THE ARCTIC UNIVERSITY OF NORWAY • UIT •

CANS
Centre for New Antibacterial Strategies

2021 Annual Report

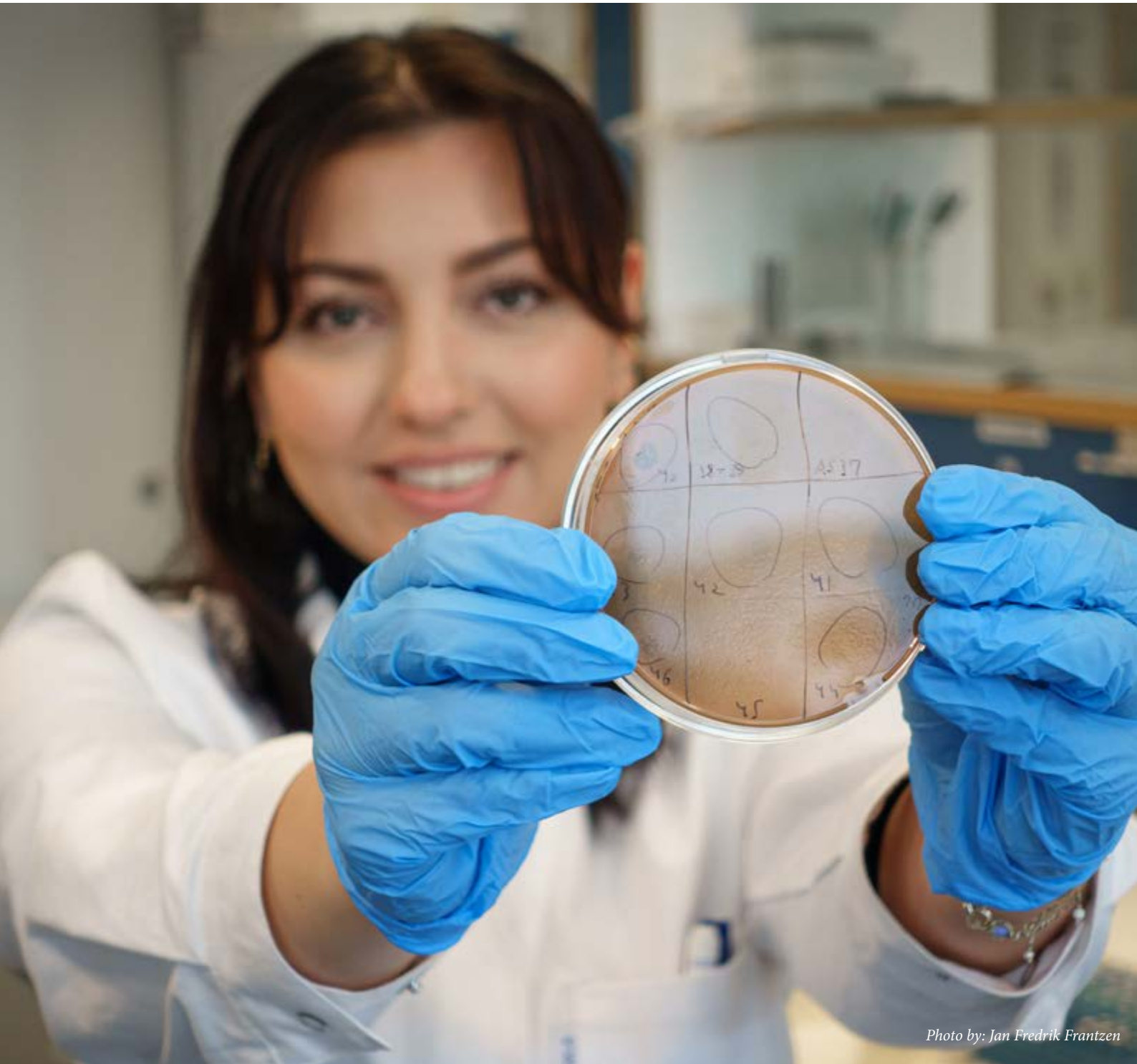

Photo by: Jan Fredrik Frantzen

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Contact information:

Centre Leader: arnfinn.sundsfjord@uit.no Coordinator: lise.nordgard@uit.no Communication advisor: jan.f.frantzen@uit.no

CANS is hosted by the Department of Medical Biology and the Faculty of Health Science at UiT the Arctic University of Norway

@cans_uit https://uit.no/research/cans

Annual activities 2021

The core centre annual activities have sustained although influenced by the pandemic. We would like to highlight the following activities:

1. The recruitment of six new associate professors funded by CANS is finalized and all PhD and PD to four of the associate professors are employed. The recruitment of the final two PhD and two postdoc positions is going on and will be finalized in 2022.

2. All five internal Ph.D.- and all three internal postdoc positions are hired.

3. In 2021 CANS research groups submitted 35 applications to internal (UiT), regional, national, and international arenas. Of these, 10 has been granted and five are still pending.

4. Within the Centre 15 Master thesis, and six PhD thesis has been completed.

5. Scientific publications in peer reviewed journals (n= 73). Se page 17 for details

6. The CANS monthly/bi-monthly digital research seminars (n= 14) continued in 2021 with internal and external presentations.

7. Other dissemination activities: Research groups in CANS has presented their research in Bioingeniøren, Farmatid and Dagens medisin.

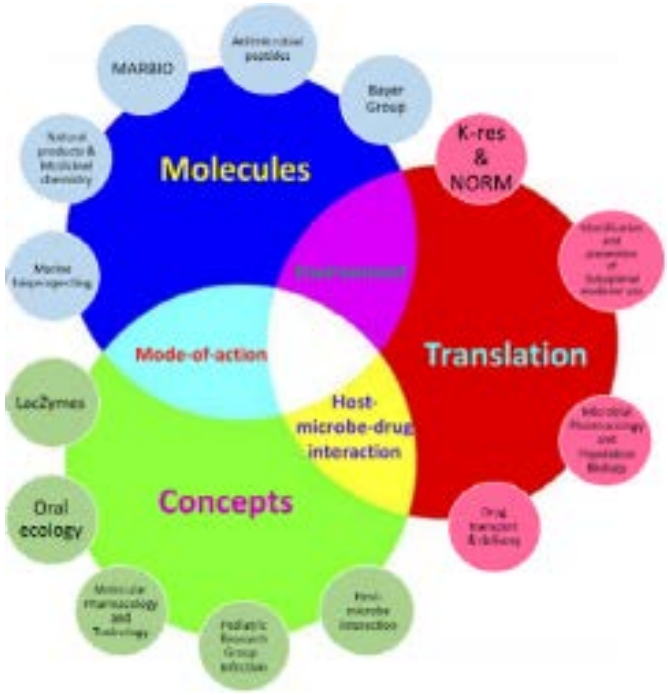
8. In 2021 The Host Microbe Interaction Group and the Health Data Lab guest researchers.

About CANS

The Centre for New Antibacterial Strategies (CANS) is an interdisciplinary centre at UiT-The Arctic University of Norway. CANS was established in 2019 and focus on antimicrobial resistance activities encompassing:

- Research
- Education
- Innovation
- Dissemination

CANS includes 15 research groups located at three different faculties at UiT, the Faculty of Health Sciences, Faculty of Science and Technology, and Faculty of Bioscience, Fisheries and Economics. Since start-up, the focus has been on recruiting new tenure-track-, associate professor-, PhD- and postdoc positions, establish arenas for interactions and communication, publications and external funding.



