

Use of WGS in an antimicrobial resistance reference lab

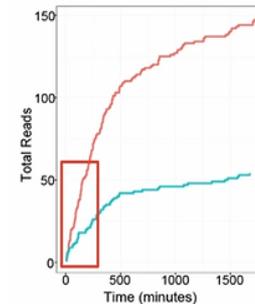
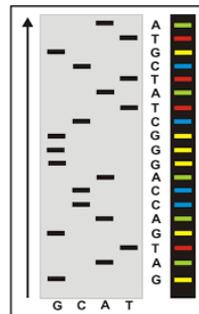
NordicAST, May 28 - 2019

Arnfinn Sundsfjord

arnfinn.sundsfjord@uit.no

K-res, University Hospital of North Norway, Tromsø

<https://unn.no/fag-og-forskning/k-res>

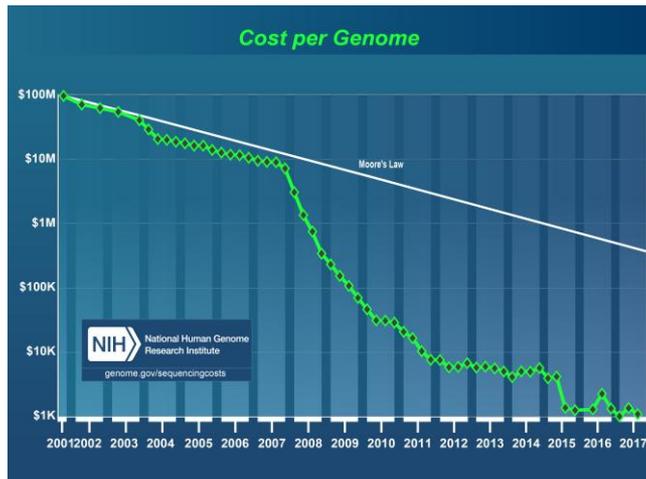
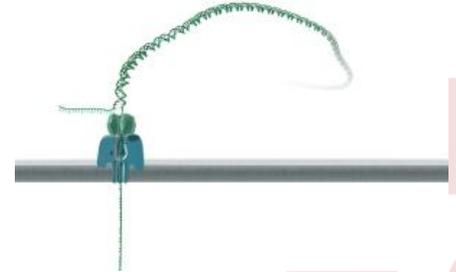
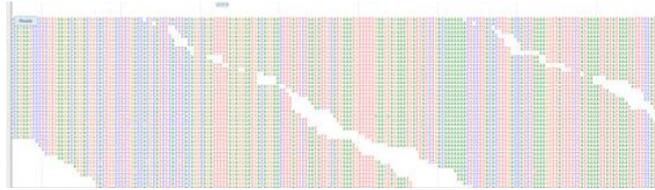
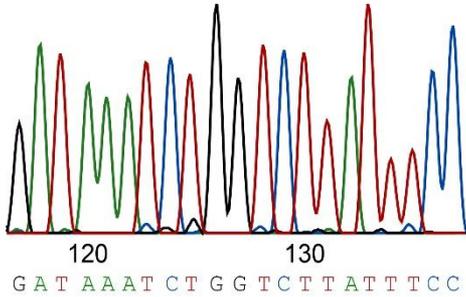


NASJONAL KOMPETANSETJENESTE
for påvisning av antibiotikaresistens

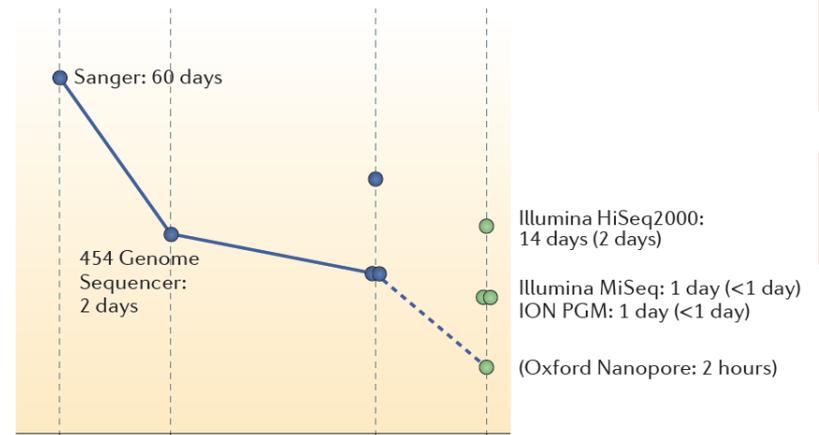




Whole genome sequencing (WGS)

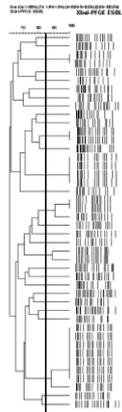
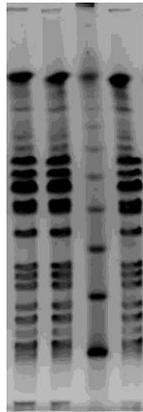


Turnaround time: bacterial genome

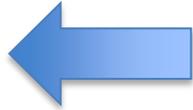




WGS in diagnostic and public health microbiology



Outbreak investigations

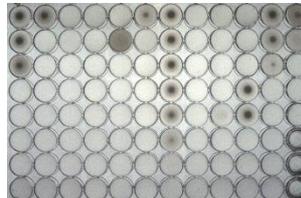
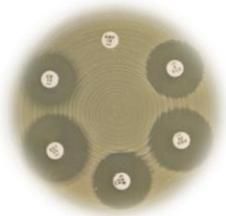


Molecular epidemiology: gene, mobile element, strain

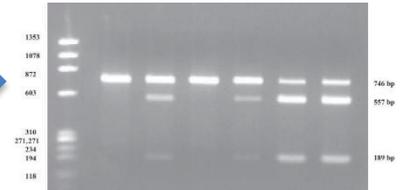


Gene	Strain A	Strain B	Strain C
oriX	G	C	G
oriH	ACTG	CCAG	ACTA
oriI	A	G	G
oriJ	C	T	T
oriK	C	C	T
oriL	CT	AG	CT
oriM	TG	TG	GA
oriN	G	G	A
oriO	TGA	AGA	TGT
Count	1 1 1 1 1 1 1	2 2 2 1 2 1 2	1 3 2 2 1 3 3

AST



Biomarker /virulence detection



Species ID





Outline

- Core functions for reference laboratories as part of the public health microbiology system – Ref: *HOD I-5/2013 + ECDC 2010*
- National reference functions
- WGS-bioinformatic pipeline and QC
- Case reports, and cluster of OXA-48 *K. pneumoniae* ST392
- Yearly reports: 2018 CRE + LRE
- Perspectives



Five core functions

1. Reference diagnostics

- The reference laboratory has *state-of-the-art validated laboratory methods* in operation and the ability to deliver accurate confirmation of diagnostic results within its field of expertise

2. Reference material resources

- If necessary, the reference laboratory develops and maintains — in accordance with international standards and procedures — a *collection of relevant reference material* that is to be shared with laboratories and organisations.

3. Scientific advice

- The reference laboratory is a *resource and coordination point for expertise* within its specific area and shares information and advice with relevant stakeholders.

4. Collaboration and research

- The reference laboratory is at the *forefront of technological and scientific development in its field of expertise*, particularly in areas relevant to public health action. Contacts with regional and international laboratory networks as well as related initiatives should be established and maintained.

5. Monitoring, alert and response

- The reference laboratory *performs or contributes to surveillance activities*, or has established channels of communication with the national surveillance body to regularly report incidence data and provide an 'alert function' for unusual occurrences.



