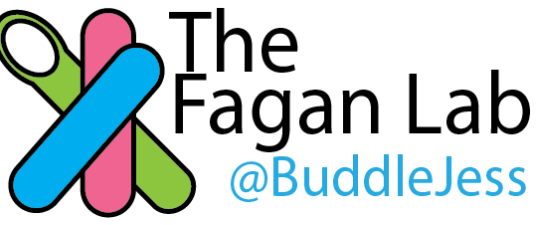


The Enchanted Journey: Unravelling the Secrets of Vancomycin Resistance in *C. difficile*

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Once upon a time...

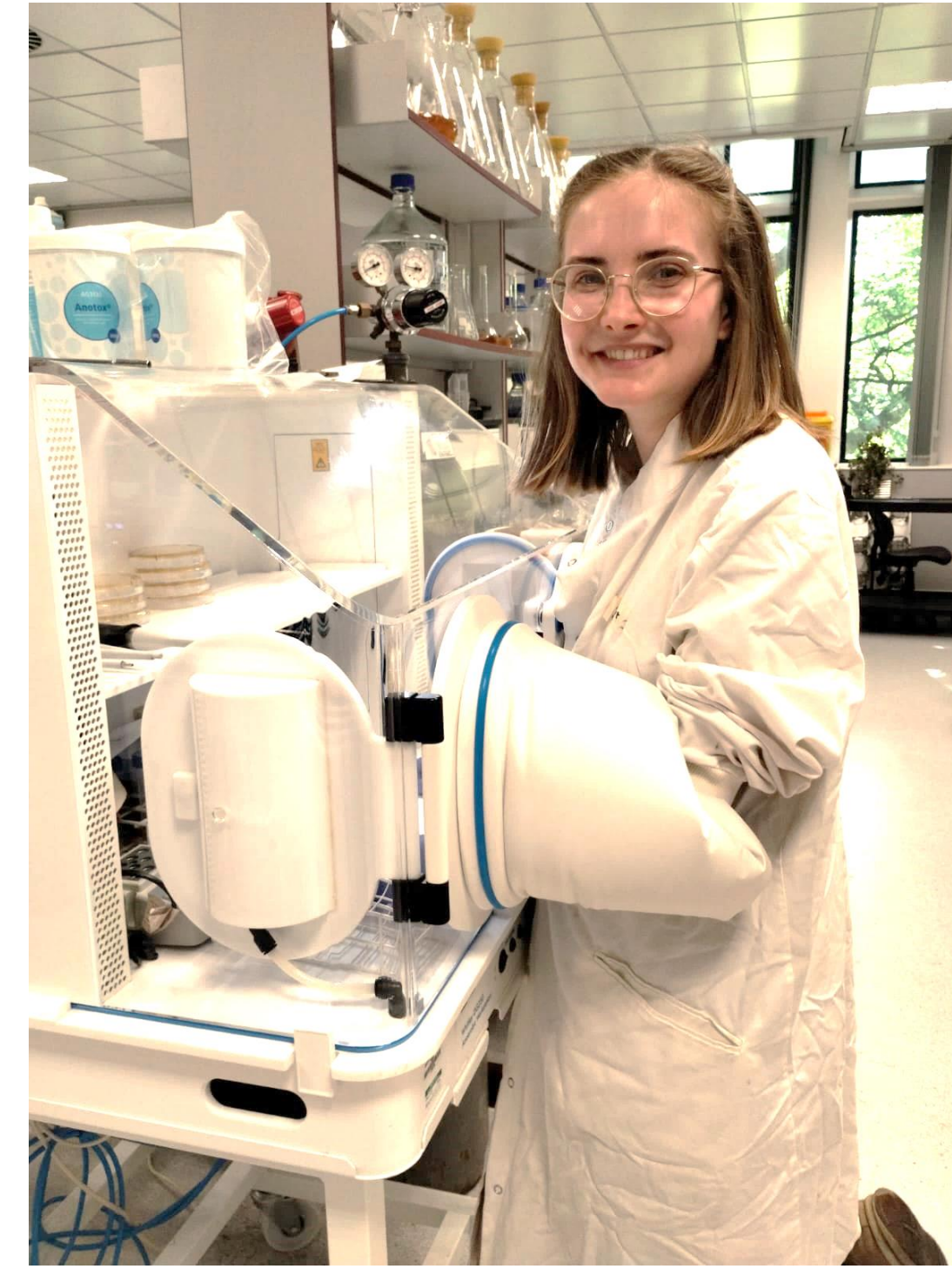
...there was a superbug, named *C. difficile*, capable of causing disease and death.

