Applied Microbiology Research

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Towards a systems understanding of key host-pathogen interactions, from molecules to populations

Hosts and pathogens share complex interactions across scales from molecules to populations. The Applied Microbiology Research group aims to understand these various levels of interactions by the identification of factors involved, with a systems biological approach. To do so we use techniques including cutting edge molecular techniques, high throughput pathogen genome sequencing, and mass spectrometry. Key findings and applications are translated into clinical applications to improve patient diagnostics of infections.

Transmission of clinically relevant viruses.
We study transmission events in the context of local outbreaks and global transmission using human influenza viruses, and most recently the pandemic SARS-CoV-2. For both viruses, we have established whole genome sequencing (WGS) and analysis pipelines and humoral immune assays. Together with our collaborating partners, we explore transmission events and spatio-temporal dynamics and models across the Basel region. With these tools we investigate viral evolution in clinically relevant contexts, such as the role of superspreading events, the effect of socioeconomics and transportation, and treatment of hospitalized patients. We explore specific mutations in the viral genome as markers for epidemiological modelling and detection of antiviral resistance.

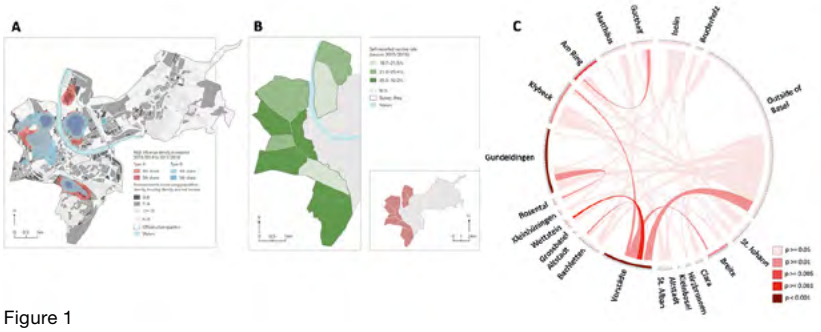

Figure 1

Transmission of clinically relevant bacteria.
We use WGS (Illumina and Oxford Nanopore) and metagenomic approaches in order to describe genetic relatedness and evolution between and within hosts. Bacterial pathogens of interest include multi-drug resistant bacteria such as ESBL- and Carbapenemase-producing and hypervirulent Enterobacteriaceae, Vancomycin resistant *Enterococcus faecium, Clostridioides difficile, Legionella pneumophila,* and Methicillin resistant *Staphylococcus aureus,* as well as interesting clinical outbreaks. Recently we have described a new bacterial species – *Mycobacterium basiliense.* A fundamental tool which we are constructing is the NRP72-funded Swiss Pathogen Surveillance Platform (www.spsp.ch): collaborating with the Universities and University Hospitals of Basel, Geneva and Lausanne, VetSuisse (University of Bern and Zurich) and the Swiss Institute for Bioinformatics, this is an interoperable molecular and classical epidemiological database for WGS and metadata sharing. This work will be extended from MRSA to multiple clinically relevant pathogens – including previously mentioned respiratory viruses.