Research communities with expertise that form the basis for CANS

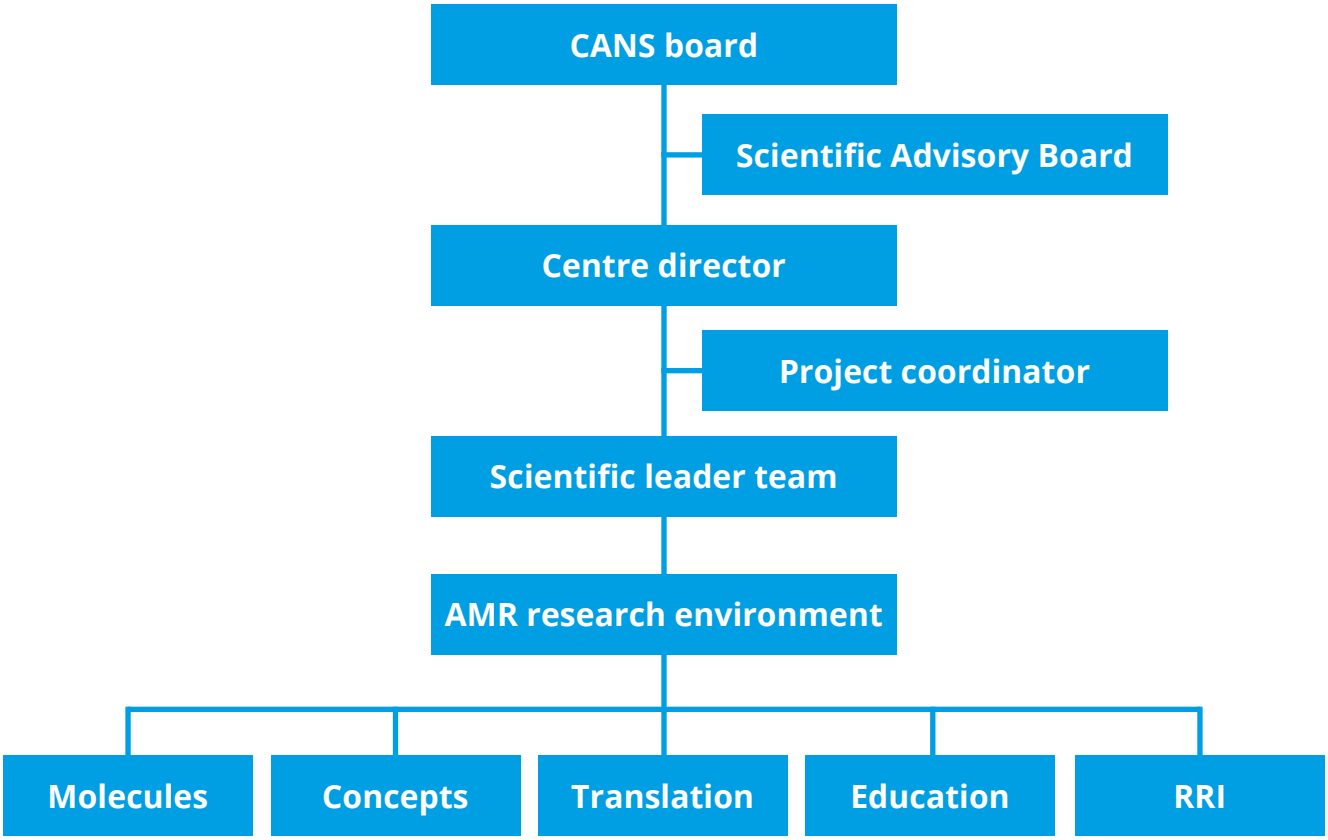
The development of CANS proceeds along three strategic axes - consolidation, fortification and direction.

Consolidation by creating and nurturing a framework for ambitious interdisciplinary collaboration generated by a centre-structure with management and overreaching strategy. Fortification by adding resources to underdeveloped important areas within the existing portfolio of activity. Finally, adding the **direction** to the AMR research by establishing new research initiatives filling the competence gaps that inhibit our ability to realize the strategy.

The centre aims to strengthen current activities, and this has been done by granting research groups at the different faculties internal PhD and postdoc positions. All together 3 PhD- and 5 postdoc positions has been granted.

The Centre also aims to support new basic research in novel concepts for sustainable activities in AMR-prevention and treatment strategies. The establishment of new research areas has been done through new permanent and temporary (tenure-track, postdoc and PhD) positions in three missing research area at UiT: human microbiota, viral bioprospection/phage therapy and bioinformatics/machine learning.

CANS organization



CANS Board

The CANS board are made up of representatives from the three faculties and the Rector. The Board is in charge of the overall direction of the Centre.

Name	Faculty
Camilla Brekke, chair	Prorector, UiT
Gunbjørg Svineng	Faculty of health sciences
Jørgen Berge	Faculty of biosciences, fisheries and economics
Arne Smalås	Faculty of Science and technology

Scientific leader team

The scientific leader team is formed of professors from the three faculties. The members hold a 10% operational role in CANS and provide academic support for the centre leader in a 50% position.

Name	Faculty
Arnfinn Sundsfjord, Centre Leader	Faculty of health sciences
Pål J. Johnsen	Faculty of health sciences
Hanna-Kirsti Schrøder Leiros	Faculty of Science and technology
Klara Stensvåg	Faculty of biosciences, fisheries and economics

Scientific Advisory Board

The scientific advisory board (SAB) consists of representatives from similar centres. The SAB will provide scientific input, evaluate CANS` activity and provide strategic advice for future activities.

Name	Affiliation
Denize Tasdemir	GEOMAR Helmholtz Centre for Ocean Research Kiel; Germany
Jörgen Johansson	Department of Molecular Biology, Umeå University, Sweden
Ursula Theuretzbacher	Center for Anti-Infective Agents, Vienna, Ausria
Ben Howden	Microbiological Diagnostic Unit (MDU) Public Health Laboratory, Melbourne, Australia

CANS research groups

CANS 16 research groups are located at three faculties and covers topics within marine bioprospecting – identification and characterization of new antibacterial activities, design and synthesis of new antibiotics and resistance inhibitors, the evolution and molecular epidemiology of AMR, host-microbe-drug interactions as well as antibiotic stewardship.

Research group	Group leader
Antibiotic resistance breakers	Anette Bayer, Chemistry (IK)
Digibiotics	John S. Mjøen Svendsen, Chemistry (IK)
Drug Transport and delivery research group	Natasa Skalko-Basnet, Pharmacy (IFA)
Health Data Lab	Lars Ailo Bongo, Informatics (IFI)
The Host-Microbe Interactions (HMI) group	Mona Johannessen, Medical Biology (IMB)
Identification and Prevention of Suboptimal medicine use	Lars Småbrekke, Pharmacy (IFA)
K-Res: Norwegain National Advisory Unit on Detection of Antimicrobial resistance	Kristin Hegstad and Ørjan Samuelsen, University Hospital (UNN)
The LacZymes group	Hanna-Kirsti S. Leiros, Chemistry (IK)
Marbio – an analytic platform for natural products	Jeanette Hammer Andersen, Fishery Science (NCFS)
Marine Bioprospecting	Klara Stensvåg, Fishery Science (NCFS)
Microbial Pharmacology and Population Biology	Pål J. Johansen, Pharmacy (IFA)
Molecular Pharmacology and Toxicology	Ingebrigt Sylte, Medical Biology (IMB)
Natural Products and Medicinal Chemistry	Terje Vasskog, Pharmacy (IFA)
NORM – Norwegian organization for surveillance of antimicrobial resistance	Gunnar Skov Simonsen, University Hospital (UNN)
Oral ecology	Mohammed Al-Haroni, Clinical Dentistry (IKO)
Pediatric research group – Infection	Trond Flægstad and Claus Klingenberg, Clinical Medicine (IKM)

Three selected Research Groups and their activities

Group leader
Associate Professor
Marius Myreng Haugland
marius.m.haugland@uit.no
Twitter: @mmhaugland

Team members
Dr Anna-Luisa Warnke
Postdoctoral fellow

Floriane Baussière,
PhD fellow

Mateusz Sowiński,
PhD fellow

Stian Rølvaag Martinsen,
Master's student

The Haugland Lab

Background

Marius holds a DPhil (PhD) in Organic Chemistry from the University of Oxford (2017), where, under the supervision of Prof. Edward Anderson, he developed a new method for the site-selective labelling of DNA with "spin labels", a technology that is orthogonal to more commonly used fluorescence-based approaches. Between 2017 and 2020, Marius held several postdoctoral fellowships at the Universities of Oxford and Edinburgh, in the groups of Prof. Edward Anderson, Prof. Scott Cockroft, and Prof. Alison Hulme. During these fellowships Marius worked on a broad range of research projects within organic chemistry and chemical biology, including synthesis of antiprotozoal natural products, bioconjugation of membrane-bound proteins, synthesis of PET radiotracers, and synthesis of small-ring molecular scaffolds for applications in pharmaceuticals.

In March 2020, Marius joined UiT The Arctic University of Norway and CANS as a tenure-track Associate Professor of Organic Chemistry.

Lab start-up at UiT

Since joining UiT, Marius has built up a fully equipped synthetic organic chemistry laboratory at the Department of Chemistry. In September 2020, Floriane Baussière became the first PhD fellow to join the group, followed by PhD fellow Mateusz Sowiński in January 2021. In the spring semester of 2021, we were pleased to host chemistry student Anne Sophie Gerhardt as she completed her Bachelor research project in our lab. Since August 2021, the group has grown to include postdoctoral fellow Dr Anna-Luisa Warnke. In March 2022 we welcomed our first chemistry Master's student, Stian Rølvaag Martinsen.

There is no question that the start-up of the lab has been impacted by the COVID-19 pandemic. While the lab has remained open except during the initial lockdown in the spring of 2020, the recruitment of PhD and postdoctoral fellows was delayed by travel restrictions. Moreover, the delivery of equipment and reagents has been affected by disruption to global supply chains. This issue still persists, at least in part, as a consequence of the international political situation. The group is, however, pleased to have filled all the positions, and remain hopeful that the supply situation will stabilize.

