Prof. Dr. Sören Abel

Assoziierter Professor, Universität Siegen

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CURRENT POSITIONS

since 01/2023	Assoziierter Professor, University Siegen (20 %)
since 08/2021	Research Professor
	(Forsker 1183, equivalent to Professor without teaching obligations)
	Division of Infection Control and Environmental Health
	Norwegian Institute of Public Health (NIPH), Norway
since 05/2015	Research group leader, Department of Pharmacy,
	University of Tromsø, Norway

PREVIOUS POSITIONS

	02/2020-07/2021	Associate Professor of Bacterial Pathogenesis at the Department of Veterinary and Biomedical Sciences
		The Pennsylvania State University, PA, USA
	05/2015-02/2020	NCMM young associate investigator at the Department of Pharmacy & Nordic
		EMBL partnership University of Tromsø, Norway
	05/2015-04/2017	Visiting Assistant Professor at the Department of Microbiology and Immunobiology
		Harvard Medical School, MA, USA
	04/2012-04/2015	Research Fellow mentored by Matthew K. Waldor
		Harvard Medical School, MA, USA &
		Postdoctoral Research Fellow
		Brigham and Women's Hospital, MA, USA
	06/2008-03/2012	Postdoctoral Researcher mentored by Urs Jenal
		University of Basel, Switzerland
E	DUCATION	
	05/2008	PhD in Molecular Microbiology
		University of Basel Switzerland

Mark -summa cum laude-

RESEARCH INTERESTS

The goal of my research is to quantify the spread of infectious diseases and decipher the molecular mechanisms underlying the successful infection of their hosts. To this end, I combine and newly develop molecular biology, genetic screens, and next-generation sequencing based methods. I apply them in combination with classical microbiology, animal models of infection, and mathematical modelling to study host-pathogen interaction and the effects of virulence mechanisms, antibiotics and antibiotic resistance on bacterial population dynamics.

PUBLICATION HIGHLIGHTS

(full publication list at <u>https://scholar.google.com/citations?user=kBjbO_AAAAAJ&hl=no&oi=ao</u>) Citations: 3075; h-index 19; i10-index: 21

Gillman AN, Mahmutovic A, Abel zur Wiesch P, *Abel S* The infectious dose shapes *Vibrio cholerae* within-host dynamics **mSYSTEMS** (2021) 6(6):e00659-21. <u>https://doi.org/10.1128/mSystems.00659-21</u> Gillman AN, Helleux A, *Abel S* A single step three-strain in vivo Gateway reaction **PLASMID** (2021) 118:102608. https://doi.org/10.1016/j.plasmid.2021.102608

Mahmutovic A, Gillman AN, Lauksund S, Robson Moe N-A, Manzi A, Storflor M, Abel Zur Wiesch P*, *Abel S**

RESTAMP–Rate estimates by sequence-tag analysis of microbial populations **COMPUT STRUCT BIOTEC** (2021) 19:1035-51. https://doi.org/10.1016/j.csbj.2021.01.017

Clarelli F, Palmer A, Singh B, Storflor M, Lauksund S, Cohen T, *Abel S**, Abel zur Wiesch P* Drug-target binding quantitatively predicts optimal antibiotic dose levels in quinolones. **PLOS COMP BIO** (2020) 16(8):e1008106

https://doi.org/10.1371/journal.pcbi.1008106

Mahmutovic A, Abel zur Wiesch P*, *Abel S** Selection or drift: The population biology underlying transposon insertion sequencing experiments **COMPUT STRUCT BIOTEC** (2020) 18: 91-804. <u>https://doi.org/10.1016/j.csbj.2020.03.021</u>

Lori C*, Ozaki S*, Steiner S, Böhm R, *Abel S*, Dubey BN, Schirmer T, Hiller S, and Jenal U Second Messenger Cyclic di-GMP acts as a cell cycle oscillator to drive chromosome replication **NATURE**, (2015) 523 (7559):236–239. https://doi.org/10.1038/nature14473

