

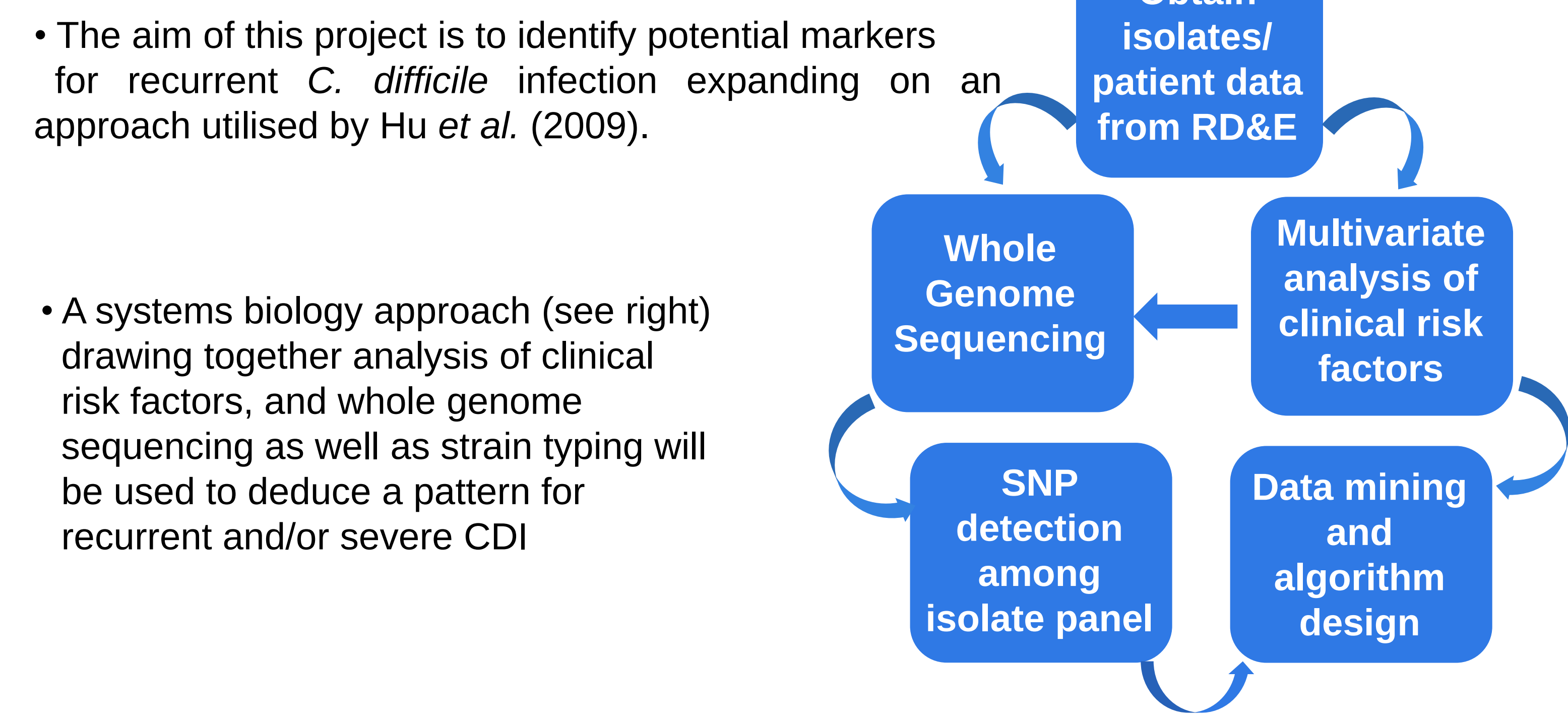
Modelling recurrent *Clostridium difficile* infection through whole genome sequencing



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Clostridium difficile is a Gram positive, anaerobic, spore forming, rod shaped bacterium, associated with nosocomial infection. Symptoms of infection range from asymptomatic carriage, mild diarrhoea and from moderate to fulminant pseudomembranous colitis (PMC). One of the most difficult challenges faced when dealing with *C. difficile* infection (CDI) is prediction and treatment of patients with recurrent infection, which occurs in approximately 20% of patients following withdrawal of antibiotics.