Research interests

Our group has a diverse range of research interest that span the wide field of organic chemistry, and with important applications across chemistry, chemical biology, biomedicine and materials science.

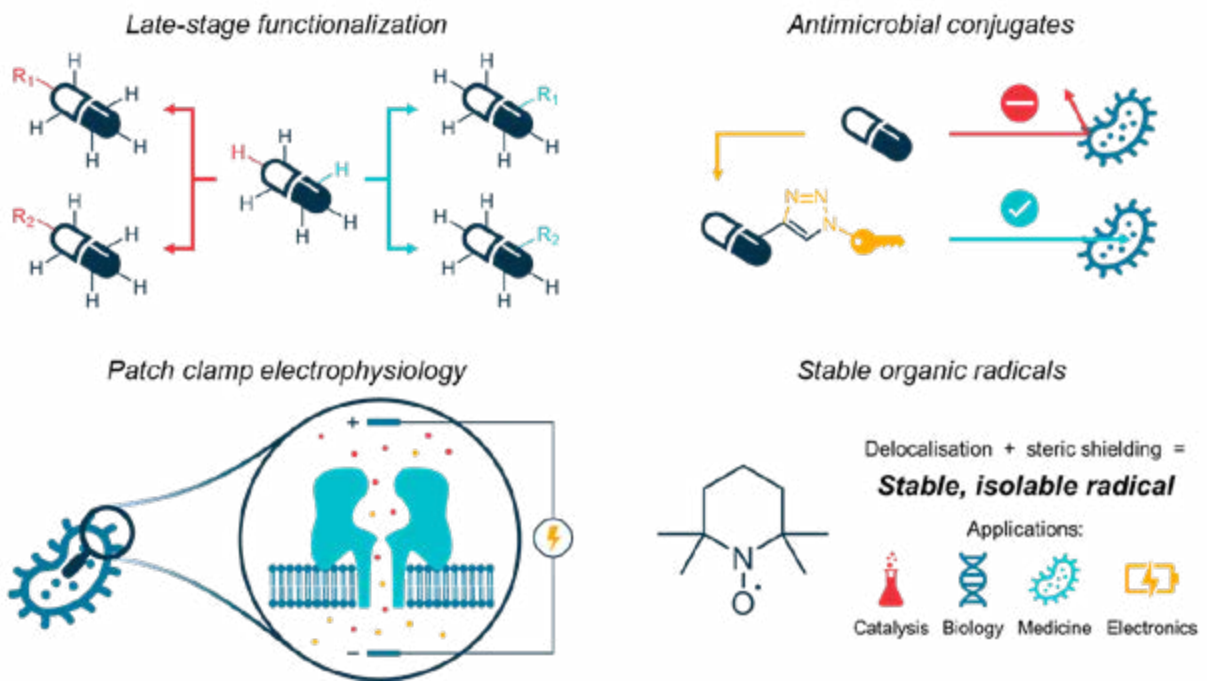
The development of new drugs usually requires the synthesis of a large number of molecular analogues, e.g. to explore the biological consequences of alterations in the chemical structure of a drug candidate. This is a laborious, slow and expensive process. Therefore, our group is interested in chemical methods that can directly diversify complex molecules to produce structurally distinct analogues, a strategy known as *late-stage functionalization*. In particular, we are aiming to modify existing antimicrobials by the introduction of chemical handles that can be used for conjugation. This will enable the formation of *antimicrobial conjugates*, where antimicrobials are covalently merged with other molecules.

Conjugation strategies can enhance bacterial uptake of antimicrobials, for example by increasing bacterial membrane penetration, or by hijacking active transport mechanisms such as iron uptake.[1] Through this approach we hope to find ways of restoring antimicrobial activity to therapeutics that have become ineffective due to antimicrobial resistance, or even to potentiate antimicrobials towards new types of pathogens.

Pore formation in bacterial membranes is important to many antimicrobials, either to facilitate bacterial uptake, or as part of the mechanism of action. To enable us to study pore-forming events in lipid bilayer membranes, our group is working to establish a *patch clamp electrophysiology* setup for use with synthetic lipid bilayers. Using this technique, we will measure tiny electrical currents to detect the formation and behaviour of membrane pores, including both porins of biological origin and transient pores formed by small, synthetic molecules.[2] Our investigations will begin using the well-established porin α-hemolysin from *Staphylococcus aureus*, but we are also interested in evaluating pore formation of other porins or small molecules. We will be pleased to hear from any CANS members that are interested in this technique.

A third focus area in our group is *stable organic radicals*, which are carbon-based molecules with an odd number of electrons. The unpaired electron imparts these radicals with unique properties, and they can therefore be used in a wide range of applications: catalysts for chemical processes, biological probes, imaging contrast agents, or even electronic conductors and energy storage materials.[3] Stable organic radicals have also been found to have anti-biofilm activity.[4] Our focus is to develop new stable organic radicals with improved properties and complementary applications, including radicals with higher stability in biological environments. We are currently preparing our first manuscript for publication in this area.

For more information about our group, please see our website: www.uit.no/project/hauglandlab



References

1. Klahn, P.; Brönstrup, M., *Nat. Prod. Rep.* **2017**, 34, 832-885.
2. Gamper, N., *Ion Channels: Methods and Protocols.* 2nd ed.; Humana Press: Totowa, NJ, 2013.
3. Chen, Z. X.; Li, Y.; Huang, F., *Chem* **2021**, 7, 288-332.
4. Verderosa, A. D.; Dhouib, R.; Fairfull-Smith, K. E.; Totsika, M., *Antimicrob. Agents Chemother.* **2019**, 64, e01685-19.

Group leader
Assoc. Prof. Christian S. Lentz,
HMI, IMB, UiT

Team members
Jonathan Hira,
Postdoc

Stephen Dela Ahator,
(Joint) Postdoc (with Mona Johannessen and Kristin Hegstad)

Roni Miah,
Postdoc (joining in 2022)

Md Jalal Uddin,
PhD fellow

Jeanette Grunnvåg,
PhD fellow

Bhupender Singh,
(Shared) HMI-technician

Kjersti Julin,
(Shared) HMI-technician

Nadia Aftab,
Master student (2021-2022)

The Chemical Biology of Bacterial Infections

Background

Our team at UiT started in 2020 and is a part of the Host-Microbe Interactions Research Group (HMI). Using a blend of chemical biology approaches, molecular biology/microbiology techniques and infection biology models, we aim to understand how bacterial pathogens adapt to survive in the course of infections. We work closely together with the other principal investigators at HMI and use our complementary expertise towards the long-term goal of developing new, innovative antimicrobial treatment and diagnostic strategies to treat and prevent bacterial infections.

Research interests

Single-cell microbial physiology and biomarker discovery. How bacteria colonize, infect and persist in a host is commonly studied using global read-outs (e.g. genomics, transcriptomics, proteomics) that are performed at the level of entire bacterial populations, providing a phenotypic snapshot of the 'averaged cell'. However, single cells or subpopulations can behave very differently. In fact, bacteria have a social life and use division-of-labor and other population-based strategies for improved survival and transmission. This phenotypic heterogeneity contributes to bacterial virulence and problems in clinical management. Two clinically relevant examples are e.g. differentiated surface-associated bacterial communities ('biofilms') that are difficult to eradicate or 'persister cell' subpopulations that are refractory to antibiotic treatment. The reason why we know so little about cellular individuality is quite simply because, for the most part, bacterial cells that are functionally different still look the same. To tell them apart, it is necessary to introduce certain labels such as fluorescent chemical probes that make hidden functional differences VISIBLE (Figure 1) (2, 3). It is the ambition of our research to establish a biomarker system that allows the detection and functional characterization of subpopulation phenotypes.

In 2021 we successfully established an experimental pipeline for fluorescence labeling, cell sorting and downstream functional analysis of single cells (Figure 2). This platform uses a combination of fluorescent reporter strains - that allow us to visualize expression of certain genes - and so-called next generation physiology probes that visualize diverse phenotypic traits such as specific enzymatic activities, general metabolism or uptake of antibiotics or nutrients in a non-destructive way. Currently, we are exploiting this platform to understand how functionally different individual cells within isogenic pathogen populations are and what relevance they have for in infection and antimicrobial resistance. By enabling the basic understanding of physiology of subpopulations and their roles for infection, we are setting the foundation to devise strategies to detect, target and manipulate clinically relevant bacterial subpopulations in the future.

