# DeepPL-guided *in-silico* mutagenesis for precision phage therapy in Hospital Pharmacy

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### Background & importance

MDR infections are rising, and because phage therapy requires strictly lytic viruses while SNVs can shift lifestyle predictions, Hospital Pharmacy needs auditable sequence-based decision support for safer lot release and patient-tailored phage cocktails.

### Aim & objectives

- Classify phage lifestyle on curated GenBank genomes
- Quantify SNV robustness via in-silico mutagenesis and map instability hotspots
- Deliver HP-ready outputs (eligibility, robustness indices, LIMS lot-release dossier) for precision phage therapy.

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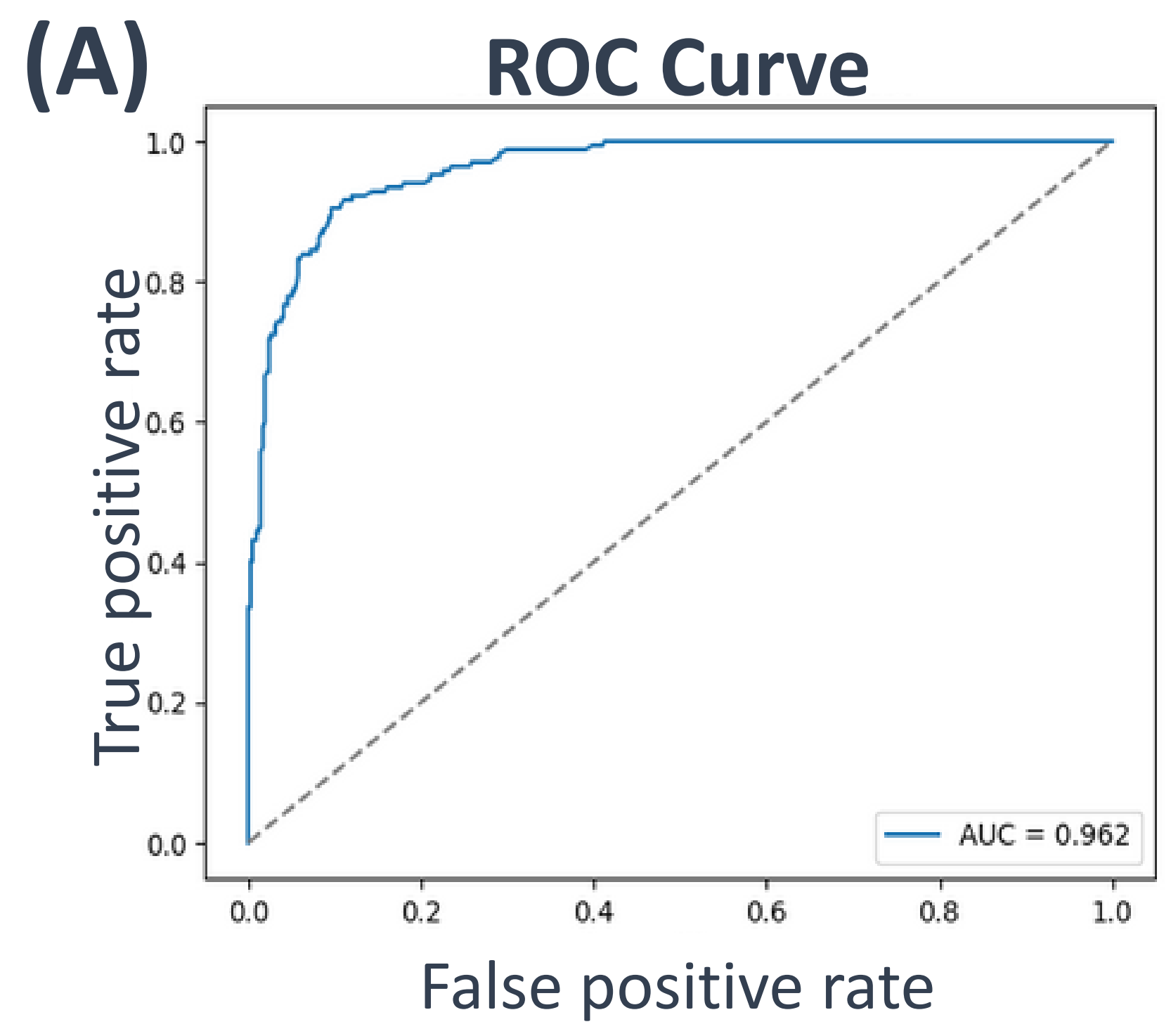
### Materials & methods

