DanCARD

ANNUAL SCIENTIFIC REPORT

2011

The Danish Centre for Antibiotic Research and Development

STATENS SERUM INSTITUT

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| CONTACTS

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| PREFACE

The second year of the Danish Centre for Antibiotic Research and Development has been interesting and eventful. Results start to show and the synergism in the DanCARD collaboration has become very distinct as indicated by the scientific reports enclosed and the gradually growing publication list.

Two DanCARD meetings (spring and fall meetings) were held in 2011, again with great attendance of both DanCARD partners and others with interest in antibiotic research and development. Axel Dalhoff, external advisory board member, participated in the fall meeting 2011.

A PhD course entitled 'Antimicrobial Resistance and Development' was successfully arranged by Reinhard Wimmer and held at Aalborg University in November 2011, with participation of most DanCARD partners and DanCARD Ph.D. fellows.

We look forward to continue the collaboration in DanCARD.

Project Head
Professor Niels Frimodt-Møller

| SCIENTIFIC REPORTS FROM COLLABORATORS

Dept. Drug Design and Pharmacology and Dept. Pharmacy, Faculty Of Health and Medical Sciences, University of Copenhagen

By Henrik Franzyk and Hanne Mørck Nielsen

The different analogs of the CPP, penetratin, have been further investigated with respect to their interaction with eucaryotes and procaryotes as well as lipid bilayers representative for these types of cells, e.g., assessment of peptide structure upon interaction with lipid bilayers was investigated by circular dichroism and the degree of membrane perturbation was assessed by calcein release from liposomes. Selected penetratin analogs have also been tested for their susceptibility to trypsin digestion. A scientific manuscript is in preparation intended for publication in 2012.

Some of the penetratin analogs were tested for their capability of killing intracellular *S. aureus* in an airway cell line, the Calu-3 cell line. For this testing, one of the DanCARD PhD students was introducedto the technology during a stay with a research group with expertise in this method (Professor Tulkens, Louvain Drug Research Institute, Brussels, Belgium). Establishment and optimization of the intracellular infection model has been initiated in our laboratory for our specific future purposes. This part is performed as a co-operation between Department of Pharmacy (Hanne M. Nielsen), Department of Drug Design and Pharmacology (Henrik Franzyk), and Hvidovre Hospital (formerly SSI) (Anne Sandberg-Schaal and Niels Frimodt-Møller). A master student associated with the DanCARD project has conducted a part of her studies in the laboratory of Prof. Martin Malmsten, Uppsala University.

A PhD project on formulation optimization of nanoparticulate drug delivery systems targeted to treat intracellular *S. aureus* infections has been initiated late 2011.

The part of the project focusing on performing the first comparative study of several differentpeptidomimetic backbones for the same sequence of side chains (aromatic and cationic) is ready for submission as a full paper.

Both homomericpeptidomimetics and chimeras consisting of alternating natural □-amino acids and unnatural residues as well as reference D- and L-peptides have been prepared by microwave-assisted SPPS.All eleven compounds in this array were examined with respect to antimicrobial activity, hemolysis, and cytotoxicity. In addition CD-spectroscopic studies have been performed in buffer with and without the presence of liposomes mimicking either human membranes or bacterial membranes.

In contrast to the inactive peptides, most peptidomimetic compounds exhibited antibacterial activity (MIC of 2-16 □M) towards the Gram-negative*E. coli* (including ESBL and NDM-1 strains), while low or no activity was found for *Klebsiellapneumoniae* and the Gram-positive *Staphylococcus aureus*(methicillin-resistant: MRSA). The degree of secondary structure as indicated by the CD-spectra correlated well with the cytotoxicity towards Hela cells, whereas the trend was much weaker for hemolysis and antibacterial effects.This part is performed as aco-operation between

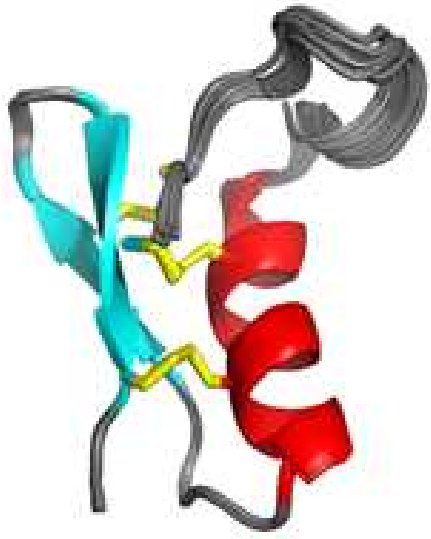
Department of Drug Design and Pharmacology (SUND – previously PHARMA) and Niels Frimodt-Møller (Hvidovre Hospital – formerly SSI).