Enzymes in bacterial virulence. Bacterial virulence is linked to the remarkable capability of pathogens to survive in different biological niches, such as different tissue sites, biotic and abiotic surfaces and in extracellular and intracellular states. These niches do not only present unique molecular surfaces and nutrient levels, but they are also characterized by different stress conditions posed e.g. by the host immune system, microbial competitors, antimicrobial agents and other environmental factors. The corresponding exposure to different molecular environments and the transitioning between niches will require cells to adapt their function. To identify enzymatic targets that are functionally relevant for bacterial survival and pathogenesis, we use a chemical proteomics technique termed activity-based protein profiling (ABPP). This technique makes use of so-called activity-based probes (ABPs), which are functionalized covalent enzyme inhibitors that can be used to detect, enrich and identify active target enzymes

(Figure 1a). Depending on the application, ABPs can be functionalized with fluorophores (for visualization of target enzyme detection) or enrichment tags such as biotin or so-called click-chemistry handles. We are using a combination of commercial and custom-synthesized ABPs provided by international collaborators from the field of chemical biology. With this toolset in hand, we are able to target a broad variety of enzyme classes including serine hydrolases (proteases, lipases, esterases, thioesterases), glycosidases or kinases and other ATP-binding enzymes.

With support of the experienced staff of the Proteomics and Metabolomics Core Facility (PRiME) at Uit, we have successfully established a chemo-proteomic pipeline for identification of probe-labelled and enriched enzymes from a variety of bacterial pathogens, including *Staphylococcus aureus, Enterococcus faecium* and *Klebsiella pneumoniae*. In the upcoming functional validation phase, we will use a combination of protein biochemistry for functional studies of the identified enzymes. We also utilize a combination of mutant and reporter strains as well as inhibitors and chemical probes for validation of the (patho)physiological roles of these enzymes *in vitro* and *in vivo*.

Selected accomplishments in 2021

- UiT Aurora Outstanding Fellow
- Start of HelseNord funded project: ´Activity-based proteomic mining of enzyme targets for clinical control of vancomycin-resistant *Enterococcus faecium*´. PhD fellow: Jeanette Grunnvåg
- Invited Topic Editor in MDPI-Journal 'Biosensors'

Publications

While the first research manuscripts of our team at UiT are still in preparation we are proud to have published our first review article:

(1) Hira, J, Uddin MJ, Haugland M, Lentz CS. From Differential Stains to Next Generation Physiology: Chemical Probes to Visualize Bacterial Cell Structure and Physiology. *Molecules*. 2020. 25(21):4949.

Further references

(2) Lentz CS, Sheldon JR, Crawford L, Cooper R, Garland M, Weerapana E, Amieva M, Skaar EP, Bogyo M. Identification of a *Staphylococcus aureus* virulence factor by activity-based protein profiling (ABPP). *Nature Chem. Biol.* (2018) 14, 609–617

(3) Lentz, CS. What you see is what you get: activity-based probes in single-cell analysis of enzymatic activities. Biol Chem. 2020;401(2): 233-248

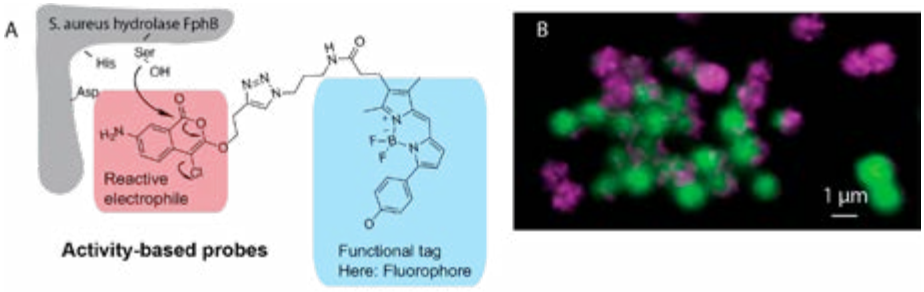


Figure 1. Chemical probes reveal cellular phenotypic heterogeneity. *A) Structure of the activity-based probe JCP251-bT. Covalent reaction with active site serine residue of the S. aureus hydrolase FphB leads to fluorescent labeling of active target protein. The image was adapted from (1). B) Confocal microscopy image revealing heterogeneity in FphB-labeling of GFP-expressing (green) S. aureus by JCP251 (magenta). The Image was reproduced from (2).*

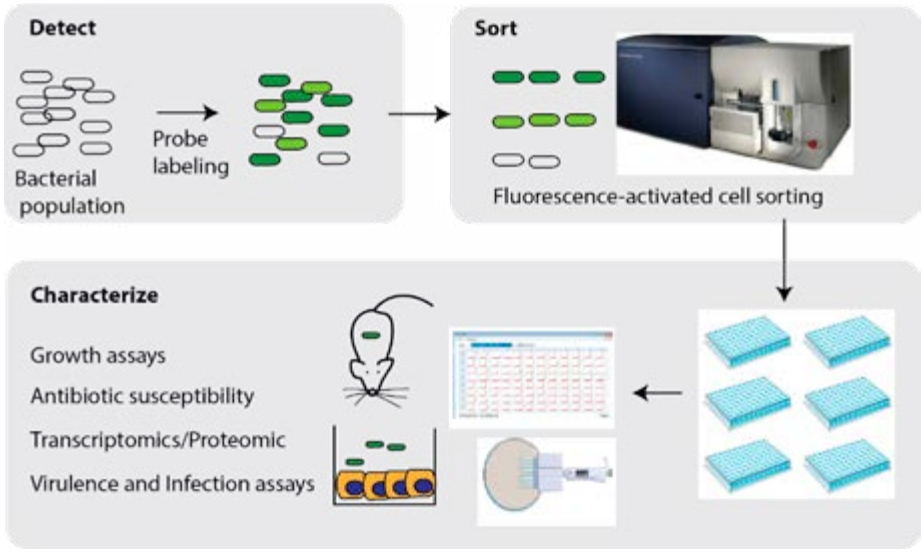


Figure 2. *An experimental pipeline to detect, sort and functionally characterize distinct subpopulations and single cells within isogenic bacterial pathogens populations.*

Group leader
Gabriel Magno de Freitas Almeida

Team members
Isabel Victoria Rey
Bachelor student

Arthur Kruse Sørensen
Bachelor student

To be hired in 2022:
One master student
One PhD
One PostDoc

Marine Bioprospecting – Bacteriophage group

Background

I joined the group as Associate Professor in October 2021 to focus on viral bioprospection. I am a virologist with experience with different host-pathogen systems, the most recent being interactions between mucosal associated bacteria and bacteriophages. My goal inside the CANS is to study the Arctic viral diversity and understand how to apply it for antibacterial measures. Starting with the isolation of viruses of microbes from the Arctic, the plan is to characterize them and then follow two main research lines. The first is focused directly on bacteriophages and how to apply them as agents of phage therapy. It will involve the build up of a CANS-UiT phage collection and exploring the prophylactic potential of phages. The second is focused on finding new giant viruses of protists and looking for viral-derived antibacterial strategies coded by their large and uncharacterized genomes. The long term goal is to build up expertise on Arctic environmental viruses and unveil their biotechnological potential.

Lab start-up at CANS-UiT

My first six months in Tromsø have been focused on establishing myself and setting up the lab space for viral work. Now we are able to work with phages in our own lab facilities and have a dedicated space in the BFE virus room for working with giant viruses. Collection of samples for viral isolation is underway.

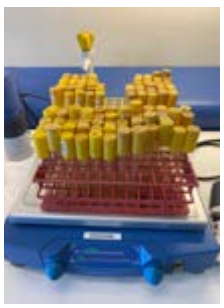
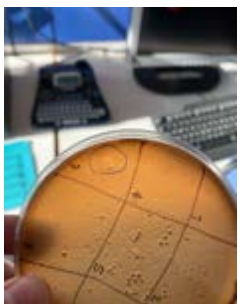
Transition: I am still finishing the last papers from my previous position (senior researcher of the University of Jyvaskyla), and they are expected to be published in 2022 with the UiT as my current address.

Grant applications: I have submited two grant applications so far, one to the Research Council of Norway and other to the FHF, tying my previous research to my future plans inside the CANS-UiT.

Recruiting: For 2022 we will have two bachelor students working with phages and one master student working with giant viruses. I will also be mentor of applicants interested in a Marie Curie Fellowship (Arctic-MSCA) and have one mobility student applying for a visit funded by the Brazilian government.

Conference participation: I have been invited as speaker to the Phage Oxford 2022 meeting and am planning to attend the Viruses of Microbes 2022 conference. Both are important conferences of the field.