Five core functions

1. Reference diagnostics

- The reference laboratory has *state-of-the-art validated laboratory methods* in operation and the ability to deliver accurate confirmation of diagnostic results within its field of expertise

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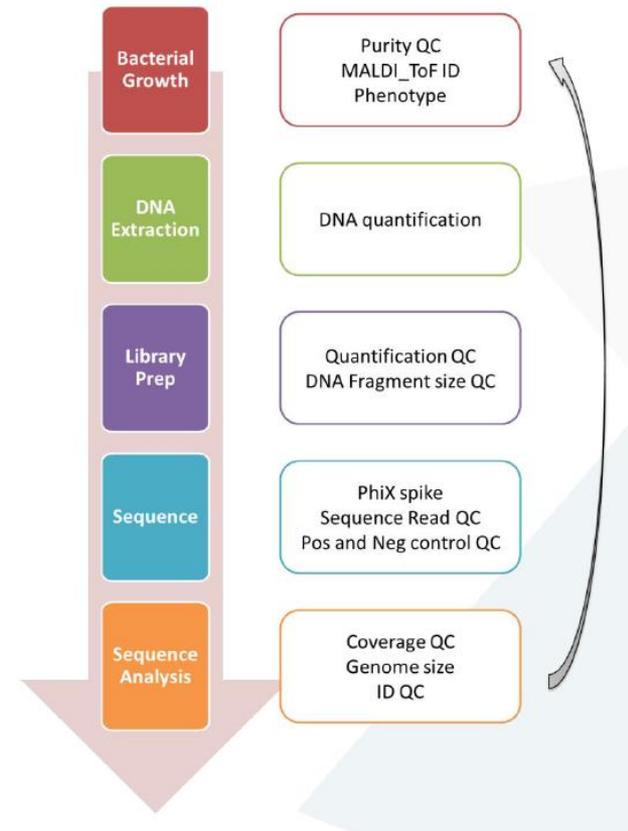
K-res: AMR reference functions

- **Linezolid** resistant enterococci (LRE)
- **Carbapenem** resistant Gram-negative bacteria
 - *Enterobacterales*, *Pseudomonas* spp. and *Acinetobacter* species
- **From late 2018:**
 - Vancomycin resistant enterococci (VRE)
 - Colistin resistant Gram-negative bacteria
- **Production line**
 - Strains are handled consecutively as they arrive
 - Phenotype:
 - MIC-profil (Sensititre, Trek diagnostic systems)
 - Additional testing for ESBL-CARBA
 - Genotype: Single and/or multiplex PCRs
 - Median response time 5 days
 - WGS of confirmed strains every month - from 2019



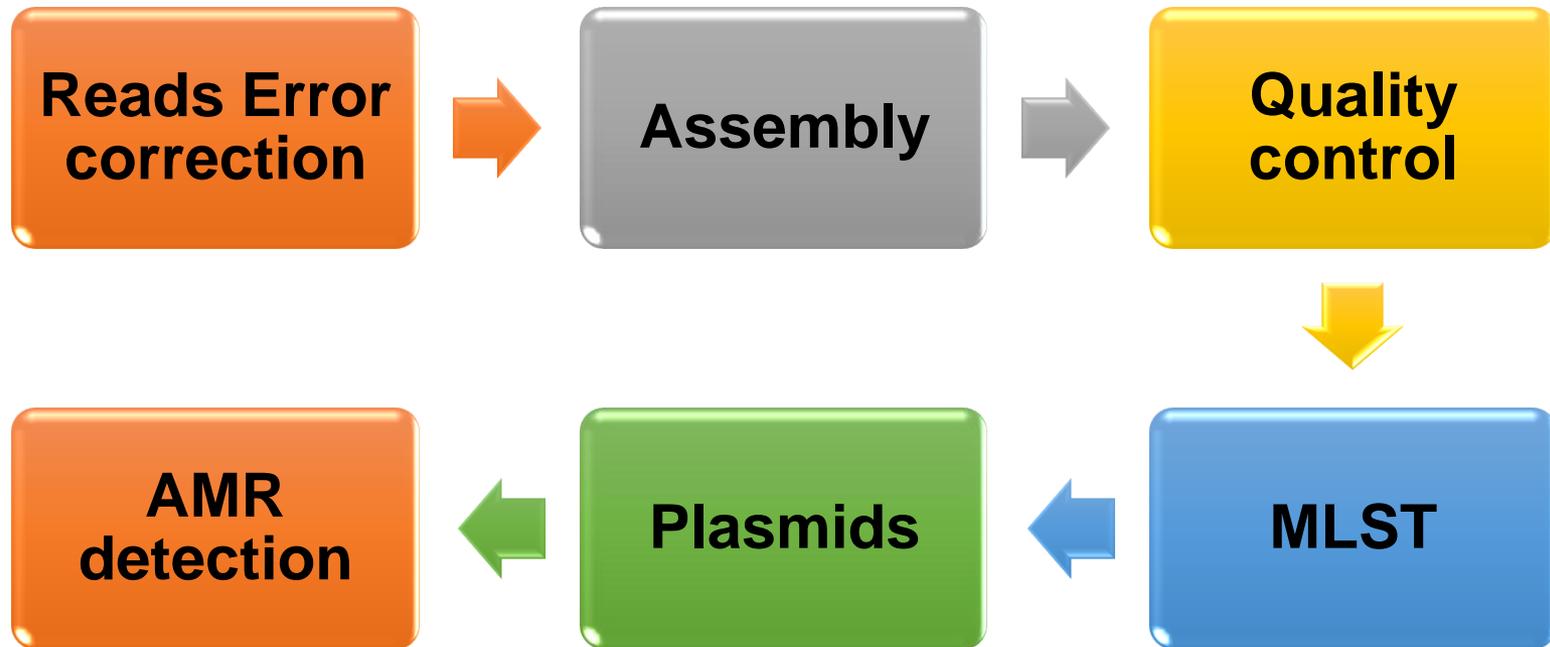
WGS-pipeline and QC

- Pure bacterial growth and DNA extraction/QC at K-res
- Library preparation and sequencing/QC:
 - Genomic core facility
 - Illumina NextSeq 550
- Bioinformatics at K-res from FASTQ files