The originally designed 8-mer peptidomimeticproved not suitable for NMR studies as one type of building blocks with methoxysubstituents proved unstable towards the strongly acidic conditions required for its release from the solid support. Subsequently, a new set of building blocks were prepared and utilized for the synthesis of a stable 8-mer peptidomimeticthat currently is being investigated for its putative folding in the presence of lipid micelles. This part is performed as a co-operationbetween Department Drug Design and Pharmacology (SUND - previously PHARMA) and Aalborg University (ReinhardWimmer).

Dept. of Biotechnology, Chemistry and Environmental Engineering, Aalborg University

By Reinhard Wimmer

- Structures of new antibiotics: a series of anoplin and anoplin derivatives were synthesized in collaboration with Paul Robert Hansen's group and tested both for antimicrobial and hemolytic activity at Statens Serum Institute. The high-resolution structures of a number of candidates were solved and their interaction with lipid mimics were elucidated. A trend linking lipid interaction with antimicrobial activity was discovered.
- Structures of peptoids: Peptoid derivatives of anoplin were synthesized in collaboration with Paul R. Hansen and NMR studies on the peptoids showed that the variants suffered from the presence of multiple conformers, presumable cis-trans isomerism around the peptide bond leading to the N-substituted glycine. Therefore, a different set of peptoids were designed and are currently being investigated. Likewise, the peptide/peptoid chimera investigated so far, did not yield high-resolution structures in solution, but an especially designed candidate is in the pipeline for structural characterization (collaboration with Henrik Franzyk).



- Structure of the insect defensinlucifensin (collaboration with Anders S. Andersen and Karen A. Krogfelt): Lucifensin, a 40 amino acid defensing from *Luciliasericata*, had previously been identified as a key player in fighting off infections during maggot debridement therapy. We have solved the 3D-structure of lucifensin. The structure follows the classical defensing motif (see figure). Analysis of the structure revealed an orientation of amino acids resembling the homologue sapecin, which has been shown to permeabilize bacterial membranes. However, as lucifensin had previously been shown to act by binding lipid II, the question remains whether lucifensin has two modes of action.

Center for Systems Biology, Technical University of Denmark (DTU)

By Søren Molin

Bacterial small regulatory RNAs (sRNAs) function in post-transcriptional control of gene expression and control a variety of processes including metabolic reactions, stress responses and pathogenesis in response to environmental signals or cell stress, such as antibiotics. A variety of approaches have been used previously to identify forty-four sRNAs in the opportunistic human pathogen *Pseudomonas aeruginosa*. We have used RNA sequencing (RNA-seq) to identify novel transcripts in *P. aeruginosa* involving a combination of three different sequencing libraries. Almost all known sRNAs and over 500 novel intergenicsRNAsare identified with this approach. Although the use of three libraries increased the number of novel transcripts identified, there were significant differences in the subset of transcripts detected in each library, underscoring the importance of library preparation strategy and relative sRNA abundance for successful sRNA detection. Nearly 90% of the novel sRNAs have no orthologous bacterial sequences outside of *P. aeruginosa*, supporting a limited degree of sequence conservation and rapid evolution of sRNAs at the species level. We anticipate that the data will be useful for the study of regulatory sRNAs in bacteria and that the approach described here may be applied to identify sRNAs in any bacterium under different growth and stress conditions

Department of Science, Systems and Models, Roskilde University (RUC)