Abel S, Abel zur Wiesch P, Chang H-H, Davis BM, Lipsitch M, and Waldor MK Sequence tag-based analysis of pathogen population dynamics **NATURE METHODS** (2015) 12 (3):223-6. https://doi.org/10.1038/nmeth.3253

GROUP MEMBERS/STUDENTS

Merete Storflor	PhD student (Tromsø)
Christina Bleis	PhD student (Tromsø)
Øyvind Lorentzen	PhD student (Tromsø)
Ying Yen	postdoc (Oslo)

FORMER GROUP MEMBERS

Silje Lauksund	Technician
Rita Raimundo	ERASMUS exchange & MSc student
	MSc in 10/2019, now microbiologist at Lonza, Netherlands
Aime Manzi	MSc student
	MSc in 07/2019, now leading hospital pharmacy, Norway
Natasha-Anne Moe	MSc student
	MSc in 07/2019, now clinical pharmacist, Norway
Alexandra Helleux	exchange student
	now PhD student at IGBMC, France
Anel Mahmutovic	postdoc
	now Associate Director at AstraZeneca, Sweden
Ida Opstad	PhD student
	PhD in 01/2021
Larissa Schröter	ERASMUS student,
	now PhD student at Hannover Medical School, Germany
Bhupender Singh	postdoc
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	now permanent position at University of Tromsø
Aaron Gillman	postdoc
	offer for faculty position, University of Colorado, USA
Maddalen Rodriguez	BSc student
-	BSc in 06/2016, now R&D Scientist at IMG Pharma, Spain

PROFESSIONAL ACTIVITIES/MEMBERSHIPS

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TEACHING INTERESTS

I am very interested in recruiting Master and PhD students to Oslo. Due to the high living costs, I would recommend applying for fellowships together. Please contact me!

Ich bin sehr daran interessiert, Masterstudenten und Diplomanden nach Oslo zu rekrutieren. Wegen der hohen Lebenskosten, wäre es das Beste, sich gemeinsam auf Stipendien zu bewerben. Bitte Kontakt aufnehmen!

GRANTS/ACTIVITIES

07/2022-12/2023 Funding from the Research Council of Norway (FriPro #262686) ~167 k€ In this grant we use genetically barcoded organisms and next-generation sequencing (RESTAMP) to directly measure replication and death rates from bacterial model organisms exposed to antibiotics. These measurements will parameterize a mechanistic pharmacodynamic model (vCOMBAT) to predict how given drug concentration affects its targeted bacteria. Specifically, our parameterized models enable us to predict bacterial responses to fluctuating antibiotic concentration that we would realistically observe in patients. These predictions will be validated in vitro. This approach will enable us to quickly and cheaply optimize dosing regiments to tread infectious diseases.

02/2020 Pennsylvania State University startup funding ~1.2 M€ Startup funding to establish a research group studying bacterial pathogenesis and population dynamics in animal models of infection. Role: PI

03/2017 NCMM collaboration seed fund ~69 k€ 'Dynamics of Protein-Lipid Interaction'. In this collaboration seed grant, we investigated the interaction between the lipid cardiolipin and the ion-transporter MgtA. Specifically, we addressed the consequences of their interaction for the protein activation, function, and subcellular localization with an interdisciplinary approach that combines structural biology and in vivo functional assays. Role: PI; Co-PI: Irep Gözen & Jens Preben Morth.

01/2017-01/2021 PhD fellowship Nano-Bio-Sys Strategic funding (UiT) ~323 k€ Advanced Nanoscopy to Decode Sub-cellular Biological Systems ('Nano-Bio-Sys'). In this interdisciplinary proposal, we developed new technologies for optical nanoscopy and apply them to study the subcellular localization of bacterial signaling components. The presently available optical nanoscopes use a 'complex microscope' with a 'simple glass slide' to hold the sample. We inverted this setup: a 'complex but mass-producible waveguide-chip' to hold and illuminate the sample and a 'standard microscope' to acquire images. Waveguide chip-based structured illumination microscopy (SIM) is already developed and we to expanded waveguide chip technology to other superresolution modalities like dSTORM. This setup allows us to run high throughput localization experiments with subcellular resolution. Role: PI; Co-Pi: Balpreet Singh Ahluwalia.