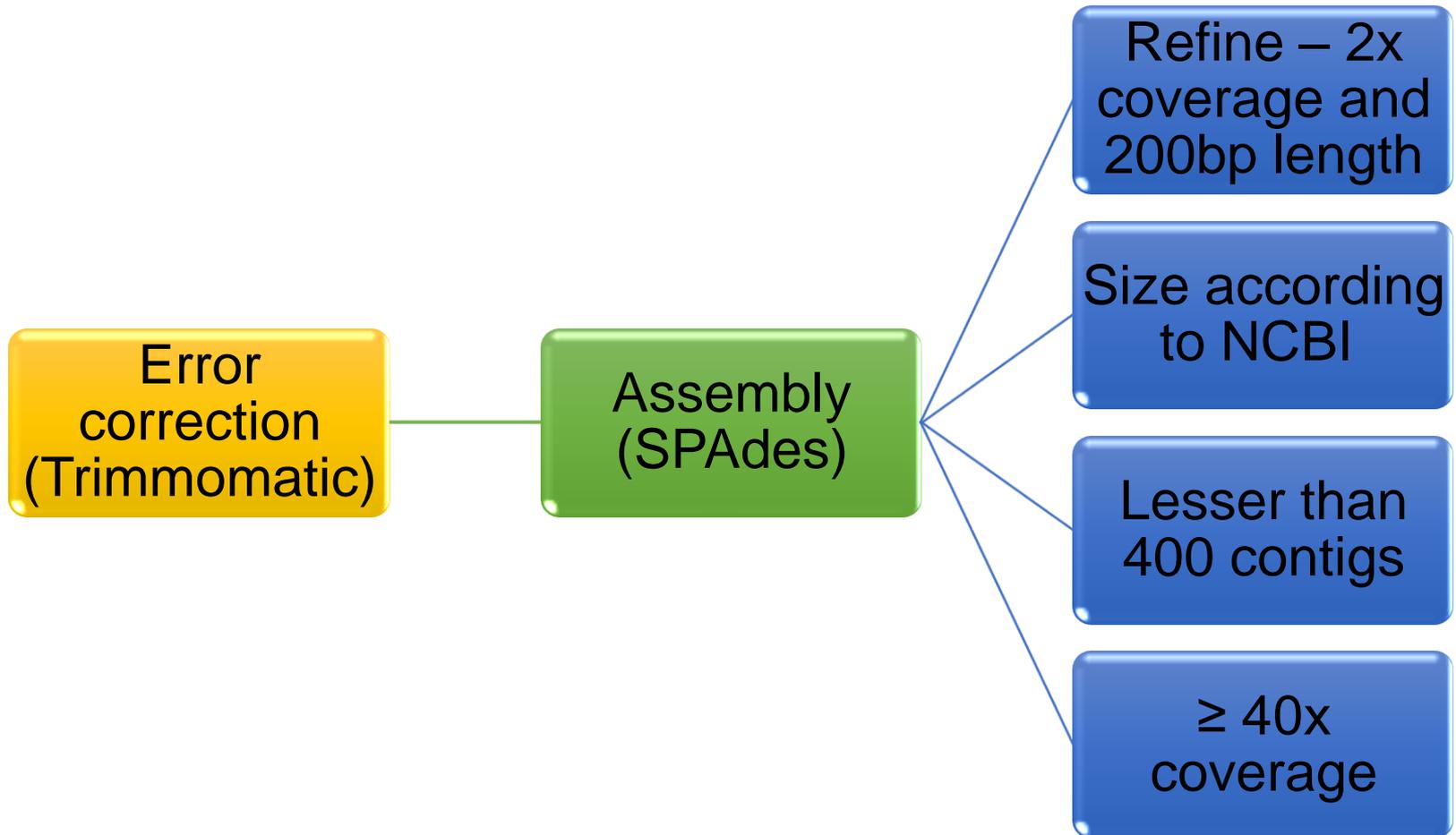


Source: MDU, Public Health Laboratory, Melbourne

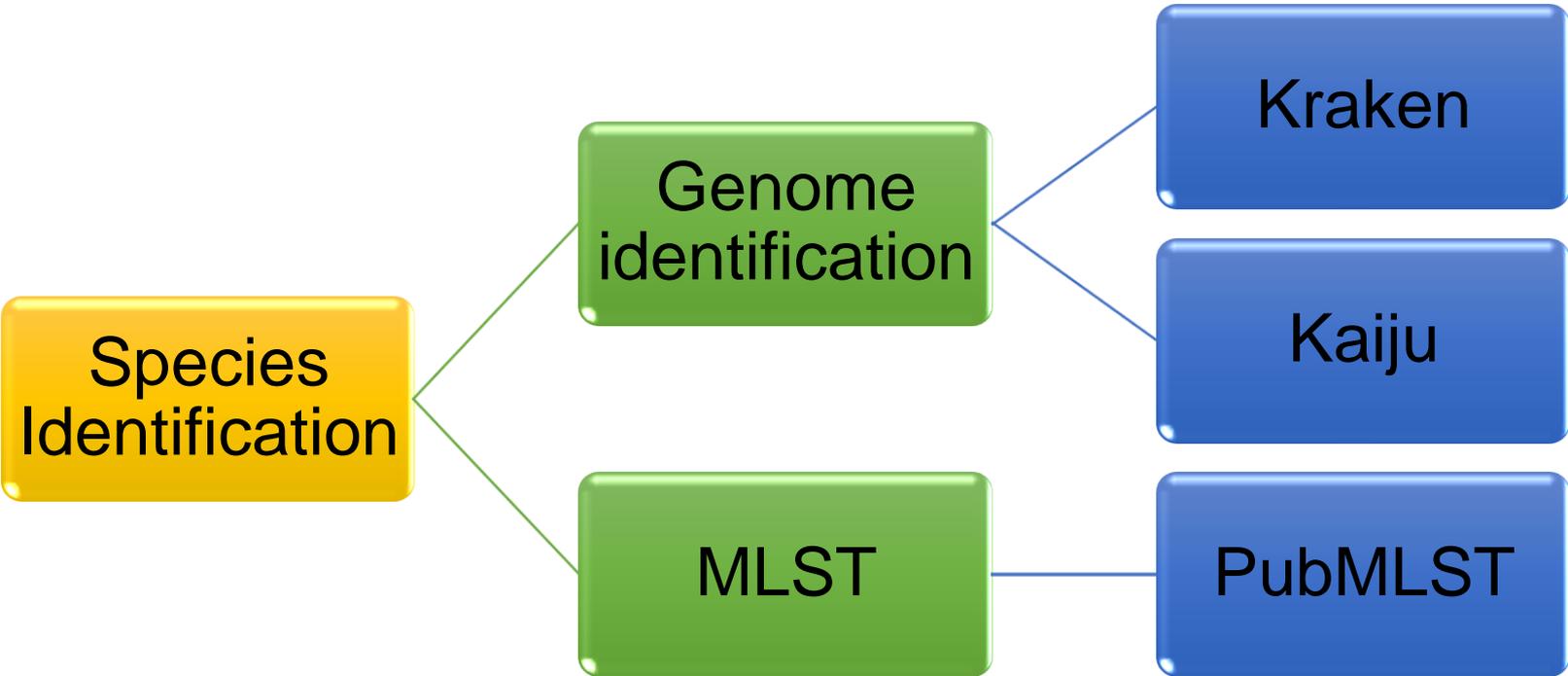
In-house bioinformatic pipeline



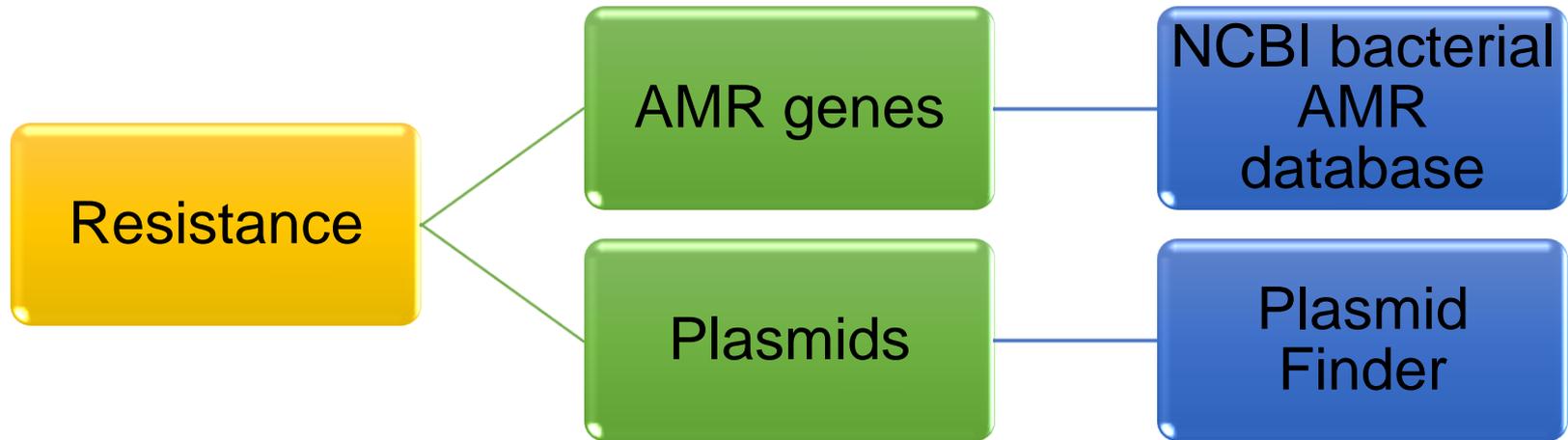
Bioinformatic - QC



Bioinformatic: species and MLST



Bioinformatic: Plasmids and AMR-genes





The WGS-report

- **Reference ID + Methods summary:**
 - Illumina technology, QC, and in-house bioinformatic pipeline
- **Assembly quality:**
 - Number of contigs, assembly length, coverage
- **Results:**
 - Species and MLST (prevalence NCBI)
 - Plasmid replicons and plasmid MLST
 - Resistance genes – two «levels»
 - minimum cutoff of 90% nucleotide identity and 90 % coverage
 - minimum cutoff of 60% nucleotide identity: Gene --> Product (Identity%, Coverage%)

```
Method summary:
Extracted genomic DNA was sequenced by Illumina technology. Paired-end Illumina reads
were assembled with SPAdes. Contigs below 200bp length and 2x coverage were removed.
The assembled genome was analyzed for species MLST type, plasmid replicons and
resistance genes using an in-house bioinformatic pipeline.

Assembly quality:
- Number of contigs: 88
- Assembly length (non-circular): 3002067bp
- Coverage: 69.0518x

Results:
a) Species & MLST type (based on https://pubmlst.org/)
Efaecalis ST-16 4.49944 (Prevalence% of this ST among the particular species
genomes in the NCBI GenBank as of March, 2019)

b) Plasmid replicons and plasmid MLST (based on PlasmidFinder https://cge.cbs.dtu.dk/
services/PlasmidFinder/ ). This analysis is only applicable for Enterobacteriaceae and
Gram positives. (p) stands for partial hits.
--rep9_1_repA(pAD1), rep6_1_repA(p703/5), rep9_4_repA2(pTEF2) (p)

c) Resistance genes (Based on PRJNA313047- Bacterial Antimicrobial Resistance Reference
Gene Database)
i) Resistance genes (identified with a minimum cutoff of 90% nucleotide identity and 90
% coverage):
Gene --> Product ( Identity%, Coverage%, Prevalence% in this ST in the NCBI GenBank as
of March, 2019)
ant(9)-Ia --> aminoglycoside nucleotidyltransferase ANT(9)-Ia (100.00, 100.00, 0.987654
)
lsa(A) --> ABC-F type ribosoma lprotection protein Lsa(A) (98.93, 100.00, 9.87654)
aph(3')-IIIa --> aminoglycoside O-phosphotransferase APH(3')-IIIa (100.00, 100.00, 7.90
123)
sat4 --> streptothricin N-acetyltransferase Sat4 (100.00, 100.00, 7.65432)
optrA --> ABC-F type ribosoma lprotection protein OptrA (99.90, 100.00, 3.7037)
fexA --> chloramphenicol/florfenicol lefflux MFS transporter FexA (99.65, 100.00, 3.4567
9)
dfrG --> trimethoprim-resistant dihydrofolate reductase DfrG (100.00, 97.59, 3.7037)
dfrE --> trimethoprim-resistant dihydrofolate reductase DfrE (97.37, 100.00, 9.87654)
tet(M) --> tetracycline resistance ribosoma lprotection protein Tet(M) (99.95, 100.00,
9.38272)
ii) Other resistance genes identified with a minimum cutoff of 60% nucleotide identity:
Gene --> Product ( Identity%, Coverage%)
tetB(60) --> tetracycline efflux ABC transporter Tet(60) subunit B ( 73.66, 10.46)
erm(A) --> 23S rRNA (adenine(2058)-N(6))-methyltransferase Erm(A) ( 87.16, 100.00)
vanR --> VanM-type vancomycin resistance DNA-binding response regulator VanR ( 68.37, 3
0.76)
tetA(46) --> tetracycline efflux ABC transporter Tet(46) subunit A ( 66.91, 15.54)
tetB(60) --> tetracycline efflux ABC transporter Tet(60) subunit B ( 71.61, 13.05)
msr(C) --> ABC-F type ribosoma lprotection protein Msr(C) ( 66.57, 22.79)
```

From WGS to laboratory result report

Method summary:

Extracted genomic DNA was sequenced by Illumina technology. Paired-end Illumina reads were assembled with SPAdes. Contigs below 200bp length and 2x coverage were removed. The assembled genome was analyzed for species MLST type, plasmid replicons and resistance genes using an in-house bioinformatic pipeline.

Assembly quality:

- Number of contigs: 88
- Assembly length (non-circular): 3002067bp
- Coverage: 69.0518x

Results:

a) **Species & MLST type** (based on <https://pubmlst.org/>)

efaecalis ST-16 4.49944 (Prevalence% of this ST among the particular species genomes in the NCBI GenBank as of March, 2019)

b) **Plasmid replicons and plasmid MLST** (based on PlasmidFinder <https://cge.cbs.dtu.dk/services/PlasmidFinder/>). This analysis is only applicable for Enterobacteriaceae and Gram positives. (p) stands for partial hits.

-rep9_1_repA(pAD1), rep6_1_repA(p703/5), rep9_4_repA2(pTEF2) (p)

c) Resistance genes (Based on PRJNA313047- Bacterial Antimicrobial Resistance Reference Gene Database)

i) **Resistance genes (identified with a minimum cutoff of 90% nucleotide identity and 90% coverage):**

Gene --> Product (Identity%, Coverage%, Prevalence% in this ST in the NCBI GenBank as of March, 2019)

ant(9)-Ia --> aminoglycoside nucleotidyltransferase ANT(9)-Ia (100.00, 100.00, 0.987654)

lsa(A) --> ABC-F type ribosoma lprotection protein Lsa(A) (98.93, 100.00, 9.87654)

aph(3')-IIIa --> aminoglycoside O-phosphotransferase APH(3')-IIIa (100.00, 100.00, 7.90123)

sat4 --> streptothricin N-acetyltransferase Sat4 (100.00, 100.00, 7.65432)

optFA --> ABC-F type ribosoma lprotection protein OptFA (99.90, 100.00, 3.7037)

fexA --> chloramphenicol/florfenicol efflux MFS transporter FexA (99.65, 100.00, 3.45679)

dfrG --> trimethoprim-resistant dihydrofolate reductase DfrG (100.00, 97.59, 3.7037)

dfrE --> trimethoprim-resistant dihydrofolate reductase DfrE (97.37, 100.00, 9.87654)

tet(M) --> tetracycline resistance ribosoma lprotection protein Tet(M) (99.95, 100.00, 9.38272)

ii) **Other resistance genes identified with a minimum cutoff of 60% nucleotide identity:**

Gene --> Product (Identity%, Coverage%)

tetB(60) --> tetracycline efflux ABC transporter Tet(60) subunit B (73.66, 10.46)

erm(A) --> 23S rRNA (adenine(2058)-N(6))-methyltransferase Erm(A) (87.16, 100.00)

vanR --> VanM-type vancomycin resistance DNA-binding response regulator VanR (68.37, 30.76)

tetA(46) --> tetracycline efflux ABC transporter Tet(46) subunit A (66.91, 15.54)

tetB(60) --> tetracycline efflux ABC transporter Tet(60) subunit B (71.61, 13.05)

msr(C) --> ABC-F type ribosoma lprotection protein Msr(C) (66.57, 22.79)

• The laboratory result report

- Species and MLST
- AMR-gene of question
- Geno- versus phenotype
- Epidemic potential
 - PubMed reference + other ...

• CASE

- *Enterococcus faecalis* ST16
- LRE: *optrA*-positive
- *E. faecalis* ST16 has previously been associated with transferable linezolid resistance (*optrA*) – Ref: *Hua R et al. Ann Lab Med 2019;39:35-42. DOI: 10.3343/alm.2019.39.1.36*
- Full report available upon request

Case report: MDR *E. coli* ST167

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Method summary:
Extracted genomic DNA was sequenced by Illumina technology. Paired-end Illumina reads
were assembled with SPAdes. Contigs below 200bp length and 2x coverage were removed.
The assembled genome was analyzed for species MLST type, plasmid replicons and
resistance genes using an in-house bioinformatic pipeline.

