

Whole genome sequencing of bacterial isolates

Resistance surveillance and outbreak analysis
in Region Östergötland

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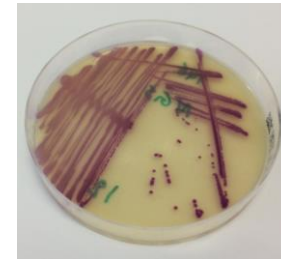
Clinical Microbiology, Linköping University Hospital



Clinical applications of WGS

- MRSA

- Subtyping (Spa typing, MLST)
- Identification of PVL gene



Whole genome sequencing (WGS) is performed on DNA from bacterial isolates

- ESBL-A, -M and -CARBA

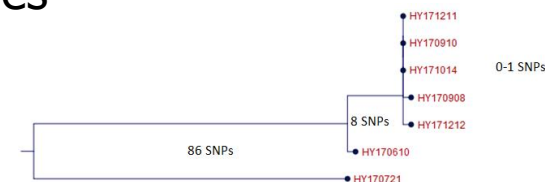
- Identification of resistance genes
- Subtyping (MLST)

In extended spectrum beta lactamase- and carbapenemase-producing bacteria (Enterobacteriales, Pseudomonas and Acinetobacter)

- Outbreak analysis

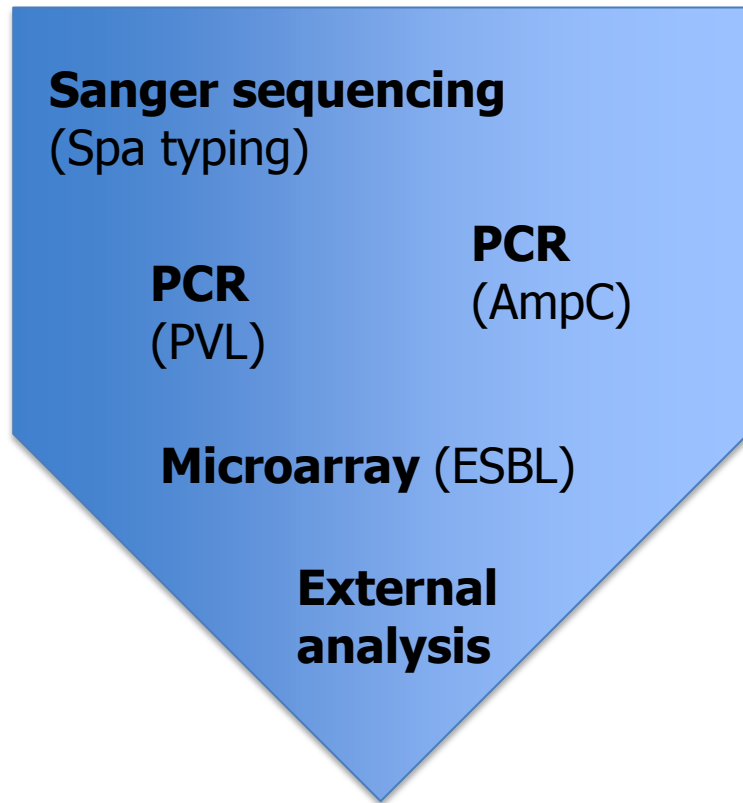
- Epidemiological typing by SNP analysis, on any species
- Can also be performed on previously produced data

(SNP; single nucleotide polymorphism)





Clinical applications of WGS



WGS

- Several molecular methods have been replaced by a single laboratory workflow
- Accredited by SWEDAC