Education and training

PhD thesis completed

Name	Research group	Title of PhD-thesis
Ole Christian Hagestad	Marbio	Bioprospecting of marine fungi from the High Arctic: A study of high latitude marine fungi from understudied taxa; bioactivity potential, taxonomy and genomics
Renate Døving Osvik	Marbio	Bioprospecting of marine phytoplankton from large scale cultivation - Effect of culture conditions on bioactivity and biochemistry of the diatom *Porosira glacialis*
Venke Kristoffersen	Marbio	Bioprospecting of Arctic marine microorganisms Exploring microbial secondary metabolite production using the one strain-many compounds approach: isolation and characterization of secondary metabolites
Bishnu Joshi	The Host-Microbe Interactions (HMI) group	Bacerial extracellular vesicles and their cargo. February 2021. Main supervisor: Mona Johannessen
Julia Maria Kloos	MicroPop	Horizontal transfer, selection and maintenance of antibiotic resistance determinants
Christopher Fröhlich	The LacZymes group	On the evolvability of OXA-48 - A comprehensive study of new functions withing the beta-lactamase OXA-48

Master's thesis completed

Name	Research group	Title of master thesis
Ella Trosten	Marbio	Identification of Bioactive Molecules from Arctic Marine Arthrobacter Isolates
Njål Rauø	Marbio	Bioactivity evaluation of underutilized marine raw materials for the management of metabolic syndrome
Heba Jawad	Marbio	Isolation, structure elucidation and bioactivity profiling of lyso-ornithine lipids from the marine bacterium Lacinutrix sp.
Daniel Salamonsen	Marbio	Securidine analogues from the marine bryozoan Securiflustra securifrons.
Mia Nilsen	MicroPop	Biofilm-related characteristics in clinical isolates of Extraintestinal Pathogenic E. coli
Marianne Svare	MicroPop	Biofilm formation in clinical isolates of Escherichia coli
Aya Ahmed Tawfeq	Drug Transport and Delivery Research Group	Localized therapy of vaginal infections: Liposomes-in-hydrogel delivery system containing curcumin.
Anna Ngoc Phung	Drug Transport and Delivery Research Group	Zwitterionic antimicrobial nanoparticles for biofilm therap
Anjanah Murugaiah	Drug Transport and Delivery Research Group	The development of electrospun chloramphenicol containing wound dressing
Daniel Engi	The Host-Microbe Interactions (HMI) group	Characterization of competition between commensal and clinical strains of *Enterococcus faecium* An *in vitro* and *in silico* study of bacteriocins
Mia Winkler	The Host-Microbe Interactions (HMI) group	Characterization of Klebsiella pneumoniae isolates by predicted serotype, CRISPR-Cas protospacer targets, and phage sensitivity.
Ira Spahiu	The Host-Microbe Interactions (HMI) group	Characterization of the interaction between Serine aspartate containing protein D and human Siglec11 and Siglec16

Name	Research group	Title of master thesis
Elin H. Sollid	The Host-Microbe Interactions (HMI) group	Bakteriofagterapi mot multiresistente Gram-negative bakterieinfeksjoner.
Bibek Chaulagain	Molecular Pharmacology and Toxicology	Inhibition of bacterial and human zinc-metalloproteases
Hanne Aanesen Holsbø	Molecular Pharmacology and Toxicology	Inhibition of zinc metalloproteases

New externally funded research projects

In 2021, CANS applied for funding from different external funds. The table shows the projects that were granted funding. Of 35 application initiatives, 14 was funded.

UiT funding

Research group	Funding source	Project title
Drug Transport and Delivery Research Group	MH2-midlene UiT	CALSCANNER equipment (state-of-the-art equipment to follow the biofilms and anti-biofilm treatment
The Host-Microbe Interaction group	Grant for establishment of collaborations with Singapore-UiT	Dissection of human-associated microbial populations using a High-Throughput Single-Cell phenotypic analysis and competition platform

*Two out of three initiatives funded

Regional funding

Research group	Funding source	Project title
MicroPop	Helse Nord	Can cancer Chemotherapy drive antibiotic resistance evolution
The Host-Microbe Interaction group	Helse Nord	Gule stafylokokker i hals: identifisering av bakterielle faktorer for infeksjonsforebygging
The Host-Microbe Interaction group	Helse Nord	Vitamin D supplement and S. aureus nasal carriage and the nasal microbiome
The Host-Microbe Interaction group	Helse Nord	Novel insights in gut microbiome-resistome composition and Klebsiella pneumoniae colonization patterns in mitigation of antimicrobial resistance: A population-based study among adults and elderly in Norway
The Host-Microbe Interaction group	Helse Nord	Activity-based proteomic mining of enzyme targets for clinical control of vancomycin-resistant Enterococcus faecium
The Host-Microbe Interaction group	Helse Nord	Gut microbiome-based biomarkers to prevent infections by antimicrobial resistant bacteria in infancy
The Host-Microbe Interaction group	Odd Berg Medisinske fond	Gule stafylokokker

*Seven out of 10 initiatives funded

National funding

Research group	Funding source	Project title
Marbio	RCN	MARINE FUNGI ON JAN MAYEN (MFJM) - TAXONOMIC DIVERSITY AND NEW ANTIBACTERIAL SECONDARY METABOLITES
Marin bioprospecting	RCN	DeepSeaQuence – Uncovering the metabolic repertoire and capacity of Arctic deep-sea hydrothermal vent microbiomes
The Host-Microbe Interaction group	NCMM	BacPac - Bacteria Capturing Programmable Artificial Cell System
The Host-Microbe Interaction group	Young "Centre for Advanced Study" fellowship	Infant Gut Microbiome Acquisition: Off to a Healthy Start
Marbio	Norwegian Biodiversity Information Centre (Artsdatabanken)	NORWEGIAN MARINE FUNGI - Distribution, diversity, taxonomy and DNA-barcoding.

*Five out of 18 initiatives funded

International funding

CANS has also showed initiatives for international funding (EU, JPIAMR-ACTION, Marie Skłodowska-Curie Actions). Of the four applications submitted, one was not funded and three are still pending.

Outreach activities

The research has been communicated in different ways. Outreach activities includes meet-ings, publications, regular scientific seminars with invited- or internal speakers. Due to Covid-19, the CANS annual conference has been postponed and there has been less outreach activities at the international level, such as conference/workshop activities, than expected.

CANS seminars

	Speaker	Title of presentation
1	Hanne Winther Larsen, Professor in Microbiology, Head of the research group MicroPath, UiO.	Bacterial extracellular vesicles in intercellular communication and vaccine development
2	Dan Andersson, Director Uppsala Antibiotic Center, Uppsala University	Unstable and transient antibiotic resistance
3	Tim Walsh, director of BARNARDS	Saving antibiotics: What we can and can't learn from COVID-19
4	Ruth Brenk, Professor, Department of biomedicine, Univeristy of Bergen	Structure-based ligand design for protein and RNA targets for new antibiotics
5	Claus Klingenberg, Professor, Pediatric Research Group UiT-The Arctic University of Norway and Pediatric Department, University Hospital of North Norway	Sepsis and antibiotic use in neonates – and research from Tromsø
6	Oskar Ljungquist, senior consultant working at the department of infectious diseases at Helsingborg hospital, south Sweden.	ESBL-producing Enterobact
7	Erik Solligård, professor, Academic Head, Anesthesia and Int. Care, St Olavs hospital/NTNU. Director Gemini-center sepsis research, NTNU	Ongoing and planned projects in sepsis research
8	Rafi Ahmad, Associate Professor in Bioinformatics / Drug Discovery at Inland Norway University of Applied Sciences, University of Tromsø, and Oslo University Hospital Norway	AMR-Diag: Rapid Diagnostics of Infection and Antimicrobial Resistance
9	Gunnveig Grødeland (UiO og OUS) og Ingvild Hausberg Sørvoll (UNN)	Vaksiner på godt og vondt
10	Lars Småbrekke, Førsteamanuensis. Samfunnsfarmasi	Antibacterial use by birth year and birth season in children 0-2 years in Norway
11	Fabrizio Clarelli, researcher at the Department of Pharmacy at UiT.	Multiple drug Model: A step towards a mechanistic approach
12	Maxim Bril'kov, PostDoc, Department of Pharmacy, UiT	Multiple drug Model: A step towards a mechanistic approach
13	Marte Jenssen, Ph.d. fellow in the Marbio research group at the Norwegian College of Fishery Science, UiT	Bioprospecting of marine fungi – the discovery of lulworthinone
14	Pål Rongved, School of Pharmacy, Dep. of Pharm. Chemistry, UiO	New AMR therapy in the 21st century. Resistance breakers and combinations