Assembly quality:
- Number of contigs: 192
- Assembly length (non-circular): 5177118bp
- Coverage: 145.478x

Results:
a) Species & MLST type (based on https://pubmlst.org/)
ecoli ST-167 0.723612 (Prevalence% of this ST among the particular species genomes
in the NCBI GenBank as of September, 2018)

b) Plasmid replicons and plasmid MLST ( based on PlasmidFinder https://cge.cbs.dtu.dk/
services/PlasmidFinder/ ). This analysis is only applicable for Enterobacteriaceae and
Gram positives. (p) stands for partial hits.
-IncY_1, IncX4_1, IncFIA_1, IncI1_1_Alpha(p), IncFIC(FII)_1(p), IncFII_1_pSFO(p)

c) Resistance genes (Based on PRJNA313047- Bacterial Antimicrobial Resistance Reference
Gene Database)

i) Resistance genes (identified with a minimum cutoff of 90% nucleotide identity and 90
% coverage):
Gene --> Product ( Identity%, Coverage%, Prevalence% in this ST in the NCBI GenBank as
of September, 2018)
erm(B) --> 23S rRNA (adenine(2058)-N(6))-methyltransferase Erm(B) (99.86, 100.00, 38.04
35)
blaCTX-M-15 --> class A extended-spectrum beta-lactamase CTX-M-15 (100.00, 100.00, 32.6
087)
blaOXA-1 --> oxacillin-hydrolyzing class D beta-lactamase OXA-1 (100.00, 100.00, 29.347
8)
blaEC-15 --> class C extended-spectrum beta-lactamase EC-15 (98.50, 100.00, 100)
blaCMY-42 --> class C extended-spectrum beta-lactamase CMY-42 (100.00, 100.00, 19.5652)
dfrA12 --> trimethoprim-resistant dihydrofolate reductase DfrA12 (100.00, 100.00, 26.08
7)
aadA2 --> ANT(3'')-Ia family aminoglycoside nucleotidyltransferase AadA2 (100.00, 100.0
0, 27.1739)
qacEdelta1 --> quaternary ammonium compound efflux SMR transporter QacE delta 1 (100.00
, 100.00, 90.2174)
sull1 --> sulfonamide-resistant dihydropteroate synthase Sull1 (100.00, 100.00, 81.5217)
ble --> bleomycin binding protein Ble-MBL (100.00, 100.00, 57.6087)
blaNDM-5 --> subclass B1 metallo-beta-lactamase NDM-5 (100.00, 100.00, 43.4783)
mph(A) --> Mph(A) family macrolide 2'-phosphotransferase (98.71, 100.00, 77.1739)
blaTEM-1 --> class A broad-spectrum beta-lactamase TEM-1 (100.00, 100.00, 55.4348)
rmtB1 --> 16S rRNA (guanine(1405)-N(7))-methyltransferase RmtB1 (100.00, 100.00, 21.739
1)
tet(A) --> tetracycline efflux MFS transporter Tet(A) (100.00, 100.00, 63.0435)
```

• Labreport

- *E. coli* ST167
- ESBL-CARBA-B NDM-5 confirmed
- In addition:
 - ESBL-A CTX-M-15
 - ESBL-M-C CMY-42
 - rmtB1 – transferable high-level broad-spectrum resistance towards aminoglycosides
- ST167 associated with MDR and NDM-5. Ref: Gronthal T et al. Euro Surveill 2018;23: DOI: 10.2807/1560-7917. ES.2018.23.27.1700497

Case report: *E. faecium* ST80

Method summary:

Extracted genomic DNA was sequenced by Illumina technology. Paired-end Illumina reads were assembled with SPAdes. Contigs below 200bp length and 2x coverage were removed. The assembled genome was analyzed for species MLST type, plasmid replicons and resistance genes using an in-house bioinformatic pipeline.

Assembly quality:

- Number of contigs: 383
- Assembly length (non-circular): 3110274bp
- Coverage: 48.6816x

Results:

a) Species & MLST type (based on <https://pubmlst.org/>)

E. faecium **ST-80** **14.2599 (Prevalence%)** of this ST among the particular species genomes in the NCBI GenBank as of September, 2018)