C. difficile was strong – resistant to many weapons the humans had designed to kill it.

In the UK, the only weapon used to kill *C. difficile* was **vancomycin...**

...The humans knew, in years to come, *C. difficile* would eventually become resistant to vancomycin too.

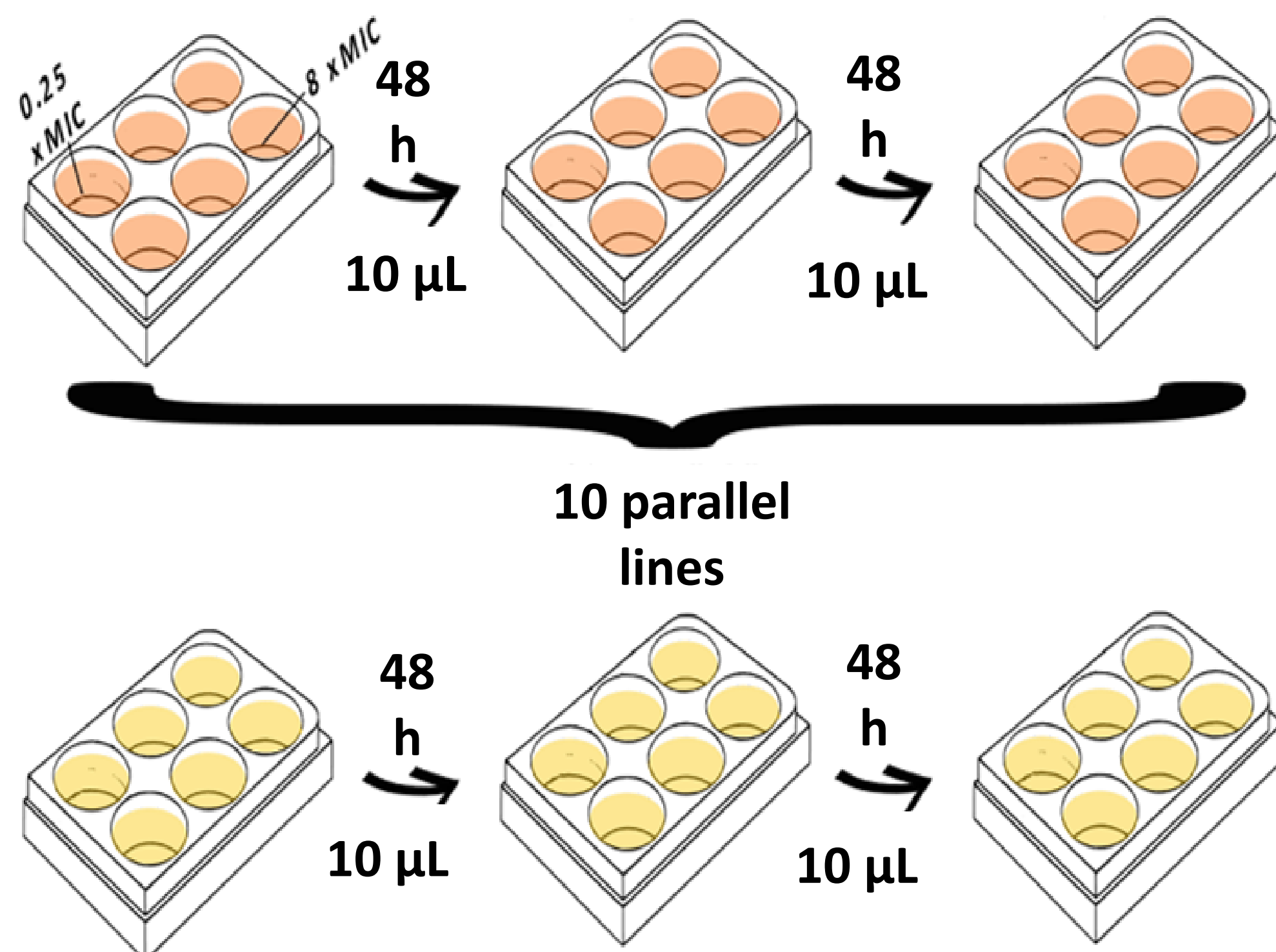
The only way to prevent this happening, **was to better understand vancomycin resistance in *C. difficile* – the mutations involved in resistance, and whether by gaining resistance, *C. difficile* became weaker.**



A brave microbiologist called Jess decided to take on this quest. She knew that by evolving resistance to *C. difficile* in the laboratory, and sequencing the *C. difficile* genome, she could understand more...

