

Translational Accuracy Regulates Competence in *Streptococcus pneumoniae*

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Wong Kai Yi, Chris
Supervisor: Prof. Margaret Ip
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Competence in *Streptococcus pneumoniae*

- Take up extracellular DNA from its environment
- Example of bacterial quorum sensing
- In response to accumulation of secreted peptide pheromone
- Induces expression of proteins for transformation
- Production of chaperones and proteases

Competence regulated by accuracy of protein synthesis

- Respond to changes in accuracy of protein synthesis

- Mutations in ribosome
- Exposure to antibiotics

- ↑ translational error rate



↑ competence

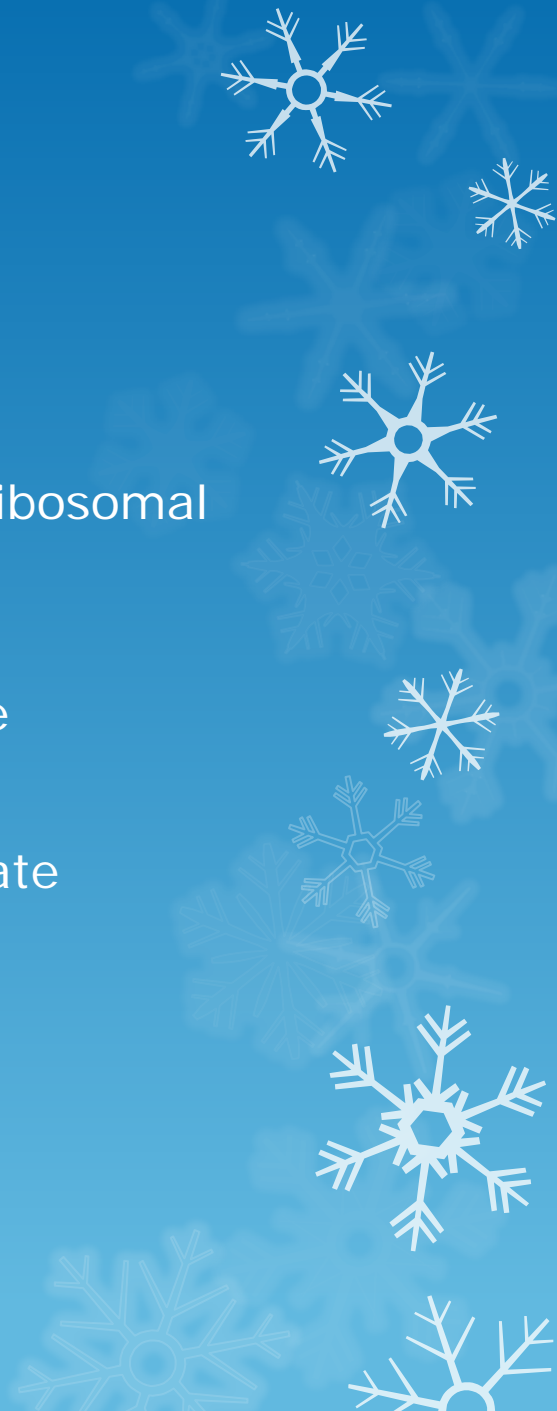
- ↓ decoding error rate below baseline level



↓ competence

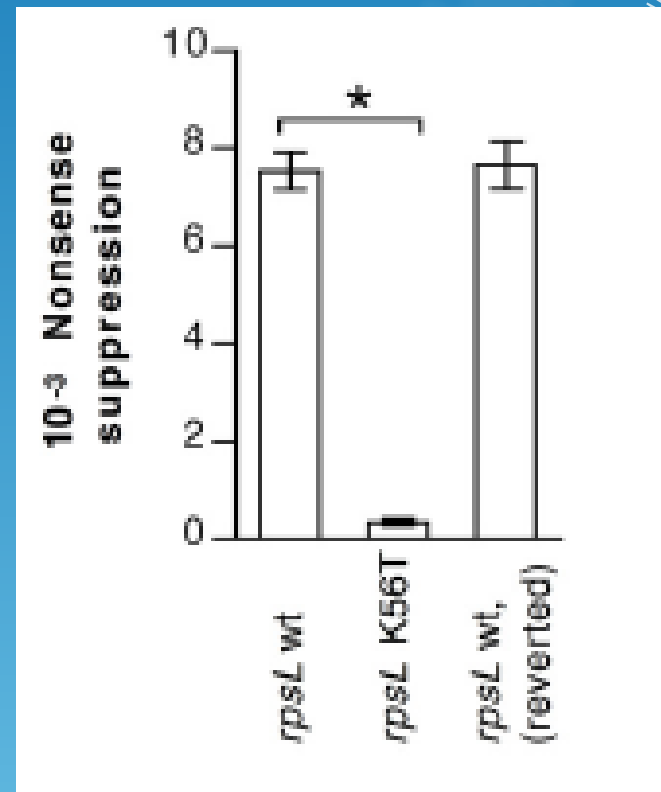
Modulation of ribosomal decoding errors and competence by antibiotic

