfor områderne: Nikotin substitution ved rygeophør, intensiv terapi, akut og kronisk smertebehandling, palliativ behandling samt eksperimentelle humane smertemodeller. Det er på nuværende tidspunkt ikke muligt at specificere eksakte projekt titler. Alle projekternes praktiske gennemførelse foregår eksternt i samarbejde med hospitals afdelinger/apoteker over hele landet. Vi tager først kontakt til de enkelte afdelinger, når vi har identificeret studerende, der er interesserede. Af hensyn til kapaciteten skal vi opfordre til, at man udfører speciale projektet to og to, men "ene opgaver" er ikke udelukkede.

Kontakt: Lona Christrup (llc@farma.ku.dk) og Janne Rømsing (jr@farma.ku.dk)

Samfundsfarmaci/Social Pharmacy

Samfundsfarmaci kan defineres som den disciplin, der behandler lægemidlernes rolle i samfundet. Samfundsfarmaceutiske problemstillinger anlægges på individ, gruppe/organisation såvel som samfunds niveau. Specialeemnerne fordeler sig på 2 temaer Lægemiddelanvendelse og Farmaceutisk praksis.

Lægemiddelanvendelse

Forskningsområde
Gruppen udfører forskning inden for en vifte af temaer i relation til forudsætninger for og konsekvens af lægemiddelanvendelse. Der udbydes specialer indenfor lægemiddelforbrug, brugerperspektiver på lægemidler, pharmacovigilance/lægemiddelsikkerhed, moderne medicin og lægemiddelanvendelse i ulande.

Information for students attending the master program of pharmaceutical sciences
The research group is conducting research in relation to the conditions and consequences of medicine use. Master theses will be offered within the research topics: medicine use, user perspectives on medicine, pharmacovigilance/medicine safety, modern medicine and medicine use in developing countries. There are limited possibilities for conducting master theses in English, and only after closer agreement with the respective supervisors.

Problemstillinger

Lægemiddelforbrug

- **Børn og unges lægemiddelanvendelse**


**Brugerperspektiver på lægemiddelanvendelse**

Det betragtes efterhånden som en selvfølge, at inddrage lægemiddelbrugernes egne erfaringer som ressource i arbejdet med at optimere af lægemiddeltherapien, men der er fortsat meget få forskningsbaserede studier og derfor mulighed for flere specialer. Mulige projekter kan f.eks. belyse børnernes betydning for brugernes hverdagsliv, stigmatisering som følge af lægemiddelanvendelse, metaforer som brugerne anvender, når de taler om medicin og deres erfaringer eller skriver om det på internettet, etc. (EHH)

**Pharmacovigilance**

Viden om lægemidlers bivirkningsprofi er begrænset, idet de kliniske forsøg som ligger til grund for registrering og markedsføring af nye lægemidler primært er designet til at hypoteseteste effekt, og ikke bivirkninger. Information om bivirkninger, som opstår ved brug af lægemidler i den almindelige befolkning er begrænset, idet kun en brøkdel af alle bivirkninger bliver rapporteret til myndighederne. Overvågning og analyse af mulige bivirkninger i relation til medicinfirmærens produkter har fået stigende betydning i samfundet. (Danish Pharmacovigilance Research Group - PREP)

- **Signalgenerering**

Analyser af spontane bivirkningsdata rapporteret til det danske bivirkningssystem og/eller de internationale bivirkningsdatabaser i WHO og EMA. Formålet med disse studier kunne være at undersøge hvilke nye bivirkningssignaler som kan identificeres via de spontane indberetninger, herunder alder og kønsfordeling på de patienter som rammes af bivirkninger og dem som rapporterer bivirkningerne. (LAA)

- **Bivirkningsestimering**

Estimering af bivirkningsfrekvenser for nye bivirkningssignaler ved registerkobling mellem lægemiddelforbruget og epidemiologiske databaser. (LAA)

- **Lægemiddelsikkerhed og risikogrupper**

Formålet med disse studier kunne være at undersøge hvor meget viden, der er til stede omkring sikkerhed ved anvendelse af lægemidler i f.eks. børn, ældre og gravide før og efter tidspunktet for markedsføring af nye lægemidler, samt hvorledes vidensniveauet kunne øges. Studier om undersøge bivirkninger ved off-label ordinater (anvendelse af lægemidler til ikke godkendte indikationer, aldersgrupper etc.), bivirkningsrelaterede indlæggelser og bivirkninger opstået i forbindelse med substitution af lægemidler er også oplagte specialemuligheder. (LAA, EHH)

- **Holdninger/opfattelser af bivirkninger**

Formålet med disse studier er at undersøge sundhedsprofessionelle og patienters holdninger/opfattelser til bivirkninger, herunder alvorlighed og anvendelse af lægemidler til risikogrupper. (EHH)

**Pharmacogenomics**

Lægemiddelsikkerhed i et globalt perspektiv
Formålet med disse studier kunne være at undersøge og sammenligne lægemiddelpolitik i forskellige lande, regioner eller kontinenter, især med fokus på overvågning af bivirkninger. Gode sprogkundskaber er en forudsætning. (LAA, EHH).