Introduction



Ribotyping *C. difficile* Isolates

- Data for this study was obtained from the Royal Devon and Exeter hospital between 2007-2009. A panel of 51 patients were identified as having recurrent CDI.
- Two new ribotypes (*) were identified

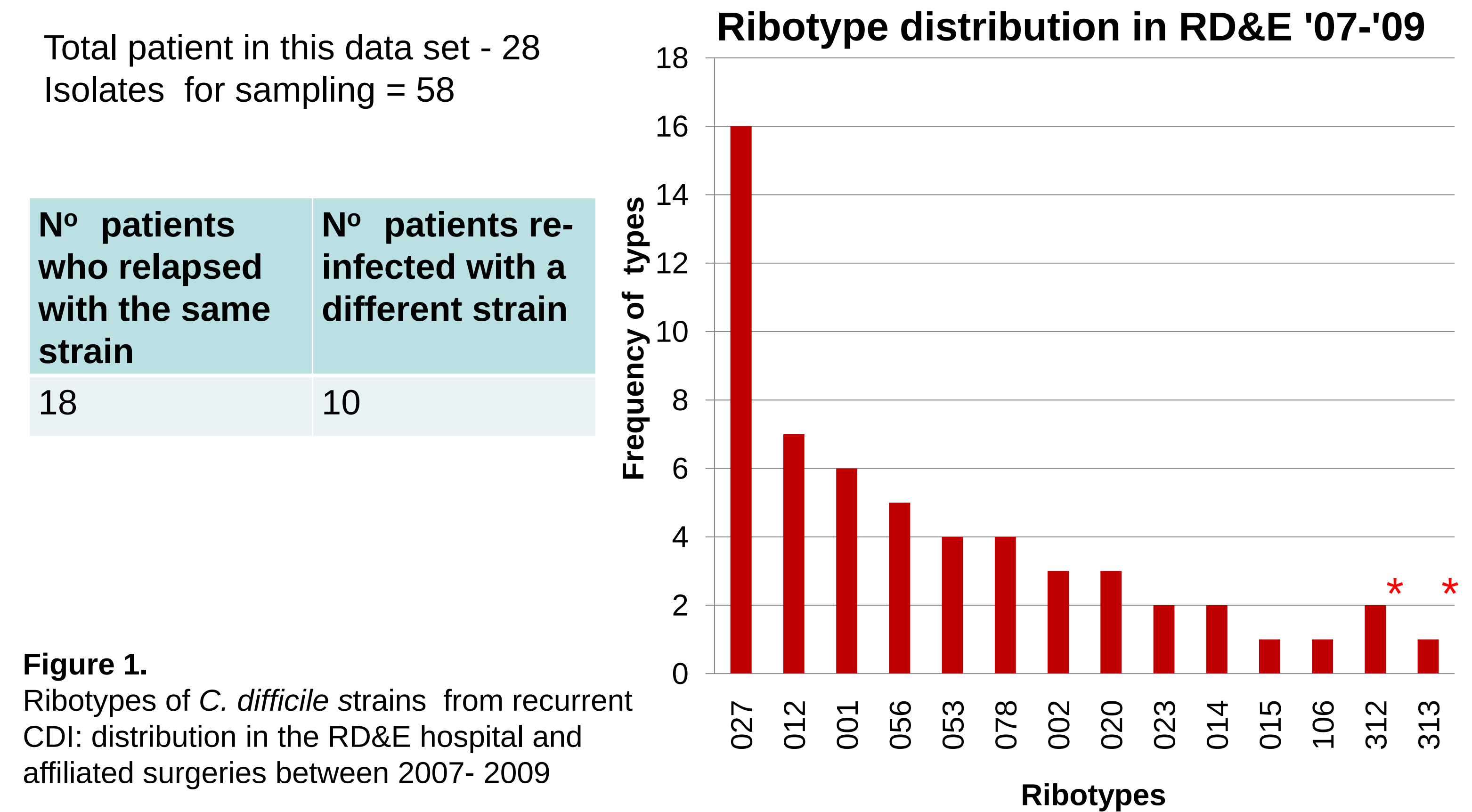


Figure 1. Ribotypes of *C. difficile* strains from recurrent CDI: distribution in the RD&E hospital and affiliated surgeries between 2007- 2009

Whole Genome Sequencing

- Whole genome sequence was determined for two *C. difficile* strains (both ribotype 002) isolated from a patient with recurrent CDI. (primary (1°) and secondary isolates (2°))
- A SNP was detected at position 652332bp in CD0547 in the 2° isolate (Fig 2) within CD0547 which encodes a 119 amino acids (aa) protein that has been annotated as a putative penicillin binding protein.