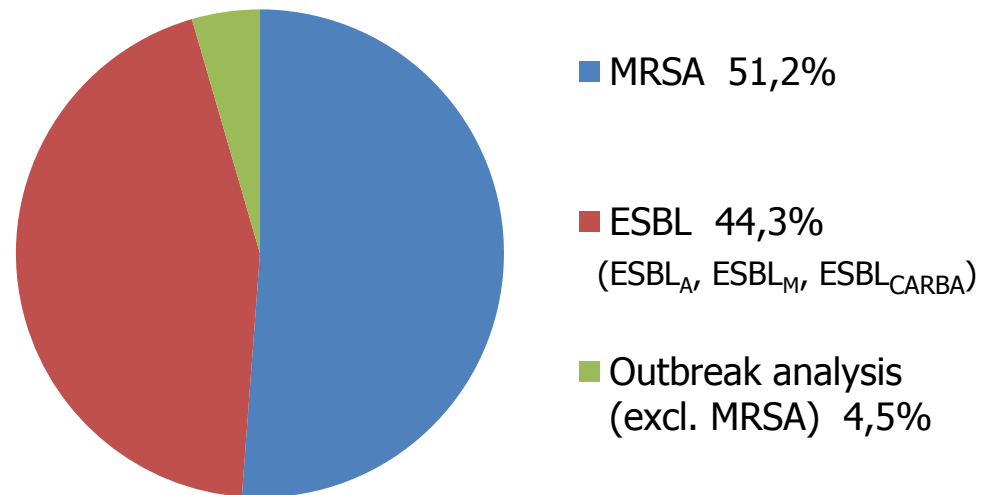


Clinical use

- Routine analysis once a week since December 2017
- 450 clinical samples/year (2018)
- Capacity: 22 samples + 2 controls/week

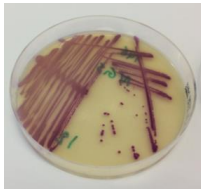
- **Research projects**

- Epidemiological typing
- Identification of virulence genes, plasmids, new resistance genes, and more





WGS workflow



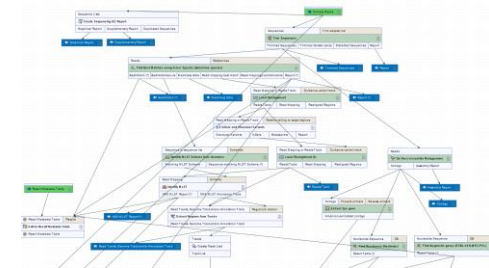
(EZ1, Qiagen)



(QIAseq, Qiagen)



(2x300 bp, MiSeq, Illumina)



(Pipeline created in CLC, Qiagen + Spa typing in BioNumerics, Applied Maths)

DNA extraction



Library preparation



Sequencing



Bioinformatics



2 days



2 days



Clinical reports

1. Whole Genome Sequencing of Bacterial Isolate - Clinical Report

1.1 Sample Name

PY1704946

1.2 Species

Staphylococcus aureus

1.3 MLST

ST 49

1.4 Diagnostic Genes

Gene	% Identity	Query / HSP Length	Contig	Predicted phenotype
mecA_10_AB51276.7	100.00	2010 / 2010	38	MRSA_(mecA)
PVL_HM584708	100.00	1918 / 1918	19	PVL

1.5 Complete List of Resistance Genes

Gene	% Identity	Query / HSP Length	Contig	Predicted phenotype
mecA	100.00	2010 / 2010	38	Beta-lactam resistance
blaZ	98.94	846 / 846	30	Beta-lactam resistance

1. Whole Genome Sequencing of Bacterial Isolate - Clinical Report

1.1 Sample Name

MRR160069

1.2 Species

Enterobacter cloacae

1.3 MLST

ST 141

1.4 Diagnostic Genes

Gene	% Identity	Query / HSP Length	Contig	Predicted phenotype
blaSHV-12	100.00	861 / 861	46	ESBL_A
blaCTX-M-9	100.00	876 / 876	53	ESBL_A
blaOXA-48	100.00	798 / 798	51	ESBL_CARBA