Lægemidler i ulande
Flere specialer er mulige inden for lægemiddelforsyning, -ordination og -forbrug samt farmaceutisk praksis. Feltarbejdet vil primært foregå i Uganda og fokusere på lægemiddelhåndtering og – brug blandt børn. (EHH)

Moderne medicin
Moderne medicin har til formål at analysere og/eller teste den sundhedsmæssige værdi af forskellige tilgange til individualiseret medicin set i et patient, sundhedsprofessionel og sundhedssystem perspektiv. Herunder compliance systemer, dosis-respons studier, medicinsk marketing etc.

- Fremtidens lægemidler er gratis – du betaler for et service abonnement!
  Med udgangspunkt i tesen om et paradigme skifte i medicinalindustrien i retning af ”from content to care” og med rationel farmakoterapi som referenceramme, ønskes en forretningsmodel for medicinalindustrien eventuelt en konkret care program udviklet. (CM)

- Dysphonic Attention Deficit Anxiety Disorder (ADHD) fremtidens sygdom?

Metoder
De ovennævnte problemstillinger kan undersøges via forskellige kvalitative og kvantitative forskningsmetoder så som registerkobling, dokumentaranalyser, spørgeskemaer, interviews, observationer, tekstmining, netnografi samt litteraturstudier. Derudover kan andre relevante metoder eller kombination af flere metoder være relevante.

Titler på tidligere specialer
- Teenagere med ADHDs erfaringer, opfattelser og vurderinger af ADHD og deres lægemiddelbehandling – et brugerperspektiv.
- Bivirkningsrelaterede indlæggelser – journalgennemgang på Akutmodtagelsen på Kolding Sygehus.
- Availability and access to medicines for children with epilepsy in Uganda.

Eksterne samarbejdspartnere
Novo Nordisk Foundation Center for Protein Research
Hospitalsafdelinger
Institut for Rationel Farmakoterapi
Statens Institut for Folkesundhed
Regionernes kvalitetssikringsenheder
Lægemiddelstyrelsen
Patientforeninger
Apoteker
Pharmakon
Danmarks Apotekerforening
Universiteter i udlandet
Lægemiddelindustrien
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Pharmacy Practice

Master thesis suggestions from the pharmacy practice team 2012
The aim of research carried out in the pharmacy practice team is threefold:
To map, evaluate and develop pharmacy practice in the primary and secondary health care sector – with a special focus on organizational aspects, tasks, resources, activities and outcomes.
To contribute to the quality development and assurance of activities carried out by pharmacists
To monitor, study and analyze the relationship and development of pharmacy and the laws and policy affecting the field including the health care sector and the pharmacy profession.

Team members:
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Susanne Kaae (ska@farma.ku.dk)
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Master thesis suggestions:

EU Pharmaceutical policy and the role of the European commission: implications for pharmacy practice in Denmark
Based on the most recent EU directives (approved as well as suggested), the thesis will analyze the consequences of EU pharmaceutical policy including economic implications; organizational implications; medicine safety; “mobile patients”; medicine substitution etc. In order to research the effects of EU policy for pharmacy practice, various methods (separate or in combination with other methods) will/can be used. Based on theories of pharmaceutical policy qualitative methods will be used, for example: document analysis; content analysis; interviews etc.

Contact: Janine Traulsen or Susanne Kaae

Liberalization/deregulation of community pharmacies in the Nordic countries
The thesis will study the economic and/or patient related consequences of recent legislation concerning community pharmacies in the Nordic countries. One approach could be to compare one or several countries, for example Iceland, Norway, Sweden or Denmark. The study will use qualitative methods based on theories and analysis of pharmaceutical polices. Based on theories of pharmaceutical policy qualitative methods will be used, for example: document analysis; content analysis; interviews etc.

Contact: Janine Morgall or Susanne Kaae

Improving communication in the pharmacy counter for chronic patients

Background: A ph.d.- project has recently documented how pharmacy staff find it difficult to communicate with chronic patients who visit the pharmacy on a regular basis (so-called “flergangskunder”). A master project is could map and suggest improvements for the content and type of communication typically provided to these customers.