07/2016-06/2019 Funding for a postdoc from HelseNord, Norway (#SFP1293-16) ~323 k€ 'Cooperative co-infection in enteric pathogens'. Enteric diseases pose a severe burden for public health in both developed and developing countries and are the second largest cause of mortality in young children worldwide with more than 2 million deaths yearly. One obstacle in curbing the spread of enteric diseases is that the relationships between pathogen uptake (overall dose and frequency) and the risk of infection and colonization are largely unknown. Here, we propose to obtain doseresponse curves for a panel of enteric pathogens in experimental animals with a focus on cooperative co-infection. These will be incorporated into mathematical models informed by Norwegian outbreak data. This will aid in setting safety limits for pathogen contamination, conducting outbreak studies, and informing vaccination policy decisions. Role: PI.

03/2016-02/2019 Funding from the Research Council of Norway (FriPro #249979) ~686 k€ 'Host defenses against Vibrio cholerae and molecular virulence mechanisms to overcome them'. In this grant, we addressed two important but understudied mechanisms V. cholerae employs to overcome host defenses: acid adaptation and host-induced hyper-infectivity. The acidic pH of the stomach is believed to be one of the major host defense mechanisms against food borne diseases and pathogens have developed specific defense mechanisms to survive it. V. cholerae increases its virulence temporarily during host-passage right before it is expelled from the host. However, the exact molecular mechanisms are not well defined. We quantified how both phenomena affect the population dynamics of V. cholerae during infection and which molecular pathways are underlying them. We used an interdisciplinary approach that combined molecular biology, genetics and population biology. We will employed animal models that closely mimic the human disease in conjunction with a next-generation-sequencing based technique (STAMP) that enabled us to quantify the population dynamic with unprecedented accuracy. Characterizing host defense mechanisms as well as the molecular mechanisms underlying the pathogens virulence helped us better understand the pathogen with respect to infection of a single host. Ultimately, this knowledge might contribute to the development of new interventions against this ancient scourge. Role: Pl.

03/2016-02/2020 PhD fellowship from the University of Tromsø, Norway ~323 k€ *C-di-GMP plays critical role during infection of* V. cholerae. Not only is the expression of the major virulence factor, cholera toxin, under direct control of this bacterial second messenger, it also contributes significantly to survival of the pathogen through the acid stomach environment, migration through the mucus lining of the GI-tract, colonization of the intestinal epithelium and the survival after excretion to the aquatic environment. All these steps are critical for the success of the pathogen, but while some can be traced back to c-di-GMP induced biofilm formation, others require the release of c-di-GMP inhibited motility and chemotaxis. This indicates that the cellular c-di-GMP concentration fluctuates in a specific and coordinated fashion during infection. Using a combination of biochemistry, molecular biology and quantitative single cell microscopy with c-di-GMP reporter proteins we will measure the concentration of the second messenger during the cause of an infection and decipher the main components responsible for regulation of the fluctuations. This will identify novel virulence factors and offer potential targets for intervention. Role: PI.

05/2015-12/2022 Funding as independent group leader

~1.2 M€

The grant is funded by the Nordic EMBL Partnership Centre for Molecular Medicine in Oslo (NCMM) and Helse-Nord is dedicated to study the adaptation of enteric pathogens to changes in their environment during infection and transmission. Our aim is to understand how enteric pathogens survive the radically different conditions it encounters during the passage through the host and into the environment. We are particularly interested in the c-di-GMP second messenger network that controls important adaptation mechanisms during infection and its impact on population dynamics, bacterial virulence and persistence under changing conditions. Role: PI.