By Anders Løbner-Olesen

Susanne Kjelstrup (Research Assistant professor paid by DanCARD) returned from maternity leave in May 2011. She is the only senior scientist that is 100% devoted to our part of the DanCARD project. After her return, Susanne has further characterized interactions in the replisome of *S. aureus* resulting in identification of additional targets. We have purified additional cyclic peptides selected as potential inhibitors of the DnaN-DnaN or DnaB-DnaB interactions. We are currently determining the MIC of these peptides. Further more, we are in the process of confirming their targets by over expression the gene encoding the target and by determining the effect of the peptides on macromolecular synthesis. We were not able to express the DnaC helicase of *S. aureus* in *E. coli* meaning that this protein is not included in the final interaction map. We have started a collaboration with Murty Madiraju, University of Texas, on a project dealing with peptides disrupting the dimerization of DnaA from *M. tuberculosis*. We received plasmids with DnaA from *M. tuberculosis* that can be used in our reverse two hybrid screening assay. We are continuing this work by mutating the screening strain in *rnhA* and *oriC* to optimize the probability of identifying any peptide disrupting this interacting. Since DnaA is widely conserved throughout the bacterial world we hope that cyclic peptides disrupting this specific interaction can be used as precursors of broad-range antimicrobial peptides.
In May 2011 Ping Fang finished her master thesis "Purification of circular peptides with antimicrobial effect and analysis by HPLC-MS" involving purification of cyclic peptides and verification of the peptides by mass spectrometry. Ping purified two peptides targeting DnaB-DnaB (the helicase loader) dimerization. The masses of the purified peptides were determined by

HPLC-MS and were consistent with the theoretical masses for the peptides confirming the structure of the cyclic peptides.
In September 2011, Paula Paulon started her master thesis "synthetic circular antimicrobial peptides" in collaboration with Poul Robert Hansen (KU) and Karen Krogfelt as formal supervisor from DTU, dealing with the synthesis of circular peptides identified from screening of our library of cyclic peptides. Paula synthesized several circular peptides but unfortunately only in very small amounts. In addition she synthesized linear variants of the peptides. Only two of the linear peptides showed antimicrobial activity against *S. epidermidis* but with very high MIC values (>200 g/ml). Our cyclic peptides had various MIC values which in general were high, with the notable exception of one peptide (called III-7; aninhibitor of DnaN-DnaN interaction) which inhibited growth of *S. epidermidis* at a concentration of 20 μg/ml. In most cases MIC values obtained from recombinant produced and purified peptides were lower than those obtained from synthesized peptides with the same sequence. The reason for this is not known at present. For future experiments we need to be able to synthesize larger amounts of cyclic peptides or we should develop a method for purification of cyclic peptides from culture supernatants.

Department of Basic Sciences and Environment, Faculty Of Health and Medical Sciences, University of Copenhagen

By Paul Robert Hansen

The primary aim of our work is to identify anoplin analogs which selectively target Gram negative species such as *E. coli.* To this end, we have synthesized and purified several anoplin analogs and subsequently characterized them with regard to their activity against five microorganisms in cooperation with SSI. Furthermore, their hemolytic activities have been determined. Several peptides with unprecedented activity and specificity towards *E.coli* relative to other microorganisms as well as human red blood cells have been identified.
Statistical analysis of the biological data obtained from the anoplin analogs has revealed mathematical relations between amino acid sequence and biological activity.
Finally, we have found that very discrete modifications of a central amino acid dramatically affect biological activity. This has been investigated in cooperation with University of Aarhus using molecular dynamics simulations in a system of water, ions and a phospholipid bilayer resembling the bacterial membrane. A clear effect of the subtle modifications is evident, observable as varying mechanisms of peptide attack on the membrane.

Department of Veterinary Disease Biology (DVSB), Faculty Of Health and Medical Sciences, University of Copenhagen

By Luca Guardabassi

DVSB is the only veterinary institution in DanCARD. The main goal at this institution is to develop alternatives to the use of veterinary systemic antibiotics, especially broad-spectrum antibiotics, in order to prevent zoonotic risks associated with the emergence of multidrug-resistant bacteria of

medical interest in food and companion animals. DandCARD supports 3 research fellows at this institution, including 1 postdoc and 2 PhD students.

The postdoc is **Peter Panduro Damborg** who is employed part-time in DanCARD for 1 year over a period of 2 years (January 2011 to December 2012). He is involved in both WP3 and WP4. In WP3, he investigates the antimicrobial effect of synthetic peptoids against the two most common pathogens in canine dermatology, *Staphylococcus pseudintermedius* and *Pseudomonas aeruginosa*. The aim of the study is to develop an effective topical product for treatment of skin infections or otitis externa in dogs. A selection of 10 peptoids developed by P. R. Hansen and his group were tested for their *in vitro* activity against these veterinary pathoges. Two peptoids exhibiting low MICs and low-level hemolysis (EC50) were selected for time kill kinetic studies and further large-scale MIC testing against 100 clinical isolates for each species. Results showed normal MIC distributions and a rapid killing by both peptoids. The next step will be to test the cytotoxicity and the *in vivo* efficacy of the two peptoids in topical formulations. For this purpose, a murine skin infection model will be performed at SSI in 2012. In WP4, Peter is presently working on the development of a new porcine intestinal model in collaboration with another project funded by the Strategic Research Council (Miniresist). The model involves surgical attachment of the caecum to the abdominal wall, allowing easy access to caecal content by needle insertion through the skin. This model will be a useful tool for future studies on resistance development and antimicrobial distribution in the intestinal tract.