b) Plasmid replicons and plasmid MLST (based on PlasmidFinder <https://cge.cbs.dtu.dk/services/PlasmidFinder/>). This analysis is only applicable for Enterobacteriaceae and Gram positives. (p) stands for partial hits.

-rep17_1_CDS29(pRUM), repUS15_ORF(*E. faecium*287), rep2_1_ORF(*E. faecium*Contig1183)_JDOE, rep18_2_repA(pEF418), rep11_1_repA(pB82), rep14_3_ORF(pRI1)(p), rep6_1_repA(p703/5)(p)

c) Resistance genes (Based on PRJNA313047- Bacterial Antimicrobial Resistance Reference Gene Database)

i) Resistance genes (identified with a minimum cutoff of 90% nucleotide identity and 90% coverage):

Gene --> Product (Identity%, Coverage%, Prevalence% in this ST in the NCBI GenBank as of September, 2018)

cfr(B) --> 23S rRNA (adenine(2503)-C(8))-methyltransferase Cfr(B) (99.91, 100.00, -)

dfrG --> trimethoprim-resistant dihydrofolate reductase DfrG (100.00, 100.00, 87.9747)

vanS --> VanA-type vancomycin resistance histidine kinase VanS (100.00, 100.00, 80.3797)

vanR --> VanA-type vancomycin resistance DNA-binding response regulator VanR (100.00, 100.00, 80.3797)

vanH-A --> D-lactate dehydrogenase VanH-A (100.00, 100.00, 78.481)

vanA --> D-alanine--(R)-lactate ligase VanA (99.90, 100.00, 77.8481)

vanX-A --> D-Ala-D-Ala dipeptidase VanX-A (100.00, 100.00, 78.481)

vanY-A --> D-Ala-D-Ala carboxypeptidase VanY-A (99.89, 99.89, 77.2152)

vanZ-A --> glycopeptide resistance protein VanZ-A (100.00, 100.00, 76.5823)

aac(6') --> aminoglycoside N-acetyltransferase AAC(6')-Ii (100.00, 100.00, 100)

msr(C) --> ABC-F type ribosome lprotection protein Msr(C) (98.99, 100.00, 100)

eat(A) --> Lsa family ABC-F type ribosome lprotection protein (100.00, 100.00, 44.9367)

erm(B) --> 23S rRNA (adenine(2058)-N(6))-methyltransferase Erm(B) (99.86, 100.00, 80.3797)

aph(3')-IIIa --> aminoglycoside O-phosphotransferase APH(3')-IIIa (100.00, 100.00, 75.3165)

sat4 --> streptothricin N-acetyltransferase Sat4 (100.00, 100.00, 62.6582)

ant(6)-Ia --> aminoglycoside nucleotidyltransferase ANT(6)-Ia (100.00, 100.00, 68.9873)

• Labreport:

- *E. faecium* ST80
- The *vanA* operon consistent with a VanA-type vancomycin resistance
- ST80 is considered a hospital adapted clone associated with MDR including VanA-type VRE. Ref: Zhou et al. J Antimicrobial Chemother 2018;73:3259-67. DOI:10.1093/jac/dky349.

Case report: *P. aeruginosa* ST235

Method summary:

Extracted genomic DNA was sequenced by Illumina technology. Paired-end Illumina reads were assembled with SPAdes. Contigs below 200bp length and 2x coverage were removed. The assembled genome was analyzed for species MLST type, plasmid replicons and resistance genes using an in-house bioinformatic pipeline.

Assembly quality:

- Number of contigs: 236
- Assembly length (non-circular): 7038765bp
- Coverage: 55.1211x

Results:

a) Species & MLST type (based on <https://pubmlst.org/>)

paeruginosa **ST-235** **4.49903** (Prevalence% of this ST among the particular species genomes in the NCBI GenBank as of March, 2019)

b) Plasmid replicons and plasmid MLST (based on PlasmidFinder <https://cge.cbs.dtu.dk/services/PlasmidFinder/>). This analysis is only applicable for Enterobacteriaceae and Gram positives. (p) stands for partial hits.

c) Resistance genes (Based on PRJNA313047- Bacterial Antimicrobial Resistance Reference Gene Database)