Methods: Observation in the counter and interviews with customers (and maybe pharmacy staff)
Theory: Communication theory

Contact: Susanne Kaae or Lotte Stig Nørgaard

Communication at the pharmacy counter

Background: It will be possible to join current research projects at the department regarding development of communication at the counter. The theme is likely to be connected to exploring differences between perceptions of patients and pharmacy...
staff regarding medicines, diseases and the role of community pharmacies and how these differences influence communication at the counter.

Methods: Interviews, observations, questionnaires and tape-recordings could all be suitable methods to achieve this aims.

Contact: Susanne Kaae

Optimal use of a database containing drug-related problems identified by medication reviews performed by clinical pharmacists

Aim: The aim of the project is to explore the optimal use of a new database containing drug-related problems identified by clinical pharmacists.

Background: The unique database has been developed as a national initiative. The database is now implemented and contains drug-related problems identified by medication reviews performed by clinical pharmacists in daily practice. There is, however, still a need for exploration of the optimal use of the database regarding various tasks such as quality assurance and research purposes. In addition, it would be of interest to identify focus areas for clinical pharmacy interventions based on the registered drug-related problems.

Methods: The methods will be based on database analyses and may be followed by surveys performed in the practice setting.

Contact: Lotte Stig Nørgaard

Identification of potential clinical pharmacy interventions in a clinical setting

Aim: The aim of the project is to explore potential clinical pharmacy interventions at a specific clinical setting e.g. pediatric ward.

Background: Before testing the effect of novel interventions, it is important to explore, whether the suggested intervention is needed, wanted and necessary in a clinical setting. This study aims to identify specific novel interventions, which can be developed and tested in the clinical setting. In that way, clinical pharmacist can optimize their interventions and support clinicians in the best possible way.

Methods: A combination of methods is optimal for this study. These could be observational studies combined with either interviews of or questionnaires by clinicians. The clinical setting is yet to be identified – but a pediatric ward would be of interest.

Contact: Lotte Stig Nørgaard

Long term implementation of cognitive services

Background: It will be possible to explore the long term development and implementation of the first publicly reimbursed cognitive service in Denmark – The Inhaler Technique Assessment Service (Tjek på inhalation) from either a macro- or micro-perspective – studying the different phases of implementation since start on basis of either actions by the Danish Pharmaceutical Association including mystery shoppers surveys (Danmarks Apotekerforening) or by the individual pharmacies. We trust to be able to co-operate directly with the Danish Pharmaceutical Association in case of the macro-level.

Contact person: Susanne Kaae

The use of medicines bought in ethnic minority patient´s country of birth

Background and research question: In connection to a study entitled “Optimal medicine use among ethnic minority Danes” and a ph.d. study entitled “Improving pharmacy practice in relation to ethnic minority patients” a master thesis on the use of medicines bought abroad is offered. Recent research has shown that ethnic minority patients buy medicines in their country of
birth. Why do they do this? How? What are the experiences, advantages and disadvantages of behavior seen from the patient’s perspective?

**Methods:** Qualitative methods

**Contact:** Lotte Stig Nørgaard, Janine Traulsen

### Automated dose-dispensing in the primary care sector

**Background:** Automated dose-dispensing in the primary care sector was introduced in Denmark in 2001 with the aim of improving and rationalising the distribution of medicines directly to the medicine users and to improve the working condition for the home care nurses. Research has shown that health care professions face challenges concerning several aspects in relation to using dose dispensing. A new external funded study aims at identifying potential risks, barriers and problems concerning use of automated dose-dispensing in order to eliminate and reduce consequences hereby and with the aim of identifying best-practice and “good stories” so that these can form the platform for solutions in the rest of Denmark concerning use of automated dose-dispensing. The study, to which the student will be attached, is run by Pharmakon in Hillerød together with Danish Society for Patient Safety and FARMA.

Other perspectives of dose-dispensing are also of research-oriented interest, such as 1) how does dose-dispensing go along with the new patient medication record system (FMK), 2) costs of dose dispensing 3) what would be the consequences for the pharmacies (economic, capacity and working routines) if more patients used dose-dispensing?

**Methods:** Qualitative methods

**Contact:** Lotte Stig Nørgaard

### Pharmacy Counseling Strategy 2010+

**Background:** The pharmacy counseling strategy implemented in all Danish pharmacies during the last 4 years is of great research interest. How do the pharmacies work with the strategy? What is the impact of the strategy in the pharmacies? What is the knowledge and impact of external partners in relation to the strategy?

**Methods:** Qualitative

**Contact:** Lotte Stig Nørgaard

### Medisam

Medisam is a research project which work with the development of HMR see www: Medicingennemgang-Medisam.
Possible topics where we invite students are:
Much data have been collected in the Medisam project which can be worked with in the form of secondary analysis of data for example:
Assessment of the clinical relevance of the medicine related problems. Eg type and relevance of interactions, type and relevance of side effects

Analysis of patient interviews e.g. selected patient groups, type II diabetics, cardiovascular patients, patients in treatment for pain, or problem areas, for example experience of adverse effects, or generic substitution.

