The molecular-matryoshka phenomenon

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IMPACT PARAGRAPH

Antimicrobial resistance (AMR) has become a global problem and has been declared an immediate threat to mankind by the World Health Organisation (WHO) requiring urgent and harmonized efforts to curb moving into a post-antibiotic age, where previously treatable common infections become untreatable. This will have serious consequences, such as a higher demands on healthcare, increased morbidity and premature death. One of the major pillars in the fight against AMR is improved surveillance to monitor the presence and dissemination of AMR bacteria. New methods for bacterial typing have been developed, such as second generation (short-read) and third generation (long-read) sequencing, giving the highest resolution in resolving phylogeny among bacterial isolates. Determining phylogeny among bacterial isolates is crucial in order to find key steps in the dissemination of AMR and prevent further spread.

Firstly, the studies in this thesis contribute to the knowledge on how to perform surveillance of bacterial pathogens by whole genome sequencing (WGS). More laboratories are moving to WGS for bacterial typing and use a plethora of methods. When WGS is utilized to characterize isolates for surveillance beyond a local level, protocols need to be harmonized to obtain comparable and interoperable data for surveillance. Without identical procedures, multi-centre outbreaks or outbreaks across a region or country may not be recognized, which may put a burden on healthcare due to decreased patient health, unnecessary isolation of patients and the general waste of time and resources if outbreaks are not contained or prevented.

One of the advantages of WGS is the detection of AMR genes, indicating putative phenotypic antimicrobial resistance of bacterial isolates. Yet, the performance of bioinformatic pipelines to identify AMR genes in the bacterial genomes is still poorly benchmarked. Work outlined in this thesis describe curated WGS datasets for AMR detection of the highest quality to enable such benchmarking, making it a valuable resource for laboratories who perform WGS and want or need to optimize their own bioinformatic data analysis. Furthermore, we identified steps in bioinformatic data processing which can hamper the detection of AMR genes. Improvement of WGS analysis for AMR identification will lead to improved decision making by clinicians and infection prevention specialists, ultimately benefitting the patient. Additionally, all WGS data generated for this thesis and associated metadata has been deposited in public repositories, available to others to retrieve and re-use.

Lastly, one of the main focus-points of this thesis is the plethora of mobile genetic elements (MGE) and their gene content. This field of study remains understudied by genomics due to the difficulties in examining these genetic units. The advances in the field of (bacterial) genomics and sequencing technologies finally made it feasible to do large scale analyses on MGEs. Outcomes of the studies described in this thesis contribute to the knowledge of the role of these MGEs in the spread of AMR and has highlighted the necessity to look further than just the contribution of bacterial iso-

lates in the spread of AMR worldwide. Dissemination of this new knowledge on MGEs and AMR has been distributed on various platforms ranging from scientific journals and conferences, bioinformatic hackathons and social media (Twitter & LinkedIn).