...She first made *C. difficile* non-pathogenic...

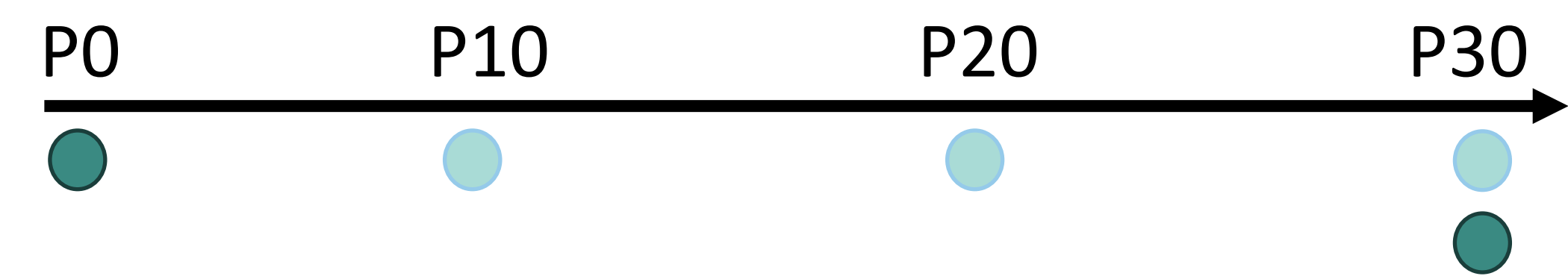
...then she evolved resistance to vancomycin:



Evolution plates – repeat for 30 passages

Control wells passaged in parallel

● Isolates sequenced
● Populations sequenced



...and sequenced individuals and populations.

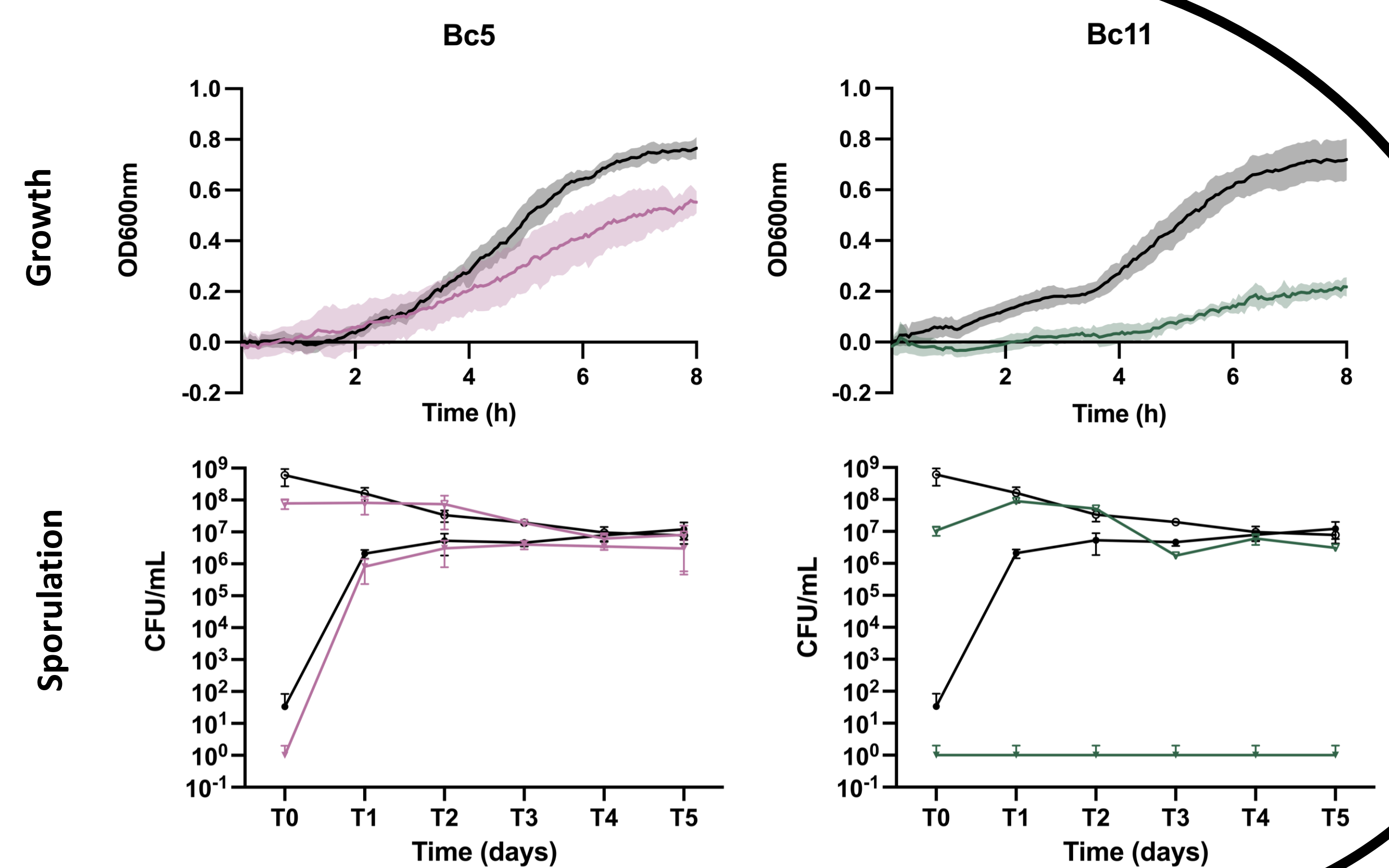
As suspected, *C. difficile* was strong – it became resistant to the powers of vancomycin quickly:

	Evolutionary line	End point MIC (µg/mL)
WT	Ancestral	1
	Bc1	32
	Bc2	16
	Bc3	16
	Bc4	16
	Bc5	32
Hypermutator	Bc7	32
	Bc8	32
	Bc9	32
	Bc10	32
	Bc11	32

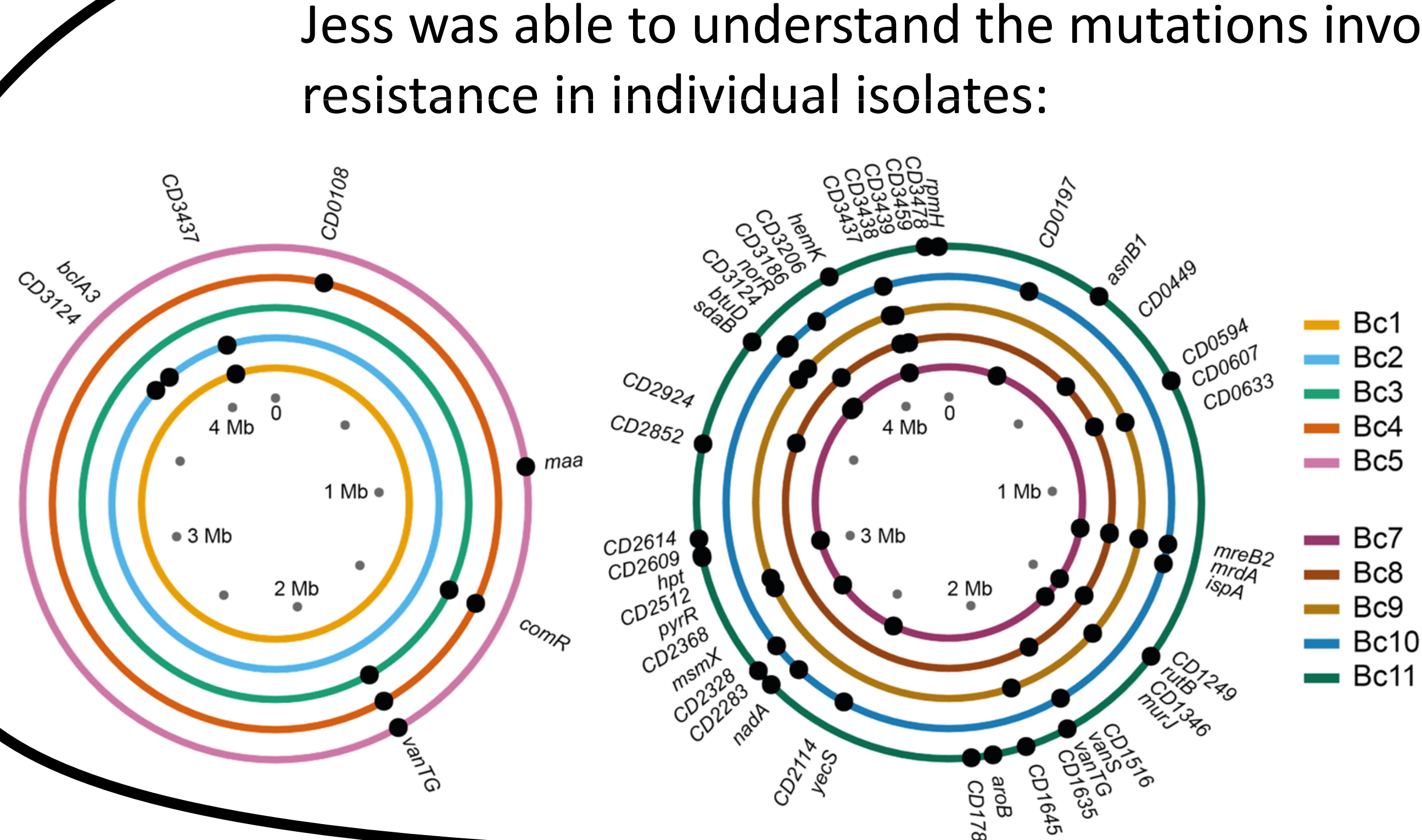
But with great power...