From 2010 all pharmacy students perform a home medication review (HMR) at the Danish training pharmacies where they are in contact with GPs, nursing homes and home care.
In which way does this influence the attitude of the training pharmacies to carry out HMR themselves? Data collection methods: analysis of questionnaire data and focus group interview with supervisors.
Patient education – the role of pharmacy

Background: Patient education as a controlled activity has been developed at Stanford University and has since been introduced in Denmark. Thus, today more than 80 out of 98 municipalities offer patients patient education programmes. The education aims at strengthening chronic patient’s health status through for instance lifestyle changes. One of the problems faced by the municipalities is how to get into contact with patients.

What role might pharmacy plays in order to recruit patients? What does it take to strengthen the cooperation between pharmacy and municipality concerning the education? What is pharmacy attitude towards entering this kind of health preventive of activity?

Methods: Qualitative methods (individual interviews and focus group interviews)

Contact: Lotte Stig Nørgaard

Patient education at the pharmacy counter

Patient education as a controlled activity has been developed at Stanford University and has since been introduced in Denmark. There is solid evidence that the programme improve health outcomes among a wide range of different patient groups. The education is based on a specific theory about self-efficacy by Albert Bandura. By the means of the self-efficacy term patients work their way through: development of actions plans, problem solving, role modeling, group dynamics and reinterpretation of symptom reasons.

The education take place in groups, but in Canada work has been initiated in order for the education to take place in a one-to-one relation, for instance between a patient and a health professional.

In the master project the student is to study if and how self-efficacy might be used as a pedagogical method in a community pharmacy setting. The aim is that pharmacies, on the long run use the methodology for supporting citizens’ life-style changes through dialogue in the pharmacy.

Method and theory: A theoretical study based on self-efficacy as a tool for developing pedagogical tools. Evt. qualitative interviews and participant observation.

It is necessary to educate the master student specifically in the methodology, which will cost about 8.000DKr.

Contact: Lotte Stig Nørgaard

Expectations to Pharmacy Practice

There is a wide consensus that understanding the expectations and preferences of pharmacy customers is important and necessary for the development of pharmacy services. Customer satisfaction surveys can be a useful tool in planning for the future, but at best these surveys provide only a partial picture of patients’ views and expectations. There are often big differences between patients’ views and expectations of pharmacy services and customer satisfaction. The aim of this project is to study the differences between what customers expect from the community pharmacy/pharmacist and what pharmacist think customers expect. This project will also look at the differences between customer expectations and customer satisfaction.

Theories of trust and the professions will/can form the basis for analysis. Qualitative methods such as interviews, observation, document analysis etc. will be used. The master’s student will become part of a research team which is working on this topic.
Improved health efforts towards socially vulnerable and marginalised groups.

**Background:** Ethnic minority Danes and people with reduced work ability face an increased amount of health problems compared to other groups. This has been shown in research and is experienced frequently by the local job centers in Denmark. Pharmakon, FARMA, a pharmacy and a local job center have applied for funding from the National Board of Health for a study with the aim of which is to improve the health status and the ability to work through an individually adapted counseling service on safe and effective implementation of medication treatment. The study is made up by a development phase and an implementation phase. A master student will be connected to the study supporting the implementation phase.

**Methods:** Qualitative and quantitative methods

**Contact:** Lotte Stig Nørgaard

Which challenges lies for patients discharged from geriatric ward at Næstved Hospital who had automatic drug dispensing (ADD) before admission to the hospital?

**Background:** In the period 01-01-2010 to 31-12-2012 geriatric ward at Næstved Hospital has employed a clinical pharmacist to optimise the quality of the medicine history for patients admitted to the ward. In that manner the clinical pharmacist identify patients receiving ADD and ensures that the ADD is paused, if there has been any changes to the patients medicine, and forward the information of ADD to the patient’s doctor. At the geriatric ward the clinical pharmacist will therefore have identified patients with ADD that potentially could be contacted regards attending in the thesis.

**Objective:** The objective of the master thesis is to investigate what happen to the patients with ADD after discharge. Following questions could be asked:
- Will the ADD be restarted after discharge?
- What are the reasons for restarting ADD?
- What kind of significance does the restart of ADD have on a potentially readmission?
- What are the reasons for not restarting ADD?
- What significance does not restarting ADD have for the patient/relatives/staff at a nursing home?
- Which actions could contribute to better patient safety for patients with ADD transferred between health care sectors?

**Method:** Interviews of patients with ADD discharged from geriatric ward before the start of the thesis.

**Contact:** Lotte Stig Nørgaard
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