1.5 Complete List of Resistance Genes

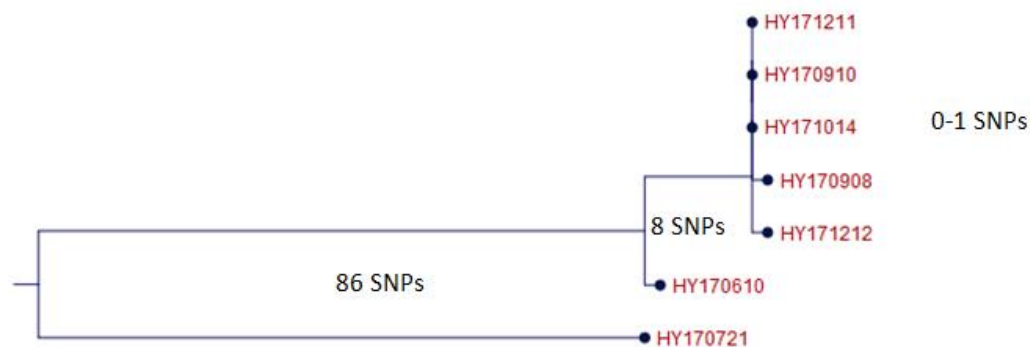
Gene	% Identity	Query / HSP Length	Contig	Predicted phenotype
aadB	100.00	534 / 534	59	Aminoglycoside resistance
blaCTX-M-9	100.00	876 / 876	53	Beta-lactam resistance
blaSHV-12	100.00	861 / 861	46	Beta-lactam resistance
blaOXA-48	100.00	798 / 798	51	Beta-lactam resistance
aac(6')Ib-cr	99.66	588 / 600	48	Fluoroquinolone and aminoglycoside resistance
catA1	99.55	660 / 660	70	Phenicol resistance
QnrA1	99.85	657 / 657	56	Quinolone resistance
sul1	100.00	927 / 927	68	Sulphonamide resistance

- Relevant genes and subtypes (MLST/spa) are reported
- Additional information on request



Outbreak analysis

- Usually requested by the [Department of Infection Control and Hygiene](#)
- Reported with phylogenetic tree and genetic distances