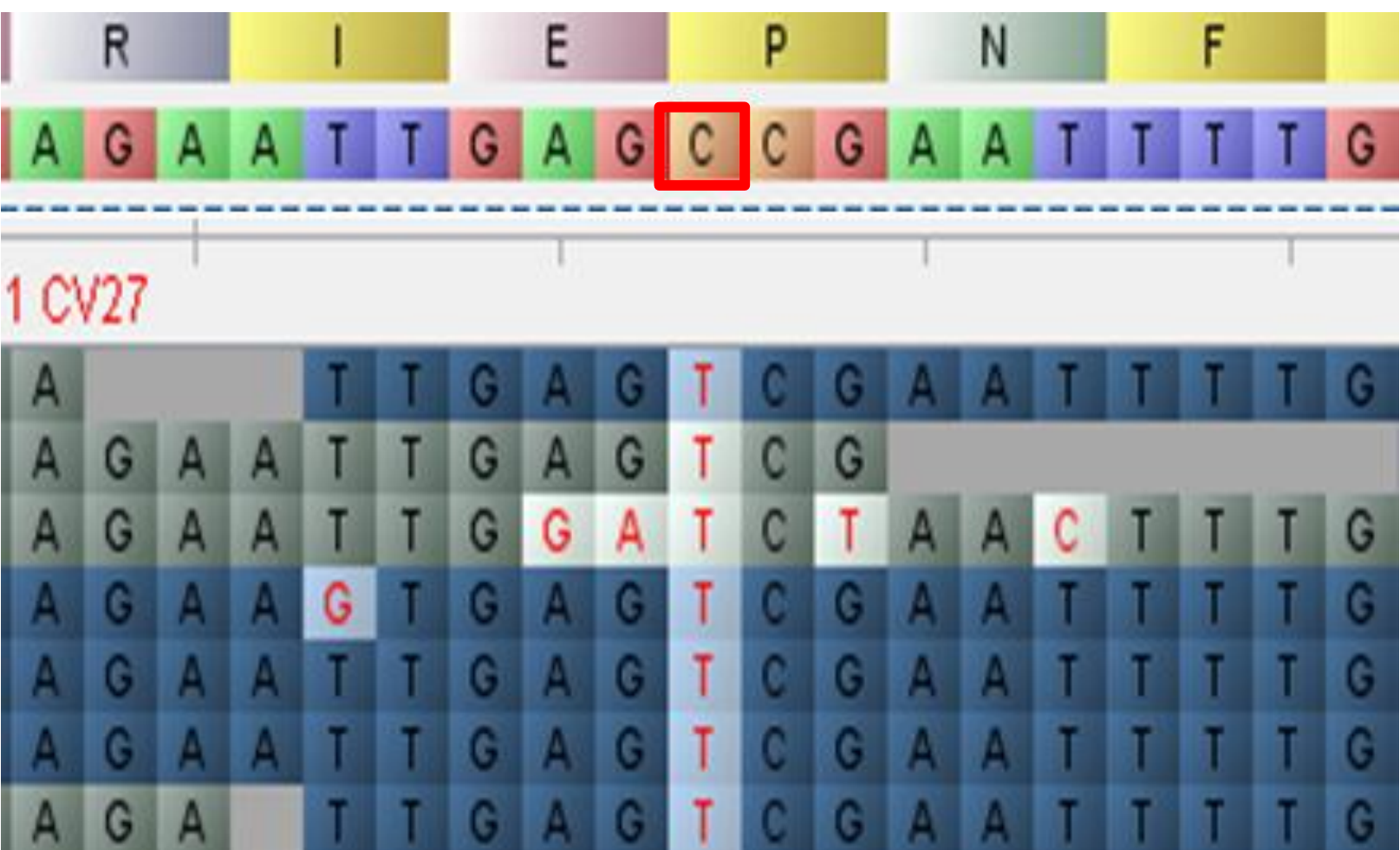


Figure 2 – Visualisation (Tablet, SCRI) of SNP called at position 652332 bp in the 2° isolate. Small highlighted C base represents reference base in *C. diff* 630

- MecI* is located within an operon (Fig 3) including *MecA* which is involved in methicillin antibiotic resistance of *Staphylococcus aureus*.
- MecI* represses activity of *MecA* when *MecA* is not under the control of *MecR* and mutations in the *MecI* (*) gene are known to infer methicillin resistance in *Staphylococcus aureus*.

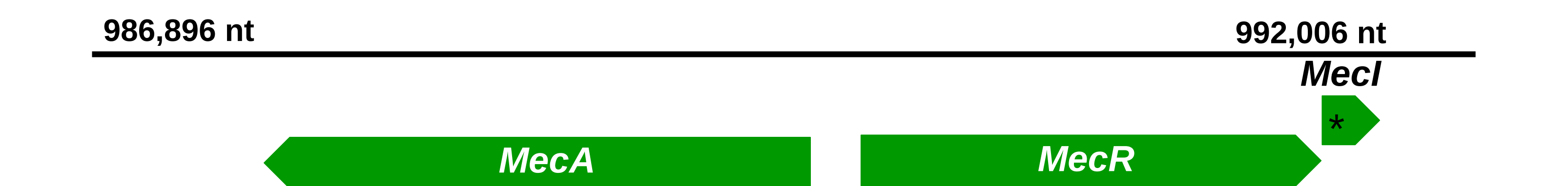


Figure 3- Organisation of the *MecA* operon of *Staphylococcus aureus*.

Conclusion

- In this collection of isolates 027 is the dominant ribotype.
- Among this cohort two new ribotypes were identified and could signify a shift in selective pressure for *C. difficile*.
- A SNP occurred within a gene putatively involved in antibiotic resistance and may confer a selective advantage enabling this strain to adapt to the host environment within the period between the 1° and 2° infection

Future work

- Coupling patient and isolate, clinical and genetic data could lead to a better understanding of recurrent CDI.

Acknowledgements

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