Marit Gaastra Maaland is a PhD-student who started on September 1st 2011 under supervision of Luca Guardabassi and Mark Papich (North Carolina State University, US). The title of her project is *"Rationalization of antibiotic therapy in dogs"*. The aim of the project is to optimize and implement the use of old antibiotics against recently emerged Multi-Drug Resistant (MDR) bacteria in dogs, namely methicillin-resistant *S. pseudintermedius* (MRSP) and extended-spectrum beta-lactamase (ESBL) -producing *E. coli.* These MDR bacteria represent a serious threat to animal health, as they are often resistant to all antibiotics commonly used in veterinary medicine. The use of human last-resort drugs for the treatment of such infections in animals is considered unwanted practice due to public health concerns. Thus there is a need for alternative antimicrobial strategies, of which one is the possible use of older antibiotics which have previously been abandoned in small animals due to poorer pharmacokinetic properties than newer drugs. The antibiotics that will be investigated in this PhD include nitrofurantoin, chloramphenicol, florfenicol, doxycycline and minocycline. For all these agents, there are no dog-specific breakpoints to evaluate susceptibility of clinical isolates, and the current dosage recommendations are largely based on insufficient or very old data. The PhD will generate the data that are missing to set clinical breakpoints and to optimize dosages, including *in vitro* data such as MIC distributions and time killing curves, *in vivo* PK/PD data, and data from clinical studies. Marit is currently working on MIC testing of canine clinical isolates by broth microdilution to determine wild-type cutoff values. Preliminary time-kill data for *E. coli* exposed to nitrofurantoin have been generated and PK/PD studies of nitrofurantoin will be soon performed using a mouse UTI model in collaboration with Lotte Jakobsen (SSI). As the project only started 6 months ago, there are no results to report at this time.

Angelika Schoster is a PhD student supervised by L. Guardabassi and cofinanced by KU-LIFE. The PhD has started on October 1st 2011 and involves national and international collaborators

such as Anders Permin (DHI), Branko Kokotovic (DTU-Vet), Per Dedenroth (Sacco srl) and Margit Andreasen (Pig Research Centre, PRC). The objective of this research project is to identify probiotic strains that can be used as an alternative to antibiotics to treat or prevent enteric clostridial disease caused by *C. difficile* and *C. perfringens* in pigs and horses. Especially the pig but also the equine industry suffers substantial economic losses from these infections. Given the amount of pigs in Denmark that have to be treated with antibiotics for neonatal enterocolitis partially due to clostridial infection, and horses that have to be treated for adult and neonatal enterocolitis due to clostridial infection, an alternative treatment method would be highly desirable to prevent antibiotic resistance from developing and spreading in these animals. A collection of 17 commercially available probiotic strains belonging to *Lactobacillus* spp, *Bifidobacterium* spp and *Proprionibacterium* spp will be tested in vitro for desirable growth characteristics (e.g. growth in bile and acid, growth in aerobic environment) and inhibitory activity against clostridia. Following this in vitro work, promising candidate strains will be taken forward into clinical trials in pigs and horses to determine whether these probiotics have a positive clinical effect and reduce levels of clostridia in the gastrointestinal system. The overall effects of probiotics on the gastrointestinal flora will be studied using molecular approaches, including metagenomics. As this project only started 5 months ago, there are no results to report at this point.

Sofia Nälgård is a MSc student affiliated to DanCARD and she has successfully defended her thesis in August 2011. The aim of her study was to investigate whether bacteriophages may be used as a tool for eradication of MRSP colonization or treatment of MRSP infection in dogs. She has isolated a number of temperate and lytic phage strains and tested the spectrum of lytic activity against MRSP and methicillin-susceptible strains. She has characterized the most promising phage strains by restriction-fragment length polymorphism (RFLP) and electron microscopy. The genome of selected phages is currently being sequenced and manuscript based on her thesis work is in preparation. The project will be extended by a PhD study funded by an EU grant to develop a phage product for treatment of MRSP skin infections in dogs.