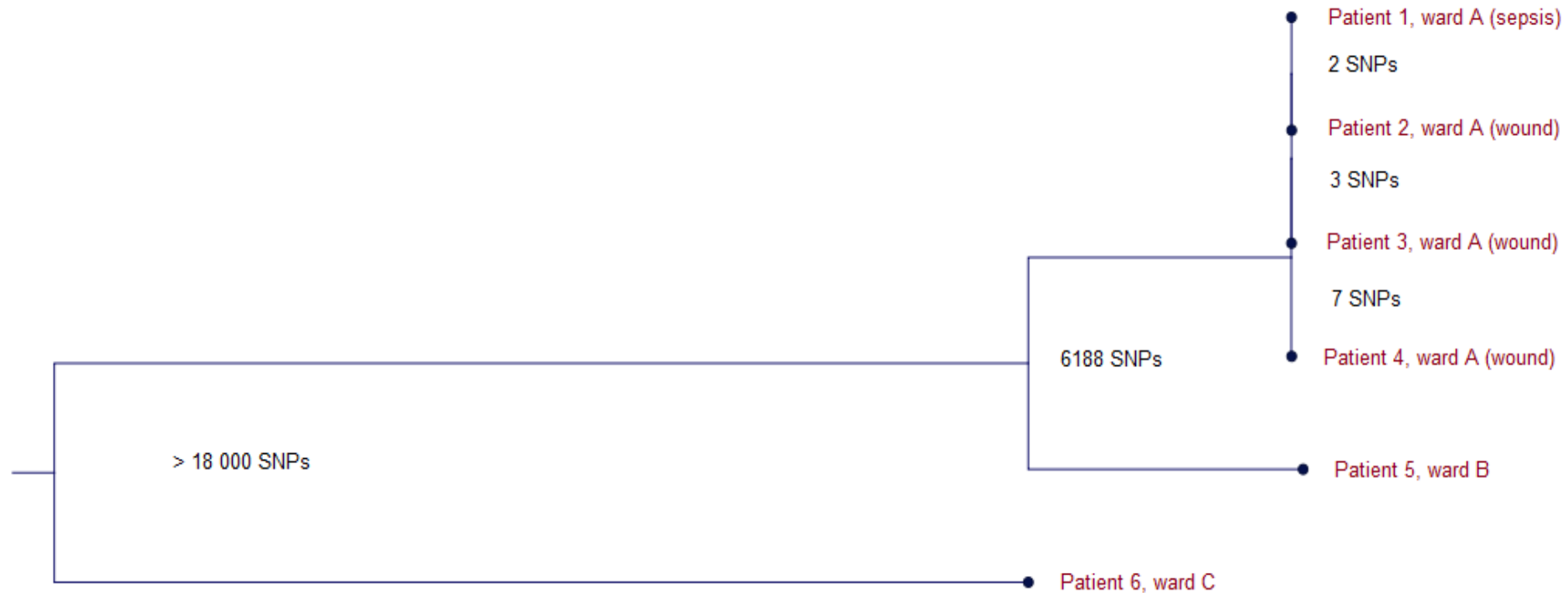


- Interpreted in view of epidemiological information



Outbreak analysis

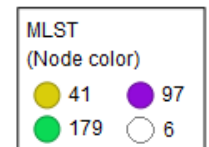
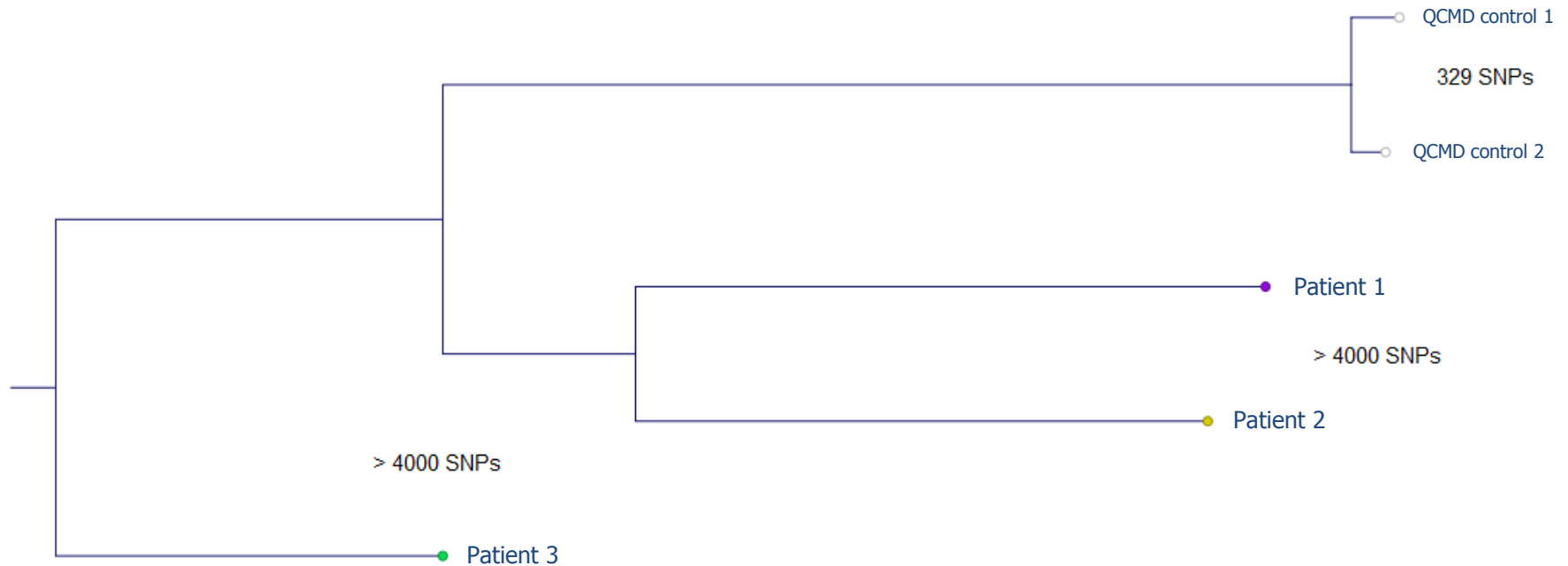
Suspected infection spreading of *Corynebacterium striatum* at the Intensive Care Unit for burn injuries





Outbreak analysis

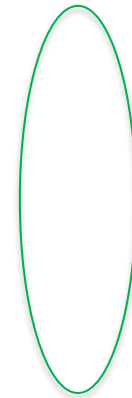
Suspected infection spreading of *Enterococcus faecalis* at the Hospital Eye Clinic





Outbreak analysis

- *Stenotrophomonas maltophilia* at the Intensive Care Unit
 - Identified in respiratory tract samples in three patients within a few days
 - *S. maltophilia* was found in samples from sinks and medical equipment...
 - ... and later in a fourth patient



Phylogenetic tree



Conclusions and future

- Several medical questions answered by one laboratory analysis
- New species and genes can be validated continuously
- High resolution comparison of isolates, where previously only subtyping was available
- Close contact with [Department of Infection Control and Hygiene](#) in suspected outbreak situations
- Future national collaboration and data sharing



Thank you

Clinical Microbiology, Diagnostic Center

Department of Infection Control and Hygiene

QIAGEN

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