Universität Basel

Research Project

Screening for multi-drug resistant pathogens: usage of rapid metagenomic technologies for screening and surveillance

Third-party funded project

Project title Screening for multi-drug resistant pathogens: usage of rapid metagenomic technologies for screening and surveillance
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Multi-drug resistant (MDR) bacteria pose a substantial threat causing significant morbidity, mortality, and healthcare costs. Understanding “who is colonized and for how long?”, “what are transmission risks and routes?” and “what is the population dynamic in the patient’s gut and hospital environment?” are preconditions for effective countermeasures. Patients at risk of being colonized are screened upon hospitalization and in some cases pre-emptively isolated to reduce nosocomial transmissions. Available culture-based methods to confirm colonisation are labour-intensive and slow. Resistance pheno- and genotypes are confirmed within 3-5 days of the sample being taken and whole genome sequencing (WGS) for typing requires another 5-10 days. WGS is increasingly important as readily available tests do not include novel and emerging resistance mechanisms. A new screening approach should aim to (i) screen resistance mechanisms significantly faster, directly from specimen without culture, but with similar sensitivities and specificities; (ii) quantify MDR loads and characterize pathogens, thereby assessing the epidemic potential; and (iii) explore the epidemiologic context by genomic comparisons. The newest technology, such as nanopore sequencing, have the potential to close these critical gaps and answer fundamental questions on population dynamics and address these challenges through unprecedented fast metagenomics, with results available in few hours. Main objective: Our goals are to: (i) understand factors influencing dynamic changes of pathogen populations in patients and source habitats over time and space; (ii) translate this knowledge of MDR pathogens colonizing patients and hospital environments to better understand pathogen transmission. Approaches/methods: We will develop a highly novel approach to screen patients for colonisation with MDR bacteria. In WP1, we will implement nanopore-based sequencing for screening, to generate long-read metagenomic data directly from swabs within few hours. We will optimize protocols and compare performances (detection rate and quantification) to current laboratory standards (culture-based and PCRs). In WP2, we will integrate real-time bioinformatics into an existing infrastructure (NRP72-funded surveillance platform). Next, we will perform a prospective observational study for screening including, (WP3) determining MDR pathogen loads and changes over time within colonized patients; (WP4) measuring the impact of colonized patients on the local hospital environment; and finally (WP5) exploring the relatedness of colonizing bacteria to public databases. Expected benefit and possible applications of results: The project will allow us to establish and assess a completely novel screening approach based on long-read shotgun metagenomics for MDR pathogens. The integration of bacterial isolates from patients and hospital environments will (i) generate a fundamental context to profoundly understand the complexity of stable ecological habitats perturbated by invading pathogens on transmission; (ii) understand transmission by integrating pathogen loads and

genes encoding proteins involved in adherence to surfaces and resistance to disinfecting agents; and (iii) explore the new technology for clinical application. This will form the basis for a novel and personalized type of hospital epidemiology. During the project, sustainable tools will be generated: (i) a metagenomic-based technical approach for diagnostics and (ii) extension of the NRP72 surveillance platform to include further metagenomic sequencing data.

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