Starting from January 2012, L. Guardabassi is the coordinator of a EU Initial Training Network (ITN) in the area of antimicrobial drug R&D (TRAIN-ASAP). The ITN supports 12 PhD students and involves 7 partners including two SMEs (Ktedogen and Davolterra) and a large pharmaceutical industry (Pfizer). TRAIN-ASAP will provide a number of synergies and opportunities for collaboration with DanCARD, including research collaborations between fellows and organization of joint training events, workshops and symposia.

The Department of Microbiological Surveillance and Research, Statens Serum Institut

1) By Karen A. Krogfelt:

Antimicrobial peptide discovery and development:
The structure of the defensin, Lucifensin, produced by *Luciliasericata* (blowfly) maggots, which is used for wound treatments, was characterized by NMR. The peptide was recombinantly produced and purified by SSI and Novozymes A/S in collaboration.The structure was analysed at AAU. A manuscript on this subject has been accepted for publication.

Synthesis and purification of cyclic peptides is currently investigated in collaboration with KU Life and RUC and a master student is working on the project.

Testing antimicrobial compounds:
Microbial resistance to ionic silver: Clinically relevant bacterial isolates have been screened for the occurrence of silver resistant isolates. No resistant isolates were identified; however, future monitoring is necessary to secure safe further use of ionic silver as an antimicrobial additive. Results were presented at an international conference and published.
A range of assays for cytotoxicity testing has been established. Antimicrobial peptoids, discovered by DanCARD partners, are currently being investigated for effects on apoptosis, cell viability and proliferation.
The antibacterial activity of a lysophospholipid is under investigation. The compound is effective against *S. aureus* strains (including methicillin resistant strains) and enhances the antibiotic activity of ampicillin against *P. aeruginosa*. Also the cytotoxicity of this compound is currently tested.

Bacteria in wounds**:**
Investigating the bacterial colonization of wounds: By comparing results obtained using three different sampling methods it was found that biopsy sampling is not needed in order to identify the bacterial species present in a wound. Data were published and well received by the community;the study was commented by John G. Bartlett, Professor of Medicine, Johns Hopkins University as follows: "I am writing about your magnificent paper on wound sampling for cultures. The reason is that I plan to report it at the annual meeting of the American College of physicians as one of the best publications in the field of infectious diseases. I like it because the bacteriology was so well done, and the issue addressed is such a common source of confusion in clinical care…"

The nasal cavity has been suggested to be the source for contamination of wounds with*S.aureus*. PFGE analysis revealed that patients harbouring *S. aureus* both in the nasal cavity and the leg ulcer had the same type both places.

2) By Niels Frimodt-Møller and Klaus Skovbo Jensen

Improvement of dosing of antibiotics in patients (Pharmacokinetics/Pharmacodynamics – PKPD):
Cefuroxime: A pharmacokinetic study of administration of intravenous cefuroxime in 2 different doses has been performed in 20 volunteers. Each volunteer receive 2 doses with en interval of 14 days. Ten plasma samples were taken after injection of each dose within a time frame of 8 hours. Cefuroxime concentrations were determined by bioassay. Plasma protein binding was determined by ultrafiltation. Mathematical analysis is ongoing. Optimal dosing regimens of patinets will be estimated by Monte-Carlo simulation. A scientific publication will be submitted later in 2011.
Phenoxymethyl penicillin: A similar study as above has been performed with 2 different oral doses of penicillinV in 20 voluteers (2 doses each). Penicillin concentrations will be detremined by LCMS at KU-Pharma. Similar mathematicl modeling will be performed as above, and a scientific paper will submitted late in 2011.
Further clinical PKPD studies are planned for dicloxacillin and penicillinG.

PKPD studies of older antibiotics in experimental animal models:
The following older antibiotics with excellent affect against multiresistant (e.g. ESBL) Enterobacteriaceae have not been studied for their optimal PKPD, i.e. to estimate the optimal dosing regimens in treatment of urinary tract infections: Temocillin, mecillinam, nitrofurantoin, fosfomycin, ciprofloxacin. The mouse urinary tract infection model and the mouse peritonitis model are usde for these studies. All 5 antibiotics are under scrutiny at the present. For each antibiotic a scientific paper will be submitted.