i) Resistance genes (identified with a minimum cutoff of 90% nucleotide identity and 90 % coverage):

Gene --> Product (Identity%, Coverage%, Prevalence% in this ST in the NCBI GenBank as of March, 2019)

ant(2'')-Ia --> aminoglycoside nucleotidyltransferase ANT(2'')-Ia (100.00, 100.00, 2.24 558)

qacF --> quaternary ammonium compound efflux SMR transporter QacF (100.00, 100.00, 0.19 1113)

fosA --> FosA family fosfomycin resistance glutathione transferase (99.02, 100.00, 8.83 899)

aph(3')-IIb --> aminoglycoside O-phosphotransferase APH(3')-IIb (98.76, 100.00, 8.79121)

blaPDC-35 --> class C beta-lactamase PDC-35 (100.00, 100.00, 8.6001)

blaOXA-488 --> OXA-50 family oxacillin-hydrolyzing class D beta-lactamase OXA-488 (99.8 7, 100.00, 8.83899)

catB7 --> type B-4 chloramphenicol acetyltransferase CatB7 (98.75, 100.00, 8.64787)

qacEdelta1 --> quaternary ammonium compound efflux SMR transporter QacE delta 1 (100.00 , 100.00, 9.50788)

sul1 --> sulfonamide-resistant dihydropteroate synthase Sull (100.00, 100.00, 8.69565)

aph(3')-VI --> APH(3')-VI family aminoglycoside O-phosphotransferase (100.00, 100.00, 0 .143335)

blaNDM-1 --> subclass B1 metallo-beta-lactamase NDM-1 (100.00, 100.00, -)

sul1 --> sulfonamide-resistant dihydropteroate synthase Sull (99.88, 100.00, 8.69565)

aac(6')-II --> aminoglycoside N-acetyltransferase AAC(6')-II (100.00, 100.00, 1.29001)

aadA6 --> ANT(3'')-Ia family aminoglycoside nucleotidyltransferase AadA6 (100.00, 100.0 0, 5.44673)

• Lab-report:

- *P. aeruginosa* ST235
- ESBL-CARBA-B NDM-1 confirmed
- ST235 is a well-known global clone associated with MDR. Ref: Genome Biol Evol 2017;9:3238-45. DOI:10.1093/gbe/evx243.

Case report: *K. pneumoniae* ST392

Method summary:

Extracted genomic DNA was sequenced by Illumina technology. Paired-end Illumina reads were assembled with SPAdes. Contigs below 200bp length and 2x coverage were removed. The assembled genome was analyzed for species MLST type, plasmid replicons and resistance genes using an in-house bioinformatic pipeline.

Assembly quality:

- Number of contigs: 109
- Assembly length (non-circular): 5590929bp
- Coverage: 162.527x

Results:

a) Species & MLST type (based on <https://pubmlst.org/>)

kpneumoniae **ST-392** **0.436535** (Prevalence% of this ST among the particular species genomes in the NCBI GenBank as of September, 2018)

b) Plasmid replicons and plasmid MLST (based on PlasmidFinder <https://cge.cbs.dtu.dk/services/PlasmidFinder/>). This analysis is only applicable for Enterobacteriaceae and Gram positives. (p) stands for partial hits.

-IncL/M(pOXA-48)_1_pOXA-48, IncFIB(K)_1_Kpn3, IncFII(pHN7A8)_1_pHN7A8(p), IncFII_1_pKP9_1(p), ColRNAI_1(p), ColRNAI_1(p)

c) Resistance genes (Based on PRJNA313047- Bacterial Antimicrobial Resistance Reference Gene Database)

i) Resistance genes (identified with a minimum cutoff of 90% nucleotide identity and 90% coverage):

Gene --> Product (Identity%, Coverage%, Prevalence% in this ST in the NCBI GenBank as of September, 2018)

fosA --> FosA family fosfomycin resistance glutathione transferase (98.79, 98.33, 100)
oqxA6 --> multidrug efflux RND transporter periplasmic adaptor subunit OqxA6 (99.83, 100.00, 100)

oqxB19 --> multidrug efflux RND transporter permease subunit OqxB19 (99.11, 100.00, 100)

blaTEM-1 --> class A broad-spectrum beta-lactamase TEM-1 (100.00, 100.00, 76.9231)