- Aminoglycoside antibiotics (e.g. Streptomycin) ↑ ribosomal decoding error rate
- 16S rRNA of the 30S subunit of bacterial ribosome
- Proofreading process, codon misreading, ↑ error rate



Effect of ribosomal mutations on decoding accuracy and competence

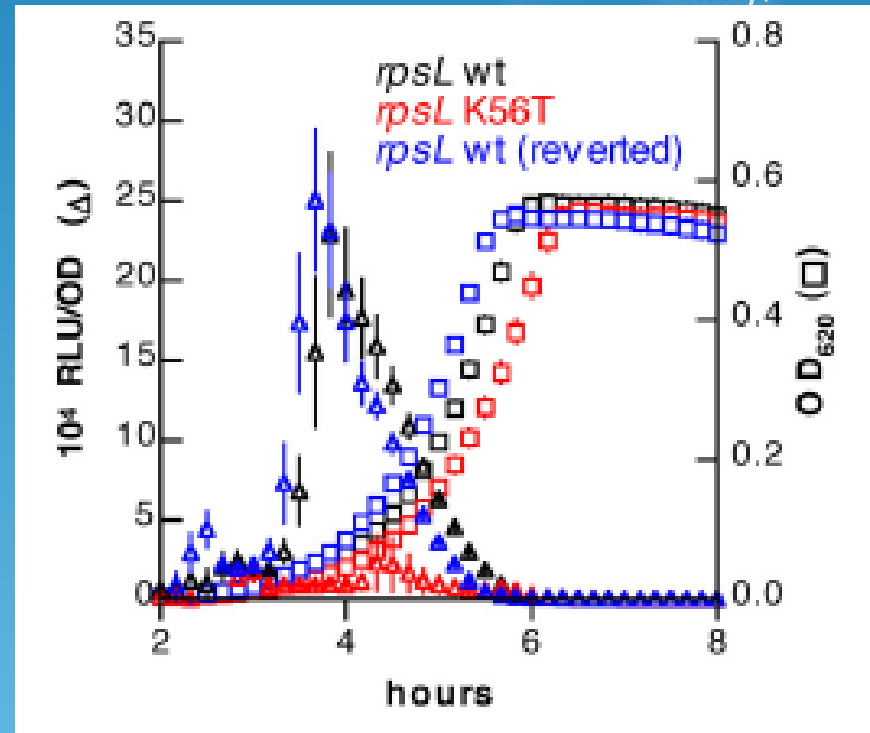
- S12 protein of ribosome, encoded by *rpsL* gene, frequent site of mutation
- Streptomycin resistance
- ↑ decoding accuracy
- *rpsL* (K546T) mutation
 - ↓ nonsense mutation
 - ↓ competence



Stevens et al, 2011

Effect of ribosomal mutations on decoding accuracy and competence

- Competence monitored by an *ssbB-luc* transcriptional fusion
- *ssbB* induced specifically during competence
- *rspL* (K546T) mutation
 - ↓ nonsense mutation
 - ↓ competence



Stevens et al, 2011

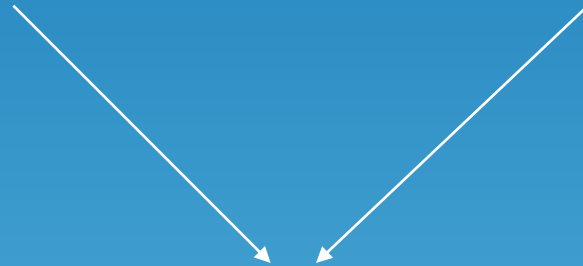
Error-sensitive modulation of competence by HtrA protease

Exposure to antibiotics
(e.g. streptomycin)

Ribosomal mutation
(*rspL* mutation)