Testing peptides in vitro and in vivo in animal models:
Peptides produced by colloborators at KU-Life and KU-Pharma are tested for their antibacterial activity against selected human pathogens by microtiter assay and time-kill curves. The most interesting compounds are further tested in the mouse peritonitis model or the mouse skin infection model. These investigations are ongoing.

Various investigations:
Various projects are ongoing on antibiotic resistance issues, comparative activity of clinically important antibiotics, toxicity studies and others. A hemolytic assay for peptides has been set up by Anne Sandberg-Schaal and is being used to test peptides and peptidomimetics from the collaborators. A master project compared the two commonly used cephalosporins, cefuroxime and cefotaxime, and has recently been submitted as a scientific paper. Projects on multi-resistant E. coli clones, which are important for the present increasing prevalence of resistance, are ongoing with focus on resistance mechanisms, plasmids and virulence factors.

| COMMUNICATION

Peer-review articles:

L. Jakobsen, V. Cattoir, K.S. Jensen, A.M. Hammerum, P. Nordmann, N. Frimodt-Møller
Impact of low-level fluoroquinolone resistance genes qnrA1, qnrB19, and qnrS1 on ciprofloxacin treatment of isogenic Escherichia coli strains in a murine urinary tract infection model
Journal of Anrimicrobial Chemother. 2012; Jun 8. [Epub ahead of print]

Gómez-Lozano M, Marvig RL, Molin S, Long KS.
Genome-wide identification of novel small RNAs in Pseudomonas aeruginosa.
Environ Microbiol. 2012; Apr 26. [Epub ahead of print]

K.L.Nielsen, T.M.Pedersen, K.I.Udekwu, A.Petersen, R.L.Skov, L.H.Hansen, D.Hughes, N.Frimodt-Møller.
Fitness cost: a bacteriological explanation for the demise of the first international methicillin-resistant Staphylococcus aureus epidemic.
Journal of Antimicrob Chemother. 2012; 67:1325-1332

T.H. Jakobsen, S.K. Bragason, R.K. Phipps, L.D. Christensen, M. van Gennip, M. Alhede, M. Skindersoe, T.O. Larsen, N. Høiby, T. Bjarnsholt, M. Givskov.
Food as a source for QS inhibitors: Iberin from Horseradish Revealed as a Quorum Sensing Inhibitor of Pseudomonas aeruginosa.
Appl. Environ. Microbiol. 2012; 78:2410-2421

T.H. Jakobsen, M. van Gennip, R.K. Phipps, M.S. Shanmugham, L.D. Christensen, M. Alhede, M.E. Skindersoe ME, T.B. Rasmussen, K. Friedrich, F. Uthe, P.O. Jensen, C. Moser, K.F. Nielsen, L. Eberl, T.O. Larsen, D. Tanner, N. Høiby, T. Bjarnsholt, M. Givskov.
Ajoene, a Sulfur Rich Molecule from Garlic, Inhibits Genes Controlled by Quorum Sensing.
Antimicrob. Agents Chemother. 2012; 56(5):2314

M. K. Nygaard, A. S. Andersen, H. H. Kristensen, K. A. Krogfelt, P. Fojan, R. Wimmer
The insect defensin lucifensin from Lucilia sericata.
Journal of Biomolecular NMR. 2012; 52:277–282

K Gjødsbøl, ME Skindersoe , JJ Christensen, T Karlsmark, B Jørgensen, AM Jensen, BM Klein, MK Sonnested, KA Krogfelt
No need for biopsies: comparison of three sample techniques for wound microbiota determination.
International Wound Journal. 2012; 9:295-302

L. Jakobsen, A. S. Andersen, A. Friis-Møller, B. Jørgensen, K. A. Krogfelt, N. Frimodt-Møller
Silver resistance: an alarming public health concern?
Int J Antimicrob Agents. 2011; 38(5):454-5

N. Christiansen, L. Nielsen, L. Jakobsen, M. Stegger, L. Hestbjerg Hansen, N. Frimodt-Møller
Flouroquinolone resistance mechanisms and their dissemination in urinary tract pathogenic Escherichia coli isolated during rapidly increasing flouroquinolone consumption in a low-use country
Microb Drug Resist. 2011; 17(3):395-406

Andersen AS, Sandvang D, Schnorr KM, Kruse T, Neve S, Joergensen B, Karlsmark T, Krogfelt KA.
A novel approach to the antimicrobial activity of maggot debridement therapy.
J Antimicrob Chemother. 2010; 65(8):1646-54.