Conferences/Workshops/Meetings

Research group	Conferences/Workshops/Meetings
Health Data Lab	Sepsis seminar. Hovde Gård, 11.11.2021.
K-res	ECCMID Postgraduate Education Course – Next-generation sequencing in routine clinical microbiology and infectious diseases, Online.
	National Consortium for Microbial Genomics Meeting. Digital
	Online course «Den stille pandemien – antibiotikaresistens», NITO Bioingeniørfaglig institutt.
	IBA Annual conference
Marbio	International Seminar for World Fungi Day; 2021-10-02 - 2021-10-02
	MarFunBioDisco project
Microbial Pharmacology and Population Biology	EMBL Conference for young Scientists
Natural Products and Medicinal Chemistry	NFIF annual conference Svalbard 2021 E132
The Host-Microbe Interactions (HMI) group	IBA annual meeting November 1st Oslo
	IBA course- Trondheim November 17th
	IMB conference 2021
	Latin American Congress of Microbiology – invited talk
	MB conference 2021, June 21st, Tromsø
	Nasjonalt Strategimøte I Bakteriologi, Folkehelseinstituttet, 27 October 2021
	Nordic Society for Clinical Microbiology and Infectious Diseases (NSCMID), Turku, Sept 3-6, 2021
The LacZymes group	Norwegian Chemical Society (NKS), avd. Nord-Norge, 28.01.2021
	German Pharmaceutical Society (DPhG) annual meeting

Visiting researchers in 2021

Name	From	Visiting
Hanne Winther Larsen	University of Oslo	The Host Microbe Interaction Group
Etienne Birmele	University of Strasbourg	Health Data Lab
Vittorio Perduca	Université de Paris	Health Data Lab

Publications

1. Achten NB, Plötz FB, Klingenberg C, Stocker M, Bokelaar R, Bijlsma M, Giannoni E, van Rossum AMC, Benitz WE. (2021) *Stratification of Culture-Proven Early-Onset Sepsis Cases by the Neonatal Early-Onset Sepsis Calculator: An Individual Patient Data Meta-Analysis.* J Pediatr. https://doi.org/10.1016/j.jpeds.2021.01.065

2. Ali Mohammed MM, Pettersen VK, Nerland AH, Wiker HG, Bakken V. (2021) *Label-free quantitative proteomic analysis of the oral bacteria Fusobacterium nucleatum and Porphyromonas gingivalis to identify protein features relevant in biofilm formation.* Anaerobe. https://doi.org/10.1016/j.anaerobe.2021.102449

3. Almeida GMDF and Sundberg LR. (2021) *The forgotten tale of Brazilian phage therapy. The Lancet Infectious Diseases.* https://doi.org/10.1016/S1473-3099(20)30060-8

4. Arredondo-Alonso S, Pöntinen AK, Cléon F, Gladstone RA, Schürch AC, Johnsen PJ, Samuelsen Ø, Corander J. (2021) *A high-throughput multiplexing and selection strategy to complete bacterial genomes.* Gigascience. https://doi.org/10.1093/gigascience/giab079

5. Beckstrøm S, Svendsen K, Småbrekke L. (2021) *Antibacterial use by birth year and birth season in children 0-2 years in Norway.* Norsk Epidemiologi. https://doi.org/10.5324/nje.v29i1-2.4044

6. Bjerkhaug AU, Granslo HN, Klingenberg C. (2021) *Metabolic responses in neonatal sepsis-A systematic review of human metabolomic studies.* Acta Paediatr. https://doi.org/10.1111/apa.15874

7. Estaleva CEL, Zimba TF, Sekyere JO, Govinden U, Chenia HY, Simonsen GS, Haldorsen B, Essack SY, Sundsfjord A. (2021) *High prevalence of multidrug resistant ESBL- and plasmid mediated AmpC-producing clinical isolates of Escherichia coli at Maputo Central Hospital, Mozambique.* BMC Infect Dis. https://doi.org/10.1186/s12879-020-05696-y

8. Fostervold A, Hetland MAK, Bakksjø R, Bernhoff E, Holt KE, Samuelsen Ø, Simonsen GS, Sundsfjord A, Wyres KL, Löhr IH (2021) *A nationwide genomic study of clinical Klebsiella pneumoniae in Norway 2001-15: introduction and spread of ESBLs facilitated by clonal groups CG15 and CG307.* J Antimicrob Chemother. https://doi.org/10.1093/jac/dkab463

9. Fostervold A, Hetland MAK, Bakksjø R, Bernhoff E, Holt KE, Samuelsen Ø, Simonsen GS, Sundsfjord A, Wyres KL, Löhr IH, Norwegian Study Group on Klebsiella pneumoniae (2021) *A nationwide genomic study of clinical Klebsiella pneumoniae in Norway 2001-15: introduction and spread of ESBLs facilitated by clonal groups CG15 and CG307.* J Antimicrob Chemother. https://doi.org/10.1093/jac/dkab463

10. Fröhlich C, Gama JA, Harms K, Hirvonen VHA, Lund BA, van der Kamp MW, Johnsen PJ, Samuelsen Ø and Leiros, H-KS. (2021) *Evolution of β-lactamase mediated efiderocol resistance*. mSphere.

11. Fröhlich C, Chen JZ, Gholipour S, Erdogan AN, & Tokuriki N. (2021) *Evolution of β-lactamase mediated efiderocol resistance.* bioRxiv. https://doi.org/10.1101/2022.01.29.478156

12. Fröhlich C, Chen JZ, Gholipour S, Erdogan AN, & Tokuriki N (2021) *Evolution of β-lactamases and enzyme promiscuity.* Protein Eng Des Sel. https://doi.org/10.1093/protein/gzab013

13. Gagliotti C, Högberg LD, Billström H, Eckmanns T, Giske CG, Heuer OE, Jarlier V, Kahlmeter G, Lo Fo Wong D, Monen J, Murchan S, Simonsen GS, Šubelj M, Andrašević AT, Žabicka D, Žemličková H, Monnet DL (2021) *EARS-Net study group participants. Staphylococcus aureus bloodstream infections: diverging trends of meticillin-resistant and meticillin-susceptible isolates, EU/EEA, 2005 to 2018.* Euro Surveill. https://doi.org/10.2807/1560-7917.ES.2021.26.46.2002094

14. Gladstone R, McNally A, Pöntinen AK, Tonkin-Hill G, Lees JA, Skytén KO, Cléon F, Christensen MOK, Haldorsen BC, Bye KK, Gammelsrud KW, Hjetland R, Kümmel A, Larsen HE, Lindemann PC, Löhr IH, Marvik Å, Nilsen E, Noer MT, Simonsen GS, Steinbakk M, Tofteland S, Vattøy M, Bentley SD, Croucher NJ, Parkhill J, Johnsen PJ, Samuelsen Ø, Corander J. (2021) *Emergence and dissemination of antimicrobial resistance in Escherichia coli bloodstream infections: a nationwide longitudinal microbial population study in Norway between 2002-2017.* Lancet Microbe. https://doi.org/10.1016/S2666-5247(21)00031-8

15. Guðmundsdóttir JS, Fredheim EGA, Koumans CIM, Hegstad J, Tang PC, Andersson DI, Samuelsen Ø, Johnsen PJ (2021) *The chemotherapeutic drug methotrexate selects for antibiotic resistance.* EBioMedicine. https://doi.org/10.1016/j.ebiom.2021.103742

16. Hagestad OC, Hou L, Andersen JH, Hansen E, Altermark B, Li C, Kuhnert E, Cox RJ, Crous PW, Spatafora JW, Lail K, Amirebrahimi M, Lipzen A, Pangilinan J, Andreopoulos W, Hayes RH, Ng V, Grigoriev IV, Jackson SA, Sutton TDS, Dobson ADW, Rämä T. (2021) *Genomic characterization of three marine fungi, including Emericellopsis atlantica sp. nov. with signatures of a generalist lifestyle and marine biomass degradation.* IMA Fungus https://doi.org/10.1186/s43008-021-00072-0

17. Haldorsen BC, Janice J, Samuelsen Ø. (2021) *Evaluation of the Amplex eazyplex® SuperBug Acineto test for detection of acquired OXA and NDM carbapenemases in Acinetobacter spp.* J Glob Antimicrob Resist. https://doi.org/10.1016/j.jgar.2021.01.019

18. Hameiri-Bowen D, Sovershaeva E, Flaegstad T, Gutteberg TJ, Ngwira LG, Simms V, Rehman AM, Mchugh G, Bandason T, Ferrand RA, Rowland-Jones S, Yindom LM. (2021) *Soluble biomarkers associated with chronic lung disease in older children and adolescents with perinatal HIV infection.* AIDS. https://doi.org/10.1097/qad.0000000000002964

19. Hemmingsen LM, Julin K, Ashan L, Basnet P, Johannessen M, Skalko-Basnet N. (2021) *Chitosomes-in-chitosan hydrogel for acute skin injuries: Prevention and infection control.* Marine Drugs. https://doi.org/10.3390/md19050269

20. Hemmingsen LM, Škalko-Basnet N, Jøraholmen MW. (2021) *The expanded role of chitosan in localized antimicrobial therapy.* Marine Drugs. https://doi.org/10.3390/md19120697

21. Hemmingsen LM, Giordani B, Pettersen AK, Vitali B, Basnet P and N. Škalko-Basne.t (2021) *Liposomes-in-chitosan hydrogel boosts potential of chlorhexidine in biofilm eradication in vitro.* Carbohydrate Polymers. https://doi.org/10.1016/j.carbpol.2021.117939