Translational error rate

Competence



Error-sensitive modulation of competence by HtrA protease



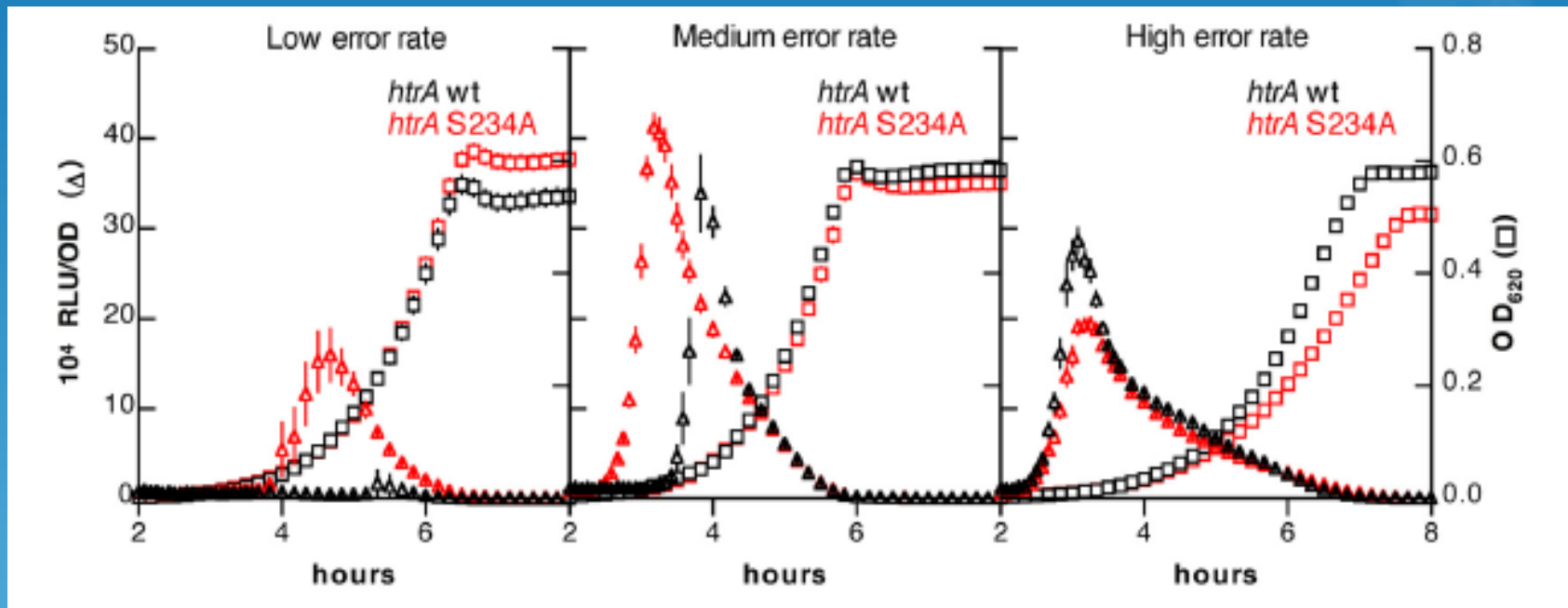
- HtrA protease ↓ competence, unknown mechanism
- Degrade misfolded protein
- Processing misfolded protein vs ↓ competence
- Translational error rate ↑, ability of HtrA to repress competence ↓

Error-sensitive modulation of competence by HtrA protease



- Wild-type *htrA* vs isogenic strain with *htrA* (S234A) mutation
- Inactivate catalytic site of the protease
- Low, medium and high error rate condition
- Low: *rpsL*(K56T) mutation
- Medium: wild-type *rpsL*
- High: wild-type *rpsL* + streptomycin

Error-sensitive modulation of competence by HtrA protease



Stevens et al, 2011

- Wild-type *htrA* \downarrow competence when decoding errors rare
- Less repression effect on competence when decoding errors more common
- Proteolytic activity of HtrA \downarrow competence as *htrA*(S234) inactivates catalytic site of the protease

Conclusion

Exposure to antibiotics
(e.g. streptomycin)

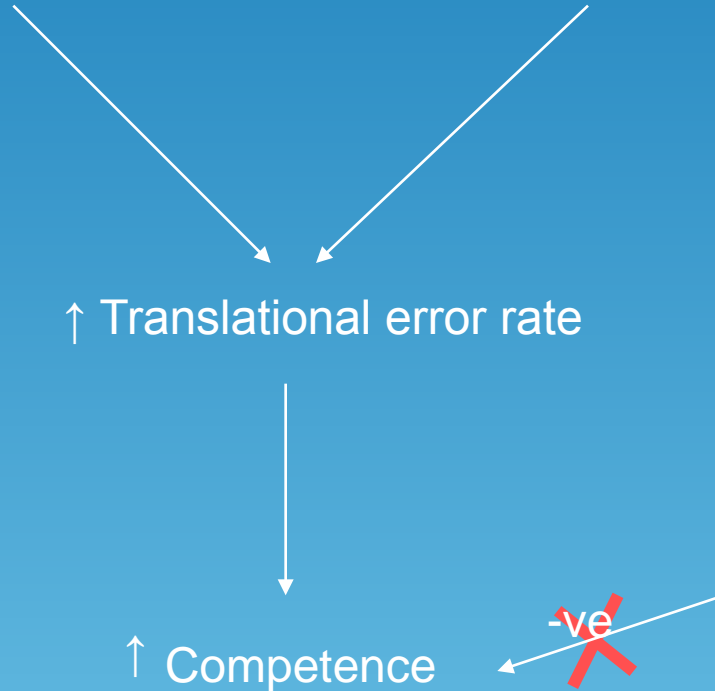
Ribosomal mutation
(*rspL* mutation)

↑ Translational error rate

↑ Competence

HtrA

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Importance

- Signaling pathway governing competence
 - Genetic transformation
 - Production of protease
- \uparrow translational error rate, \uparrow competence
- Monitor accuracy of information used for protein synthesis
- Immediate challenge of misfolded protein through production of chaperones and proteases



Importance

- Address upstream coding errors
 - Intrinsic protein folding defects
- Strategy dealing with upstream coding error by \uparrow competence for genetic transformation
- Maintain the coding integrity of the genome
- Ensure production of functional proteins
- Prevent accumulation of toxic misfolded protein



References

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