Abstracts:

P. Damborg, P.R. Hansen, L. Guardabassi
Two novel synthetic peptoids eexhibit rapid in vitro killing of methicillin-resistant Staphylococcus pseudintermedius.
2nd ASM-ESCMID Conference on methicillin-resistant staphylococci in animals, Washington DC, September 8-11, 2011

L.G.Schoster, H.R. Arroyo, P.E.Staempfli, P.E. Shewen, J.S. Weese
Epidemiologic investigation of Clostridium Difficile and Clostridium perfringens in healthy horses.
7th International Conference on the Molecular Biology and Pathogenesis of the Clostridia (ClosPath 2011). Ames, Iowa, October 25-30, 2011.

S. Kjelstrup and A. Løbner-Olesen
Synthetic peptide inhibitors of DNA replication in Staphylococcus aureus.
1st European Conference of Microbiology and Immunology, Budapest, Hungary, May 12-15, 2011

A. S. Andersen, L. Jakobsen, A. Friis-Møller, B. Jørgensen, N. Frimodt Møller & K. A. Krogfelt.
Susceptibility to Silver in Community and Hospital Acquired Bacterial Pathogens.
Nordic-NIAID Symposium on Antimicrobial Resistance, Copenhagen, Denmark. November 2010

P.R. Hansen and N. Frimodt-Møller
Antimicrobial activity of small 3-(2-naphthyl)-L-alanine containing peptides.
The 31st European Peptide Symposium, Copenhagen, Denmark. September 2010.

R. K. Bojsen, K. S. Jensen, N. Frimodt-Møller
PKPD in vitro and in vivo of Cefotaxime (CTX) and Cefuroxime (CFR) against E. coli
Poster A1-1373. 50th Interscience Conference on Antimicrobial Agents and Chemotherapy, Boston, USA. September 2010.

R. Jahnsen; K. Knapp; H. Franzyk
Comparative study of antibacterial alpha- and beta-peptoid/alpha-peptide chimeras
The 31st EPS (European Peptide Symposium), Bella Center, Copenhagen, Sep. 6-9, 2010.

Master Theses:

Paula Melo Paulon Hansen
Synthetic Cyclic Antimicrobial Peptides
The Danish Technical University (biotechnology and medical microbiology), March 2012

Anja Sloth Nielsen
Metabolic profiling of pathogenic bacteria
Aalborg University, June 2011

Mads Erlin Nygaard Kristensen
Structural Characterization of New Antibiotics from Maggots
Aalborg University, June 2011

Sofia Nälgård
Phage as a tool for control of skin infection caused by multidrug-resistant staphylococci in dogs
University of Copenhagen (LIFE), September 2011

Tanja Juul Poulsen
New Antibiotics Based on Anoplin from Wasps: Synthesis, Characterisation and Activity
Aalborg University, June 2011

Delima Sebamalairashan
Evaluation of gentamicin pharmacokinetics and pharmakodynamics in experimental urinary tract infections in mice
Roskilde University, March 2011

Jesper Søborg Bahnsen
Characterization and optimization of truncated and structurally modified penetratin analogs.
Faculty of Pharmaceutical Sciences, December 2010.

Rasmus Jahnsen
Influence of the backbone structure on the activity of antimicrobial peptidomimetics.
Faculty of Pharmaceutical Sciences, August 2010.

R. K. Bojsen.
Comparative investigations of cephalosporins. In vivo and in vitro study of cefuroxime and cefotaxime: bactericidal
activity, ESBL selection ability and frequency of resistance.
Technical University of Denmark. August 2010

Oral presentations:

L. Jakobsen, K. A. Krogfelt, N. Frimodt-Møller
Silver as a putative health concern
Conference on Nanosilver, Federal Institute for Risk Assessment, Berlin 8-9 February, 2012

A. Løbner-Olsen:
Development of synthetic circular peptides directed against DNA replication in. S. aureus
Invited speaker at the 1st Annual Symposium of Antimicrobial Research (SAR-2011), Beijing, China, December 1-3, 2011

Other communication:

DanCARD PhD-course:
Antimicrobial Resistance and Development
Aalborg University, November 28 to December 1, 2011

Organizer: Reinhard Wimmer