22. Hemmingsen LM, Julin K, Ahsan L, Basnet P, Johannessen M, and Škalko-Basnet N. (2021) *Chitosomes-in-chitosan hydrogel for acute skin injuries: prevention and infection control.* Wound Healing Potential of Marine Natural Products. https://doi.org/10.3390/md19050269

23. Hermansen JU, Wojcik DM, Robinson N, Pahnke J, Haugland HK, Jamtøy AH, Flaegstad T, Halvorsen H, Lund B, Baumbusch LO, Munthe-Kaas MC. (2021) *The Norwegian childhood cancer biobank.* Cancer Rep (Hoboken) https://doi.org/10.1002/cnr2.1555

24. Håkansson J, Cavanagh JP, Stensen W, Mortensen B, Svendsen JS, Svenson J. (2021) *In vitro and in vivo antibacterial properties of peptide AMC-109 impregnated wound dressings and gels.* J Antibiot (Tokyo) https://doi.org/10.1038/s41429-021-00406-5

25. Imai K, Saito R, Ezawa T, Sugiyama S, Sylte I, Kurita N. (2021) *Proposal of selective inhibitor for bacterial zinc metalloprotease: Molecular mechanics and ab initio molecular orbital calculations.* J. Mol. Graphics and Modeling. https://doi.org/10.1016/j.jmgm.2021.108047

26. Janice J, Agyepong N, Owusu-Ofori A, Govinden U, Essack SY, Samuelsen Ø, Sundsfjord A, Pedersen T. (2021) *Carbapenem Resistance Determinants Acquired through Novel Chromosomal Integrations in Extensively Drug-Resistant Pseudomonas aeruginosa.* Antimicrobial Agents Chemother. https://doi.org/10.1128/AAC.00289-21

27. Jenssen M, Rainsford P, Juskewitz E, Andersen JH, Hansen EH, Isaksson J, Rämä T, Hansen KØ (2021) *Lulworthinone, a New Dimeric Naphthopyrone from a Marine Fungus in the Family Lulworthiaceae with Antibacterial Activity Against Clinical Methicillin-Resistant Staphylococcus aureus Isolates.* Front Microbiol. https://doi.org/10.3389/fmicb.2021.730740

28. Jenssen M, Kristoffersen V, Motiram-Corral K, Isaksson J, Rämä T, Andersen JH, Hansen E, Hansen KØ. (2021) *Chlovalicin B, a Chlorinated Sesquiterpene Isolated from the Marine Mushroom Digitatispora marina.* Molecules. https://doi.org/10.3390/molecules26247560

29. Johnsen PJ, Gama JA, Harms K. (2021) *Antibiotic Resistance: Bacterial evolution on demand.* Elife. https://doi.org/10.7554/eLife.68070

30. Joshi B, Singh B, Nadeem A, Askarian F, Wai SN, Johannessen M *, K Hegstad* (2021) *Transcriptome Profiling of Staphylococcus aureus Associated Extracellular Vesicles Reveals Presence of Small RNA-Cargo.* Front Mol Biosci. https://doi.org/10.3389/fmolb.2020.566207

31. Karlsen EA, Stensen W, Juskewitz E, Svenson J, Berglin M, Svendsen JSM. (2021) *Anti-colonization effect of Au surfaces with self-assembled molecular monolayers functionalized with antimicrobial peptides on S. epidermidis.* Antibiotics. https://doi.org/10.3390/antibiotics10121516

32. Klingenberg C, Tembulkar SK, Lavizzari A, Roehr CC, Ehret DEY, Vain NE, Mariani GL, Erdeve O, Lara-Diaz VJ, Velaphi S, Cheong HK, Bisht SS, Waheed KAI, Stevenson AG, Al-Kafi N, Roue JM, Barrero-Castillero A, Molloy EJ, Zupancic JAF, Profit J. (2021) *COVID-19 preparedness-a survey among neonatal care providers in low- and middle-income countries.* J Perinatol. https://doi.org/10.1038/s41372-021-01019-4

33. Kloos J, Gama JA, Hegstad J, Samuelsen Ø, Johnsen PJ. (2021) *Piggybacking on Niche Adaptation Improves the Maintenance of Multidrug-Resistance Plasmids.* Mol Biol Evol. https://doi.org/10.1093/molbev/msab091

34. Kloos J, Johnsen PJ, Harms K. (2021) *Tn1 transposition in the course of natural transformation enables horizontal antibiotic resistance spread in Acinetobacter baylyi.* Microbiology. https://doi.org/10.1099/mic.0.001003.

35. Kranjec C, Kristensen SS, Bartkiewicz KT, Brønner M, Cavanagh JP, Srikantam A, Mathiesen G, Diep DB. (2021) *A bacteriocin-based treatment option for Staphylococcus haemolyticus biofilms.* Sci Rep. https://doi.org/10.1038/s41598-021-93158-z

36. Kristoffersen V, Jenssen M, Jawad HR, Isaksso J, Hansen E, Rämä T, Hansen KØ, Andersen JH. (2021) *Two Novel Lyso-Ornithine Lipids Isolated from an Arctic Marine Lacinutrix sp. Bacterium.* Molecules. https://doi.org/10.3390/molecules26175295

37. Kuwelker K, Langeland N, Löhr IH, Gidion J, Manyahi J, Moyo SJ, Blomberg B, Klingenberg C. (2021) *Use of probiotics to reduce infections and death and prevent colonization with extended-spectrum beta-lactamase (ESBL)-producing bacteria among newborn infants in Tanzania (ProRIDE Trial): study protocol for a randomized controlled clinical trial.* Trials. https://doi.org/10.1186/s13063-021-05251-3

38. Kumaraswamy M, Wiull K, Joshi B, Sakoulas G, Kousha A, Vaaje-Kolstad G, Johannessen M, Hegstad K, Nizet V, Askarian F. (2021) *Bacterial Membrane-Derived Vesicles Attenuate Vancomycin Activity against Methicillin-Resistant.* Microorganisms. https://doi.org/10.3390/microorganisms9102055

39. Laulund AS, Schwartz FA, Christophersen L, Høiby N, Svendsen JSM, Stensen W, Thomsen K, Cavanagh JP, Moser CJ. (2021) *Lactoferricin inspired peptide AMC-109 augments the effect of ciprofloxacin against Pseudomonas aeruginosa biofilm in chronic murine wounds.* Glob Antimicrob Resist. https://doi.org/10.1016/j.jgar.2021.12.015

40. Lund BA, Thomassen AM, Carlsen TJW & Leiros H-KS. (2021) *Biochemical and biophysical characterization of the OXA-48-like carbapenemase OXA-436.* Acta Crystallogr F Struct Biol Commun. https://doi.org/10.1107/S2053230X21008645

41. Lupattelli A, Karlstad Ø, Egeland A, Småbrekke L et al. (2021) *The Norwegian Society for Pharmacoepisemiology.* Norsk Epidemiologi. https://doi.org/10.5324/nje.v29i1-2.4039

42. Mohammed MMA, Pettersen VK, Nerland AH, Wiker HG, Bakken V. (2021) *Label-free quantitative proteomic analysis of the oral bacteria Fusobacterium nucleatum and Porphyromonas gingivalis to identify protein features relevant in biofilm formation.* Anaerobe. https://doi.org/10.1016/j.anaerobe.2021.102449

43. Mäklin T, Kallonen T, Alanko J, Samuelsen Ø, Hegstad K, Mäkinen V, Corander J, Heinz E, Honkela A. (2021) *Bacterial Genomic Epidemiology with Mixed Samples.* Microbial Genomics. https://dx.doi.org/10.1099%2Fmgen.0.000691

44. Mundal HS, Rønnestad A, Klingenberg C, Stensvold HJ, Størdal K. (2021) *Antibiotic Use in Term and Near-Term Newborns.* Pediatrics. https://doi.org/10.1542/peds.2021-051339

45. Nordal EB, Granslo HN, Esaiassen E, Leknessund CBB, Forsdahl BA. (2021) *Bronchiolitis should not be treated with glucocorticoids or antibiotics.* Tidsskr Nor Laegeforen. https://doi.org/10.4045/tidsskr.21.0862

46. Palica K, Vorácová M, Skagseth S, Rasmussen AA, Allander L, Hubert M, Sandegren L, Leiros, H-KS, Andersson H & Erdélyi M. (2021) *Metallo-β-lactamase inhibitor phosphonamidate monoesters.* ACS Omega. https://dx.doi.org/10.1021%2Facsomega.1c06527

