The research commercialisation office of the University of Oxford, previously called **Isis Innovation**, has been renamed **Oxford University Innovation**

All documents and other materials will be updated accordingly. In the meantime the remaining content of this Isis Innovation document is still valid.

URLs beginning www.isis-innovation.com/... are automatically redirected to our new domain, www.innovation.ox.ac.uk/...

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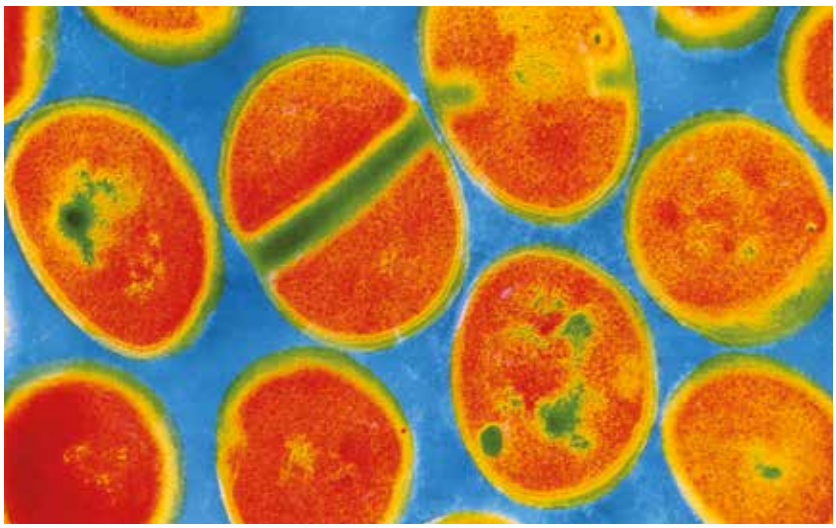
Mykrobe predictor – Antibiotic resistance prediction for *S. aureus* and *M. tuberculosis* from whole genome sequence data

Rapid and accurate antibiotic resistance prediction software that enables discovery of low-frequency resistant subpopulations for *S. aureus* and *M. tuberculosis*, as well as determination of species and

Rapid and accurate detection of antibiotic resistance in pathogens is an urgent need, affecting both patient care and population-scale control. Microbial whole-genome sequencing promises much, but many barriers exist to its routine deployment. Here, we address these challenges, using a "de Bruijn graph" comparison of clinical isolate and curated knowledge-base to identify species and predict resistance profile, including minor populations. This is implemented in a software package, Mykrobe predictor, for *S. aureus* and *M. tuberculosis*, that can run in under three minutes on a laptop from raw data.



For *S. aureus*, we train and validate in 495 and 471 samples, respectively, finding error rates comparable to gold-standard phenotypic methods. The software detected *S. aureus* with a sensitivity of 99.3% and predicted resistance with specificity of 99.5% across 12 drugs.

For *M. tuberculosis*, we identify species and predict resistance with specificity of 98.5% (training and validating on 1920 and 1609 samples, respectively). Sensitivity of 82.6% is limited only by current understanding of genetic mechanisms.

As new mechanisms are revealed, the software can be updated easily. We also show that analysis of minor populations increases power to detect phenotypic resistance in second-line drugs without appreciable loss of specificity. Finally, we have demonstrated the feasibility of using an emerging single-molecule sequencing technique, the Oxford Nanopore Technologies MinION.

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