...came great fitness burdens.

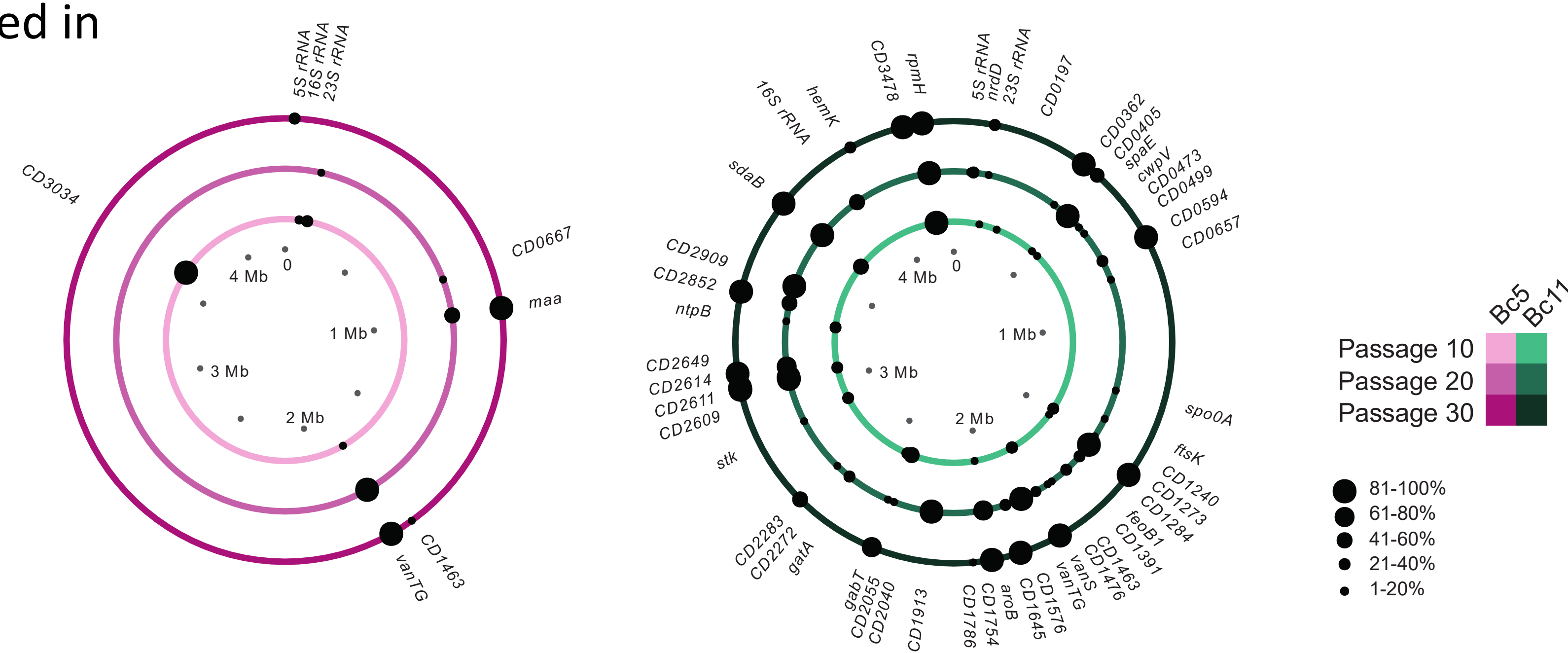
C. difficile showed reduced growth and sporulation compared to its susceptible ancestor.



With the help of genomics and bioinformatic analysis, Jess was able to understand the mutations involved in resistance in individual isolates:



...and in whole populations.



She is now validating mutations of interest to understand their contribution to resistance and fitness...

...The end.