47. Paulsen MH, Engqvist M, Ausbacher D, Anderssen T, Langer MK, Haug T, Morello GR, Liikanen L, Blencke HM, Isaksson J, Juskewitz E, Bayer A, Strøm MB. (2021) *Amphipathic Barbiturates as Mimics of Antimicrobial Peptides and the Marine Natural Products Eusynstyelamides with Activity against Multi-resistant Clinical Isolates.* J Med Chem. https://doi.org/10.1021/acs.jmedchem.1c00734

48. Pettersen VK, Antunes LCM, Dufour A, Arrieta MC. (2021) *Inferring early-life host and microbiome functions by mass spectrometry-based metaproteomics and metabolomics.* Comput Struct Biotechnol J. https://doi.org/10.1016/j.csbj.2021.12.012

49. Pettersen VK, Steinsland H, Wiker HG. (2021) *Front Cover: Distinct Metabolic Features of Pathogenic Escherichia coli and Shigella spp. Determined by Label-Free Quantitative Proteomics.* PROTEOMICS. https://doi.org/10.1002/pmic.202000072

50. Phiri AFND, Abia ALK, Amoako DG, Mkakosya R, Sundsfjord A, Essack SY, Simonsen GS. (2021) *Burden, Antibiotic Resistance, and Clonality of Shigella spp. Implicated in Community-Acquired Acute Diarrhoea in Lilongwe, Malawi.* Trop Med Infect Dis. https://doi.org/10.3390/tropicalmed6020063

51. Raffelsberger N, Hetland MAK, Svendsen K, Småbrekke L, Löhr IH, Andreassen LLE, Brisse S, Holt KE, Sundsfjord A, Samuelsen Ø, Gravningen K. (2021) *Gastrointestinal carriage of Klebsiella pneumoniae in a general adult population: a cross-sectional study of risk factors and bacterial genomic diversity.* Gut Microbes. https://doi.org/10.1080/19490976.2021.1939599

52. Rahman F, Nguyen T, Adekoya OA, Campestre C, Tortorella P, Sylte I and Winberg JO. (2021) *Inhibition of bacterial and human zinc-metalloproteases by bisphosphonate- and catechol-containing compound.* Journal of Enzyme Inhibition & Medicinal Chemistry. https://doi.org/10.1080/14756366.2021.1901088

53. Rahman F, Wushur, I, Malla, N, Åstran, OAH, Rongved P, Winberg, JO, Sylte I. (2021) *Zinc-Chelating Compounds as Inhibitors of Human and Bacterial Zinc Metalloproteases.* Molecules. https://doi.org/10.3390/molecules27010056

54. Riibe MØ, Sørbye SW, Simonsen GS, Sundsfjord A, Ekgren J, Maltau JM. (2021) *Risk of cervical intraepithelial neoplasia grade 3 or higher (CIN3+) among women with HPV-test in 1990-1992, a 30-year follow-up study.* Infect Agent Cancer. https://doi.org/10.1186/s13027-021-00386-z

55. Rubaye MTSAL, Janice J, Bjørnholt JV, Jakovljev A, Hultström ME, Sundsfjord A, Hegstad K. (2021) *Novel genomic islands and a new vanD-subtype in the first sporadic VanD-type vancomycin resistant enterococci in Norway.* PLoS ONE. https://doi.org/10.1371/journal.pone.0255187

56. Rämä T, Quandt CA. (2021) *Improving Fungal Cultivability for Natural Products Discovery.* Frontiers in Microbiology. https://doi.org/10.3389/fmicb.2021.706044

57. Rypdal V, Jørandli S, Hemmingsen D, Solbu MD, Klingenberg C. (2021) *Exposure to an Extended-Interval, High-Dose Gentamicin Regimen in the Neonatal Period Is Not Associated With Long-Term Nephrotoxicity.* Front Pediatr. https://doi.org/10.3389/fped.2021.779827

58. Rypdal M, Rypdal V, Jakobsen PK, Ytterstad E, Løvsletten O, Klingenberg C, Rypdal K. (2021) *Modelling suggests limited change in the reproduction number from reopening Norwegian kindergartens and schools during the COVID-19 pandemic.* PLoS One. https://doi.org/10.1371/journal.pone.0238268

59. Saito R, Imai K, Yamamoto S, Ezawa T, Sugiyama S, Evenseth LSM, Sylte I, Kurita N. (2021) *Specific interactions between the alkaline protease of P. aeruginosa and its natural peptide inhibitor: ab initio molecular simulations.* J. Mol. Modeling. https://doi.org/10.1007/s00894-021-04991-y

60. Sanabria AM, James J, Hjerde E, Simonsen GS and Hanssen AM. (2021) *Shotgun-metagenomics based prediction of antibiotic resistance and virulence determinants in Staphylococcus aureus from periprosthetic tissue on blood culture bottles.* Scientific Reports. https://doi.org/10.1038/s41598-021-00383-7

61. Schulte-Werning MA, Singh B, Johannessen M, Engstad RE, Skasko-Basnet N, Holsæter AM. (2021) *Multifunctional Nanofibrous Dressing with Antimicrobial and Anti-Inflammatory Properties Prepared by Needle-Free Electrospinning.* Pharmaceutics. https://doi.org/10.3390/pharmaceutics13091527

62. Stensen DB, Småbrekke L, Olsen K et al. (2021) *Circulating sex-steroids and Staphylococcus aureus nasal carriage in a general female population.* Eur J Endocrinol. https://dx.doi.org/10.1530%2FEJE-20-0877

63. Stensen DB, Småbrekke L, Olsen K, Grimnes G, Nielsen CS, Sollid JUE, Simonsen GS, Almås B, Furberg AS (2021) *Circulating sex-steroids and Staphylococcus aureus nasal carriage in a general female population.* Eur J Endocrinol. https://dx.doi.org/10.1530%2FEJE-20-0877

64. Tansirichaiya S, Moyo SJ, Al-Haroni M, Roberts AP. (2021) *Capture of a novel, antibiotic resistance encoding, mobile genetic element from Escherichia coli using a new entrapment vector.* J Appl Microbiol. https://doi.org/10.1111/jam.14837

65. Thaulow CM, Lindemann PC, Klingenberg C. (2021) *Antibiotic resistance in paediatric UTIs in Norway.* Tidsskr Nor Laegeforen. https://doi.org/10.4045/tidsskr.20.0889

66. Thaulow CM, Lindemann PC, Klingenberg C, Berild D, Salvesen Blix H, Myklebust TÅ, Harthug S. (2021) *Epidemiology and Antimicrobial Susceptibility of Invasive Bacterial Infections in Children-A Population-Based Study From Norway.* Pediatr Infect Dis J. https://doi.org/10.1097/inf.0000000000003013

67. Van Hal SJ, Willems RJL, Gouliouris T, Ballard SA, Coque TM, Hammerum AM, Hegstad K, Westh HT, Howden BP, Malhotra-Kumar S, Werner G, Yanagihara K, Earl AM, Raven KE, Corander J, Bowden R and Enterococcal Group (2021) *The global dissemination of hospital clones of Enterococcus faecium.* BMC Genome Med. https://doi.org/10.1186/s13073-021-00868-0

68. Vanić Ž, Jøraholmen MW and Škalko-Basnet N. (2021) *Nanomedicines for the topical treatment of vulvovaginal infections: addressing the challenges of antimicrobial resistance.* Advances in Drug Delivery for Women's Health. https://doi.org/10.1016/j.addr.2021.113855

69. Vatne A, Klingenberg C, Rettedal S, Øymar K. (2021) *Early-Onset Sepsis in Neonates - A Population-Based Study in South-West Norway From 1996 to 2018.* Front Pediatr. https://doi.org/10.3389/fped.2021.634798

70. Wagner TM, Janice J, Sivertsen A, Sjögren I, Sundsfjord A, Hegstad K. (2021) *Alternative vanHAX promoters and increased vanA-plasmid copy number resurrect silenced glycopeptide resistance in Enterococcus faecium.* J Antimicrob Chemother. https://doi.org/10.1093/jac/dkaa541

71. Winter M, Buckling A, Harms K, Johnsen PJ, Vos M. (2021) *Antimicrobial resistance acquisition via natural transformation: context is everything.* Current opinion in microbiology. https://doi.org/10.1016/j.mib.2021.09.009

72. Øvsthus KK, Sjåvik K, Lier T, Klingenberg C. (2021) *Antibiotic Therapy of an Infant With a Brevibacterium casei Ventriculoperitoneal Shunt Infection.* Pediatr Infect Dis J. https://doi.org/10.1097/inf.0000000000003267

73. Østlyngen RM, Wergeland SS, Simonsen GS, Sundsfjord A, Ekgren J, Maltau JM. (2021) *Risk of cervical intraepithelial neoplasia grade 3 or higher (CIN3+) among women with HPV-test in 1990-1992, a 30-year follow-up study.* Infect Agent Cancer. https://doi.org/10.1186/s13027-021-00386-z

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