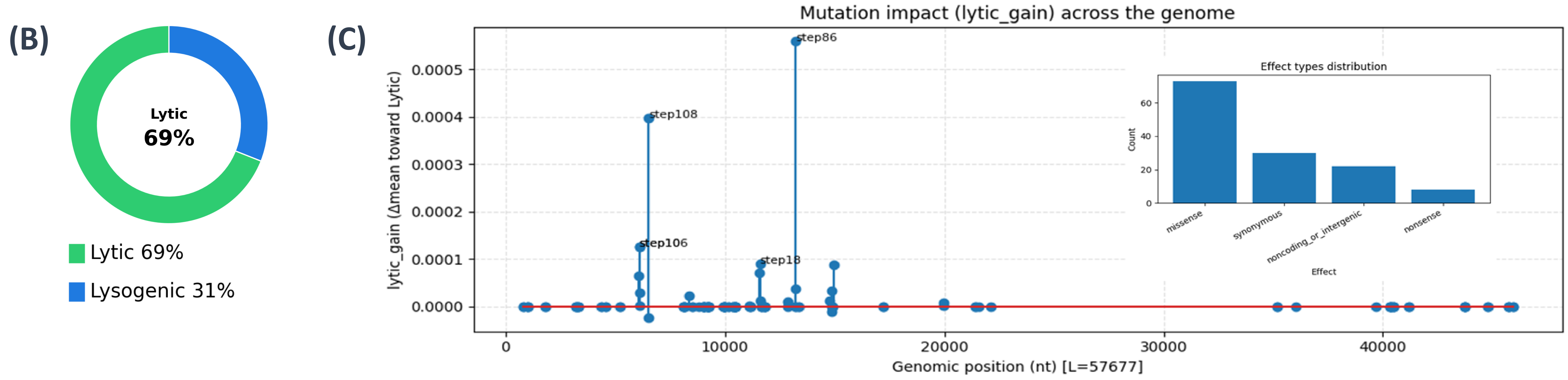
- GenBank phage genomes
- DeepPL lifestyle classification
- Score performance ≈ decision threshold
- Stress-test with in-silico mutagenesis
- Sensitivity hotspots via greedy search

### Results

- **High discrimination:** AUC ≈0.96, accuracy 0.87–0.90 **(A)**
- **Clear class structure:** predictions split into 69% lytic and 31% lysogenic, silhouette >0.5 **(B)**
- **SNV robustness:** mutagenesis indicates high-confidence genomes remain stable, borderline genomes show a dose-dependent rise in class switches **(C)**

## Graphs





**Graphs**: **(A)** ROC curve. Receiver operating characteristic for DeepPL lifestyle classification on curated GenBank phage genomes, showing high discriminative performance (AUC ≈ 0.96) at the selected decision threshold.**(B)** Lifestyle distribution. Donut chart summarising predicted classes across the full dataset: lytic 69% (n=1,347) vs lysogenic 31% (n=598). **(C)** Genome-wide mutational sensitivity map. DeepPL-guided in-silico SNV mutagenesis on a 57,677-nt case genome: lollipop plot reports Δp (“lytic_gain”, change in lytic score) by genomic position, highlighting high-impact hotspots prioritised by the greedy KL-filtered search; inset shows the distribution of predicted mutation effect types.

### Hospital Pharmacy outputs

- **Eligibility sheet**: lifestyle, confidence, decision threshold, exclusion flags
- **Robustness profile**: switch-rate vs SNV burden; hotspot map for sensitivity
- **Lot release dossier**: traceable model versioning, parameters, inputs/outputs; exportable to LIMS
- **Precision cocktail support**: prioritise lytic & robust phages; flag borderline genomes for extra QC / wet-lab confirmation.

### Conclusions & Relevance

DeepPL combined with in-silico mutagenesis enables reliable lifestyle assignment and quantitative robustness profiling in Hospital Pharmacy, producing traceable and auditable outputs that support LIMS-integrated lot release and patient-specific cocktail design to advance antimicrobial stewardship and precision phage therapy.

### Limitations & next steps

Sensitivity maps provide decision support and should be paired with wet-lab confirmation (host range, lytic activity); next steps include integrating virulence/AMR gene screening and prophage markers, followed by prospective evaluation within routine Hospital Pharmacy workflows.

## Key take-home message

DeepPL classification combined with *in-silico* mutagenesis provides **auditable lifestyle calls** and **quantitative SNV-robustness scores**, enabling **LIMS-ready lot release** and **patient-tailored phage cocktail design** for precision phage therapy in Hospital Pharmacy.

### References

- Zhang Y. et al. DeepPL. PLoS Comput Biol (2024).
- Ji Y. et al. DNABERT. Bioinformatics (2021).
- WHO/Europe. Evidence for bacteriophages against AMR (2024-2025).

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