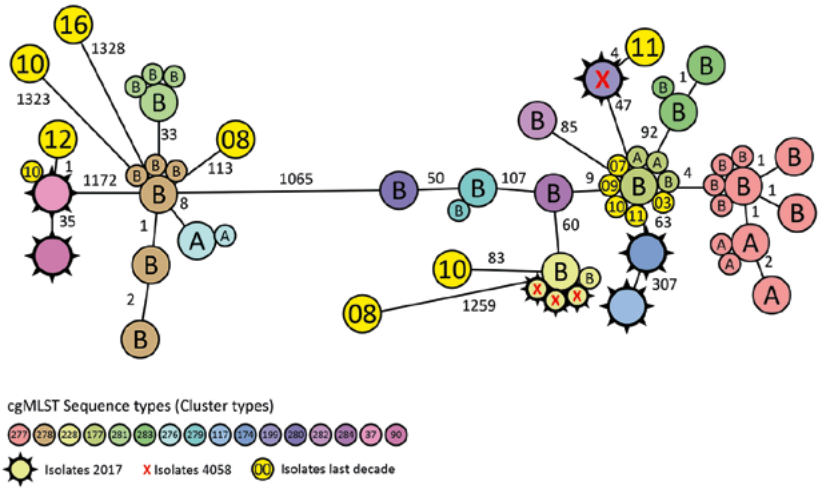

Figure 2

Understanding pathogens and populations.
Our research group also focuses on pathogen dynamics and prediction of invasiveness within a single host. In a SNF-funded project, we are also developing metagenomic tools to determine MDR colonization status of hospital patients directly from swabs, aiming to monitor microbiota changes over time within the patient during hospitalization. In a Gebert-Rüf funded project, we look into the dynamics of ESBL *E. coli* colonization and carriage in healthy individuals who travelled to high endemic regions. Our goal is to identify (i) microbiological factors affecting whether the subject remains colonized or spontaneously clears the pathogen and (ii) which pan-sensitive natural microbial displace resistant bacteria such as ESBL *E. coli*. Finally, we also study the factors driving invasiveness of colonizing *E. coli* isolates causing pyelonephritis and uro-sepsis. We use WGS data to predict ribosomal marker masses in order to determine phylogroups in MALDI-TOF MS spectra. These phylogroups allow the prediction of clinical phenotypes.

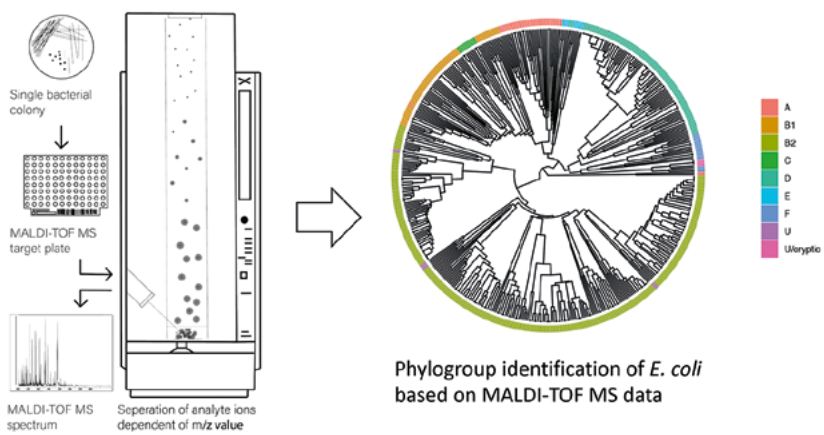

Figure 3

Connection to Clinical Practice

Prof. Manuel Battegay and team
Infectious Diseases and Hospital Epidemiology

Bridging pathogen characterization to clinical application

Being embedded in the division of Clinical Bacteriology and Mycology provides access to clinical isolates, and interesting cases. Together with colleagues from the Division of Infectious Diseases and Hospital Epidemiology, we explore these patients and use the new discoveries and insights to improve the diagnostic process. In parallel, there is a constant need to accelerate diagnostics, providing the best of new technologies for patients, and much of our work also focuses on this aspect. We want to translate our findings into clinical practice, developing novel diagnostic strategies and preventive measurements to reduce pathogen transmission and expedite patient treatment.
An example is the combination of mass-spectrometry and antibiotic resistance profiles. Using machine learning, we have developed together with Prof. Karsten Borgwardt (ETH Zurich) an algorithm to predict antibiotic resistance about 24h before classical phenotypic assays.

Selected Publications

Egli A, Schrenzel J, Greub G. Digital microbiology. Clin Microbiol Infect. 2020 Oct;26(10):1324-1331. doi: 10.1016/j.cmi.2020.06.023. Epub 2020 Jun 27.

Syedbasha M, Bonfiglio F, Linnik J *et al.* Interferon-λ Enhances the Differentiation of Naive B Cells into Plasmablasts via the mTORC1 Pathway. Cell Rep. 2020 Oct 6;33(1):108211. doi: 10.1016/j.celrep.2020.108211.

Seth-Smith HMB, Imkamp F, Tagini F *et al.* Discovery and Characterization of *Mycobacterium basiliense* sp. nov., a Nontuberculous *Mycobacterium* Isolated From Human Lungs. Front Microbiol. 2019 Jan 8;9:3184. doi: 10.3389/fmicb.2018.03184. eCollection 2018.

Seth-Smith HMB, Casanova C, Sommerstein R, *et al.* Phenotypic and Genomic Analyses of *Burkholderia stabilis* Clinical Contamination, Switzerland. Emerg Infect Dis. 2019;25(6):1084-1092. doi:10.3201/eid2506.172119.

Wüthrich D, Gautsch S, Spieler-Denz R, *et al.* Air-conditioner cooling towers as complex reservoirs and continuous source of *Legionella pneumophila* infection evidenced by a genomic analysis study in 2017, Switzerland. Euro Surveill. 2019;24(4):1800192. doi:10.2807/1560–7917.ES.2019.24.4.1800192.