aph(6)-Id --> aminoglycoside O-phosphotransferase APH(6)-Id (100.00, 100.00, 80.7692)

aph(3'')-Ib --> aminoglycoside O-phosphotransferase APH(3'')-Ib (100.00, 91.97, 76.9231)

qnrB1 --> quinolone resistance pentapeptide repeat protein QnrB1 (100.00, 100.00, 84.6154)

dfrA14 --> trimethoprim-resistant dihydrofolate reductase DfrA14 (100.00, 100.00, 96.1538)

tet(A) --> tetracycline efflux MFS transporter Tet(A) (100.00, 100.00, 73.0769)

aac(3)-IIa --> aminoglycoside N-acetyltransferase AAC(3)-IIa (99.77, 100.00, 61.5385)

blaOXA-48 --> carbapenem-hydrolyzing class D beta-lactamase OXA-48 (100.00, 100.00, 19.2308)

blaOXA-1 --> oxacillin-hydrolyzing class D beta-lactamase OXA-1 (100.00, 100.00, 92.3077)

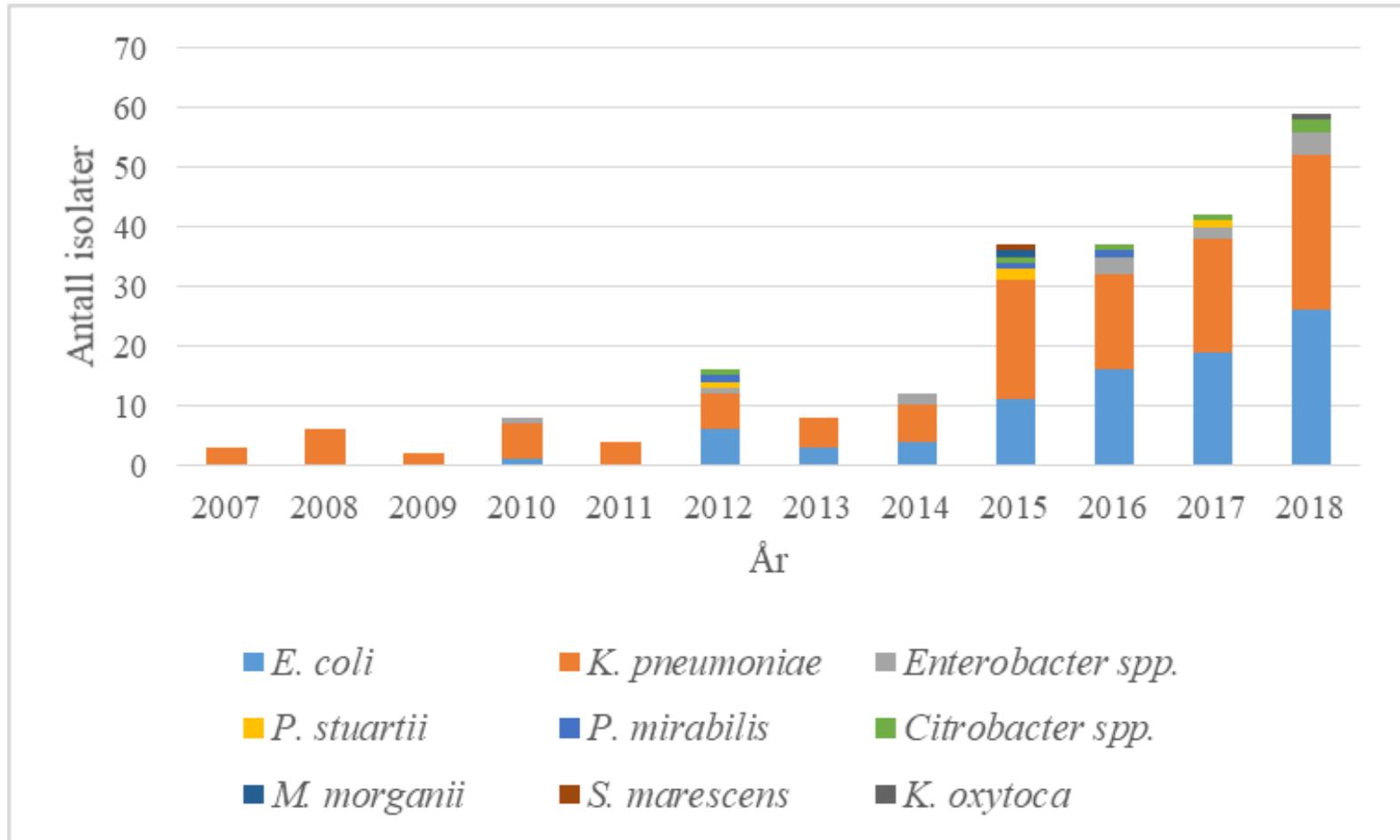
blaCTX-M-15 --> class A extended-spectrum beta-lactamase CTX-M-15 (100.00, 100.00, 115.385)

blaSHV-11 --> class A broad-spectrum beta-lactamase SHV-11 (99.77, 100.00, 96.1538)

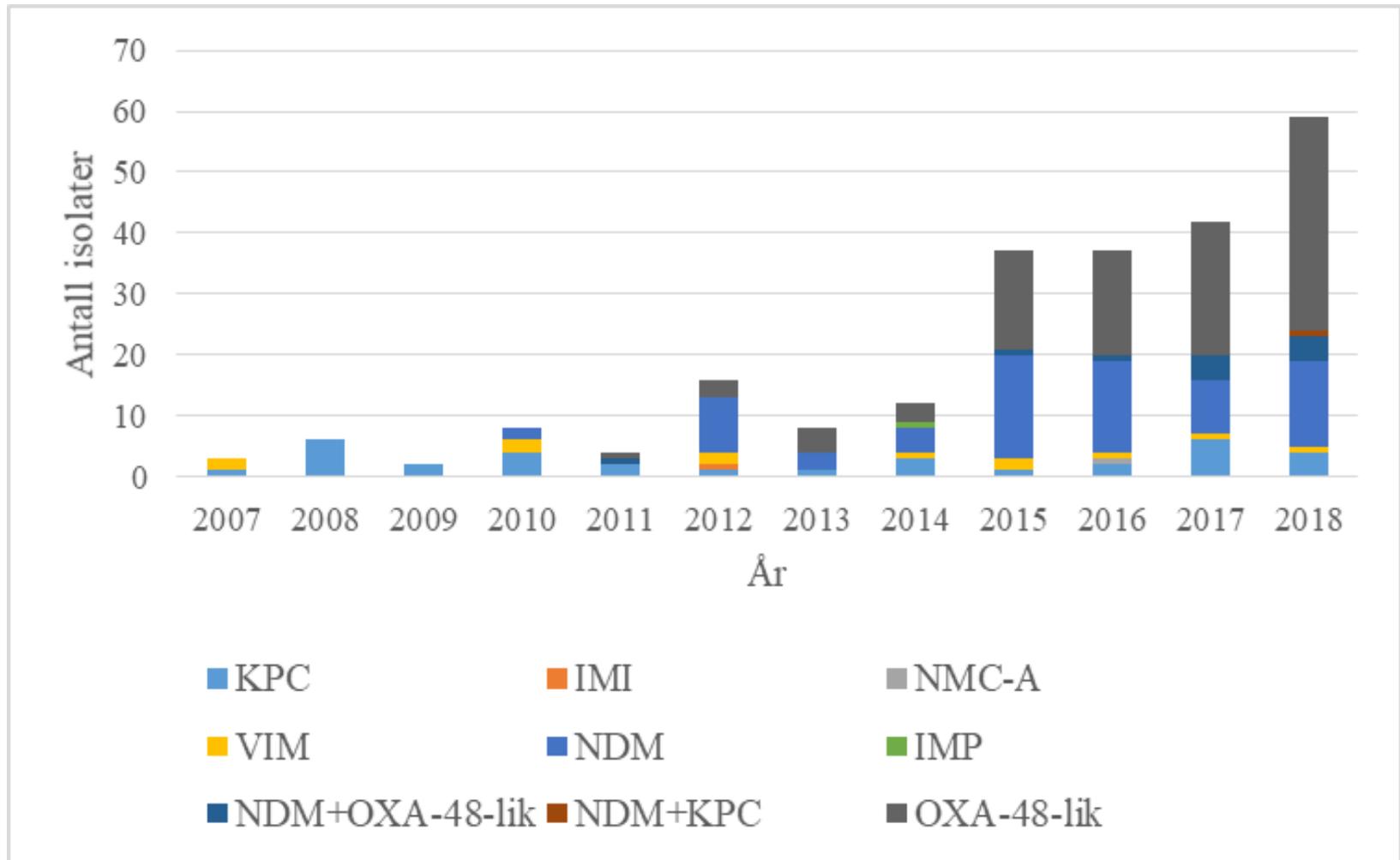
• Lab-report:

- *K. pneumoniae* ST392
- ESBL-CARBA-D OXA-48
- In addition:
 - ESBL-A CTX-M-15
 - qnrB1 – transferable quinolone resistance
 - Epidemic IncL/M (pOXA48) plasmid
- ST392 OXA-48 is associated with travellers returning from and having been hospitalised in Gran Canari, Spain in 2018. Ref: ECDC report 2018

Carbapenemase-producing *Enterobacterales* (CRE) Norway 2018- report (n=59 strains from 54 patients)



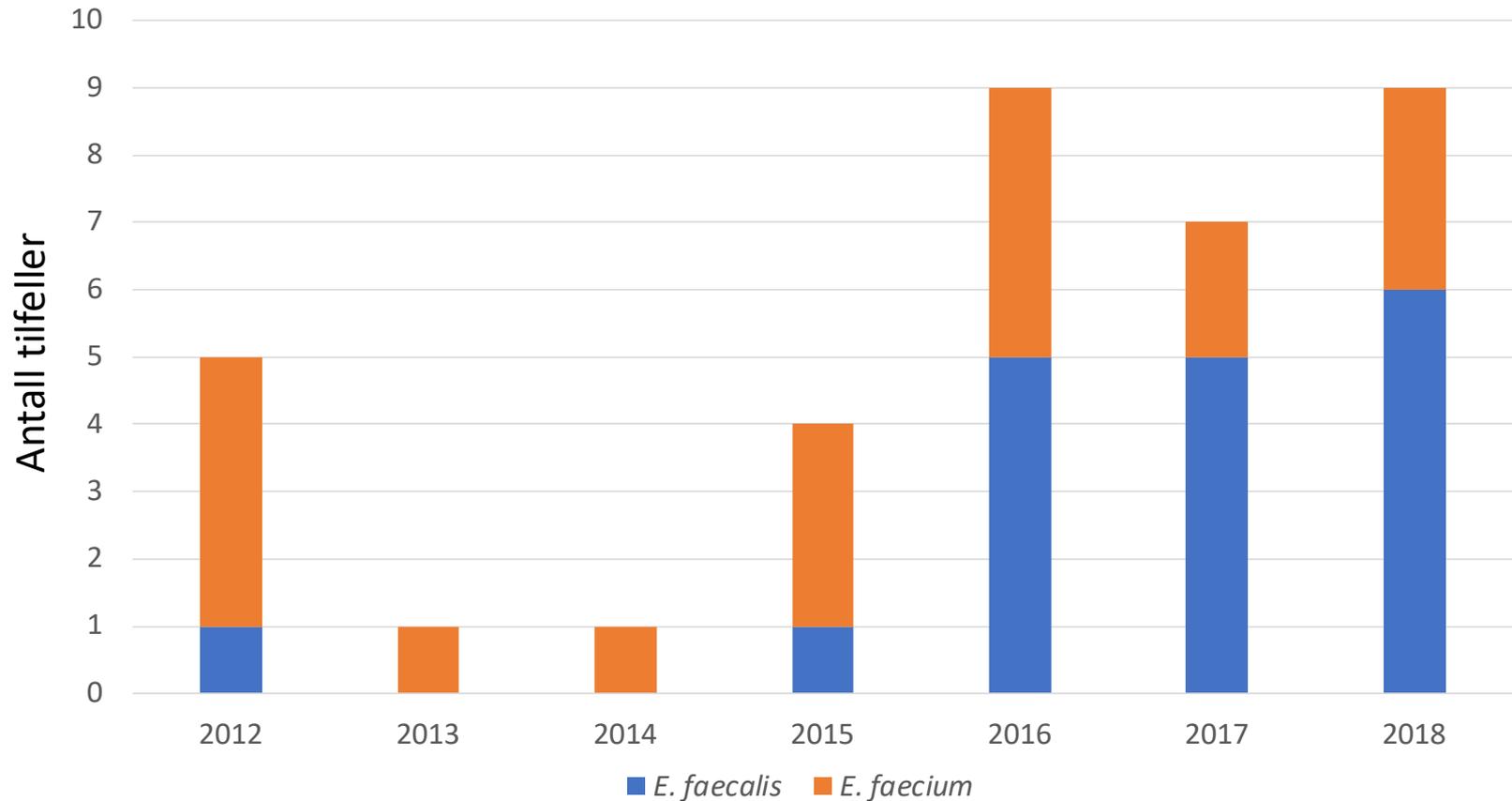
CRE Norway 2018 - report



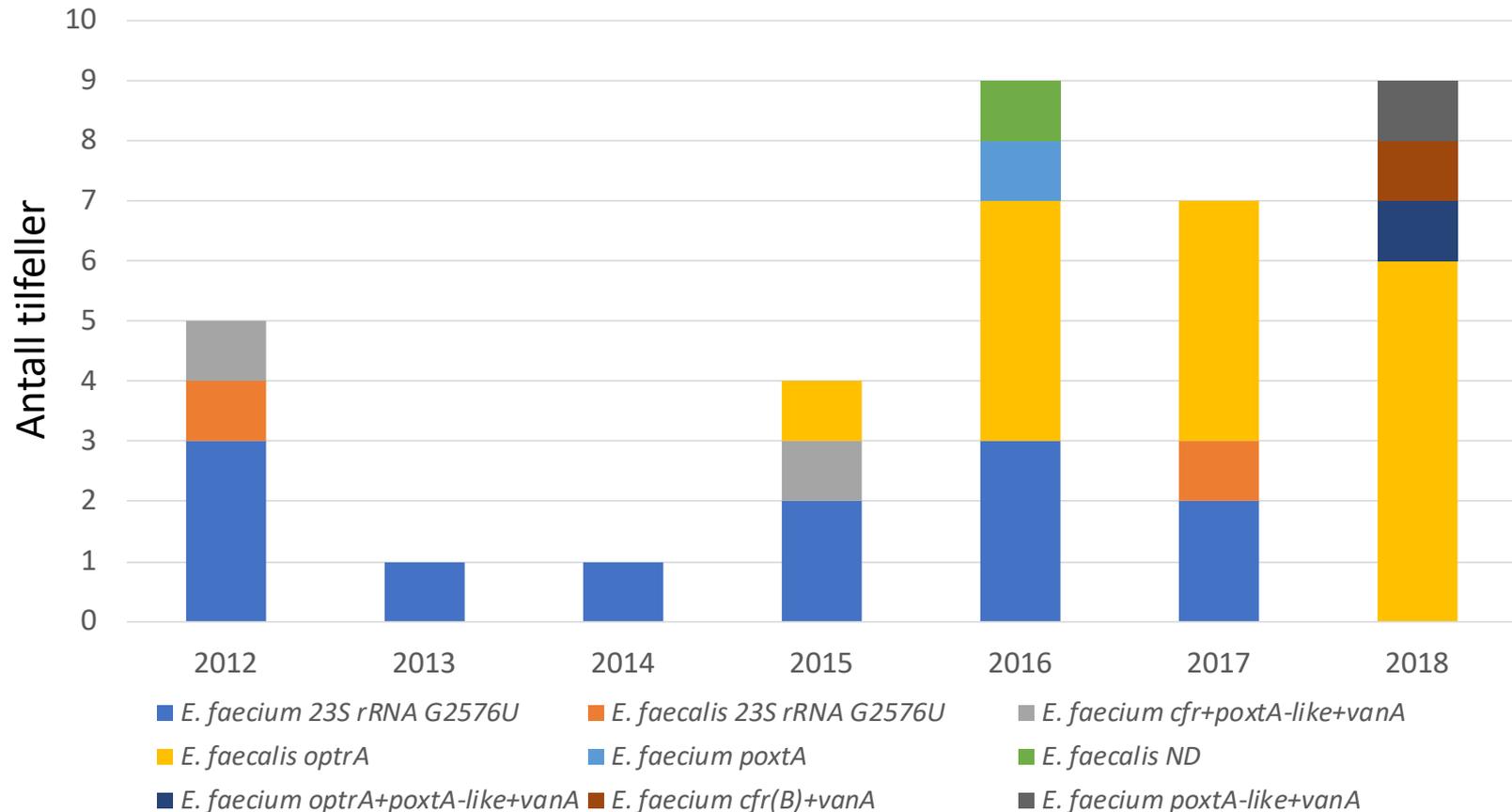
WGS-data linked to epidemiology (MSIS): no suspicion of patient-to-patient transmission of CRE in Norway in 2018

LRE Norway 2018 – report

(n=9 strains from 9 patients)



LRE Norway 2018 – report

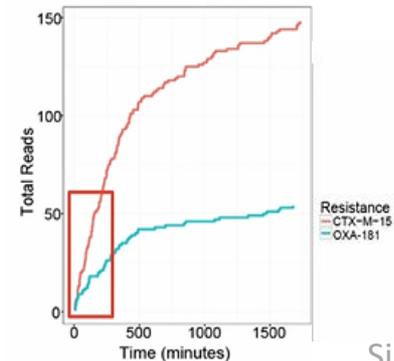


WGS-data linked to epidemiology (MSIS): no suspicion of patient-to-patient transmission of LRE in Norway in 2018

Oxford Nanopore Technology - evaluation

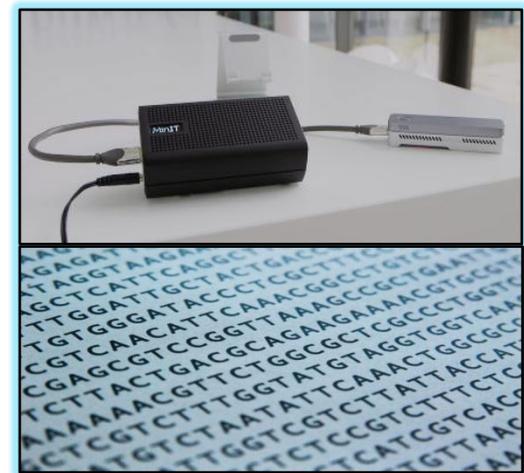
Aims:

- Internal validation study
- Rapid identification of microbe, resistance-virulence-clonal markers
 - flexible and in real-time
- Identify variants of resistance determinants and their support
 - plasmids and other mobile elements
- Molecular epidemiology
 - Phylogenetic analyses



Sample	OXA-181 detection time	CTX-M-15 detection time
4	4.8 min	2.8 min
8	10.3 min	3.6 min
9	10.73 min	9.37 min
10	0.99 min	1.00 min
12	13.07 min	6.04 min

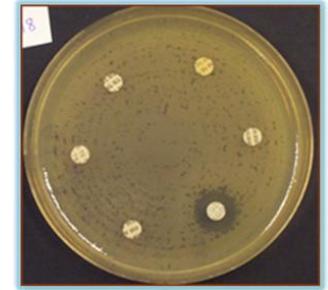
Simner *et al*, 2018, JAC



Perspectives

- Broad implementation of sequence technology and bioinformatics
- Quality control aspects
- Integration i LIS, databases and privacy aspects
- Pheno- versus genotype AST
 - The quality of biocuration – databases
 - Organize and make biological information accessible
 - Robust, well-funded institutions
 - Databases combining genotypic and phenotypic data
 - Shift from AMR genotype to prediction of AMR phenotype

Thanks to K-RES



MDs:



Administrative head:



Bioinformatician:



PhDs:



Biomedical laboratory technicians:



Postdoc and students

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- Norwegian Ministry of Health and Care Services
- Northern Norway Regional Health Authority



- University Hospital of North Norway



- Research grants
- UiT



Thanks

