Resistance to Beta-Lactams in *Staphylococcus aureus*

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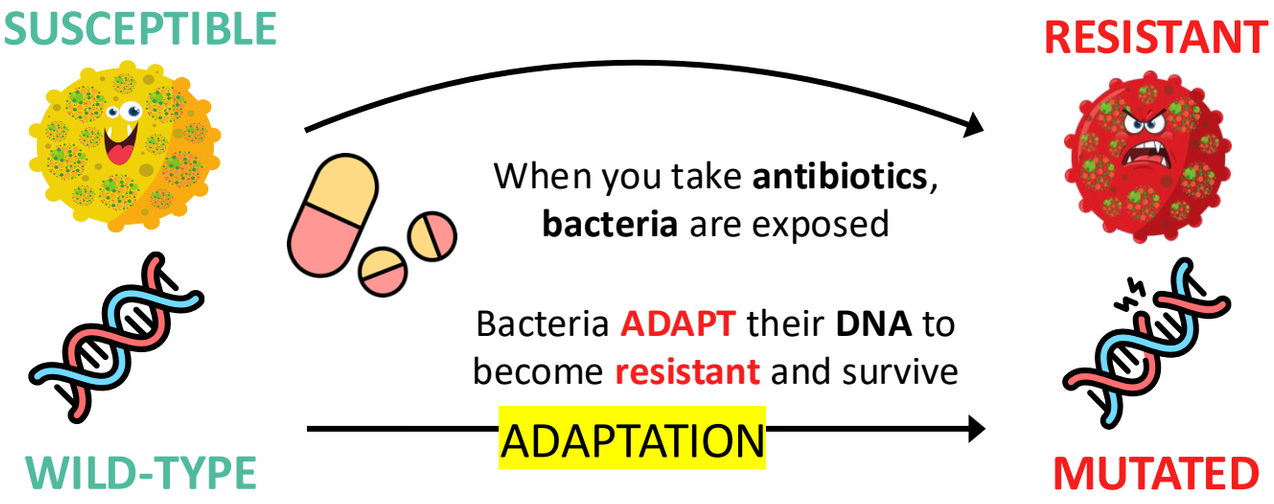
Background

- Increasing resistance rates → **fewer antibiotic available** for resistant infections

- *Staphylococcus aureus* bacteraemia treated with beta-lactams → Need to investigate **which mutations cause beta-lactam resistance**



Aim & Hypothesis

A: Generate resistant bacteria after beta-lactam exposure and identify **mutations** responsible for beta-lactam resistance.

H: During beta-lactam exposure, *Staphylococcus aureus* accumulate DNA mutations, which make it **genetically different and more resistant** than susceptible bacteria.

Methods

- Infection Stage: expose **susceptible bacteria to beta-lactams** to generate resistant bacteria.

- Bioinformatic Stage:

1. **DNA extraction** (both susceptible and resistant bacteria)
2. **Whole genome sequ**encing (reads)
3. **Quality Control** of reads
4. **Assembly** of reads into complete DNA (assembly)
5. **Variant Calling** between susceptible and resistant bacteria

Results

Mutation	Gene	Type	Effect	AA Pos	Nucleotide Change
H499D, H499Q	pbp1	Substitution	Non-synonymous	499	1495C>G, 1497C>A
S746Y, S746F	rpoB	Substitution	Non-synonymous	746	2237C>A, 2237C>T

Mutations in *pbp1* and *rpoB* genes detected only in resistant *Staphylococcus aureus* (not in susceptible bacteria). Mutated genes lead to **mutated proteins**, which are **not recognized by antibiotics**.

Key Takeaway

Bacteria with mutations (and mutated proteins) are resistant to antibiotics. If we know in which genes mutations are more likely to occur, we can look for them and predict which bacteria are likely to be resistant, improving correct diagnosis and treatment.