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Impact of genomic adaptation on stress response and virulence of sequential urinary isolates of *Pseudomonas aeruginosa*

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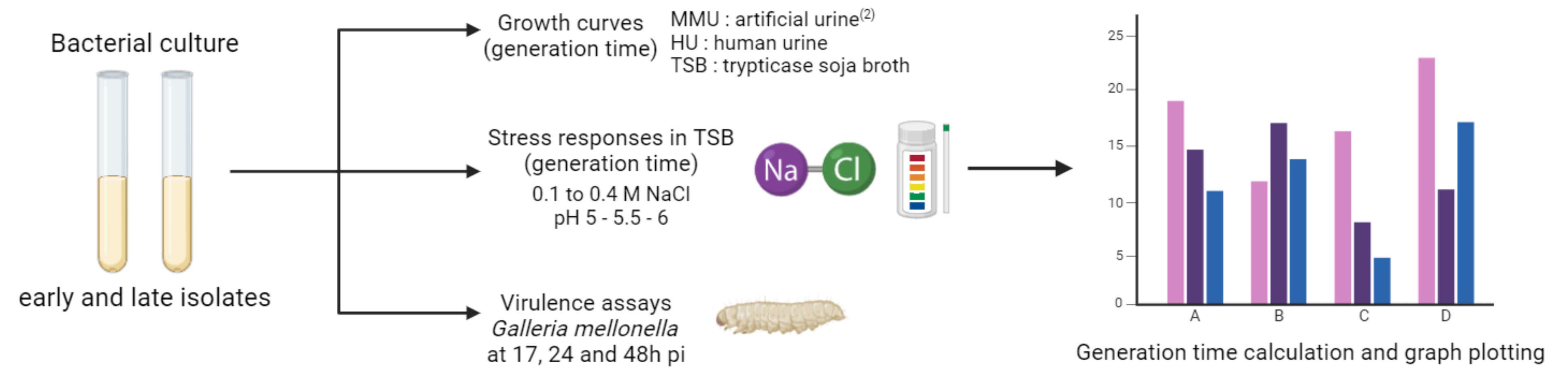
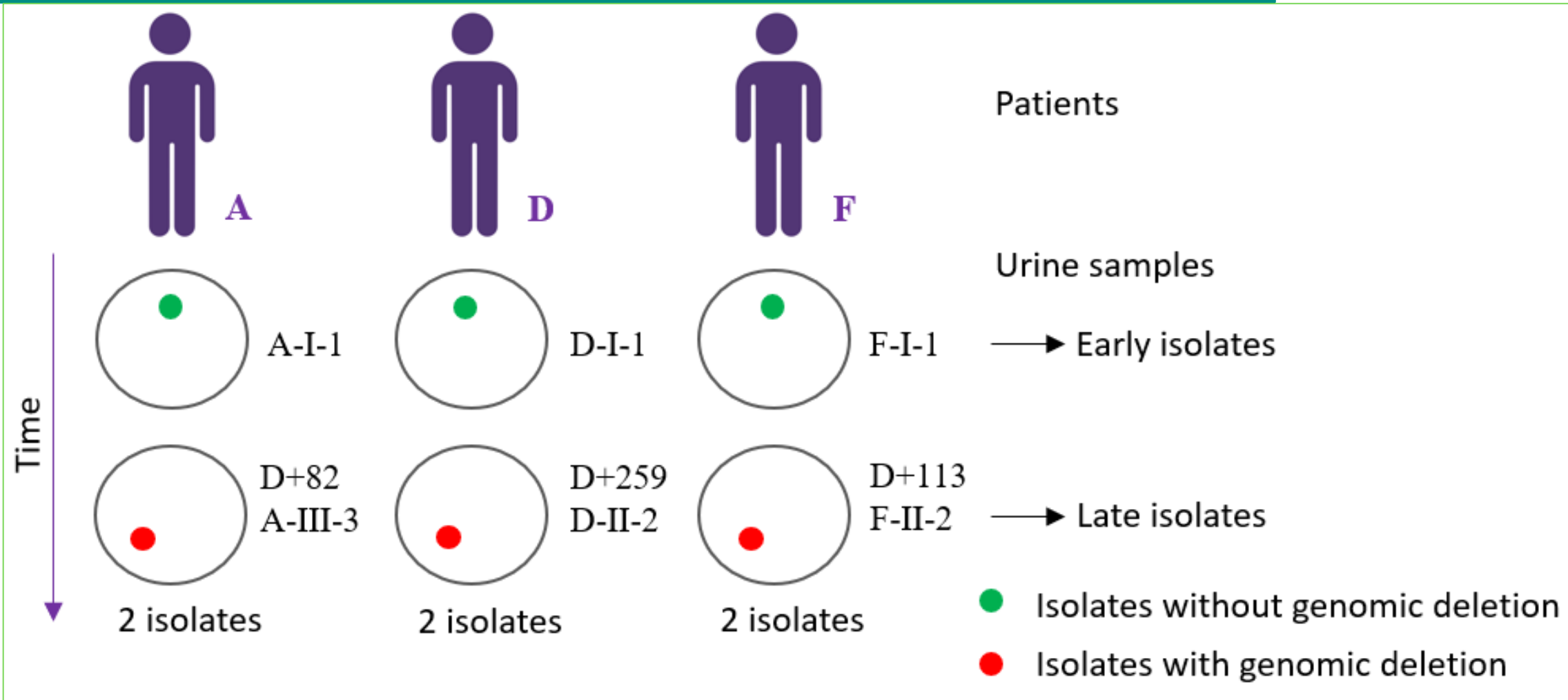
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Background

Pseudomonas aeruginosa (PA) contributes to approximately 10% of hospital-acquired urinary tract infections (UTI) which can lead to bacterial persistence and relapses. Within-host adaptation of urinary *P. aeruginosa* isolates includes large genomic deletions⁽¹⁾; their impact on response to urinary-like environment stresses and virulence has not yet been explored.

Methods

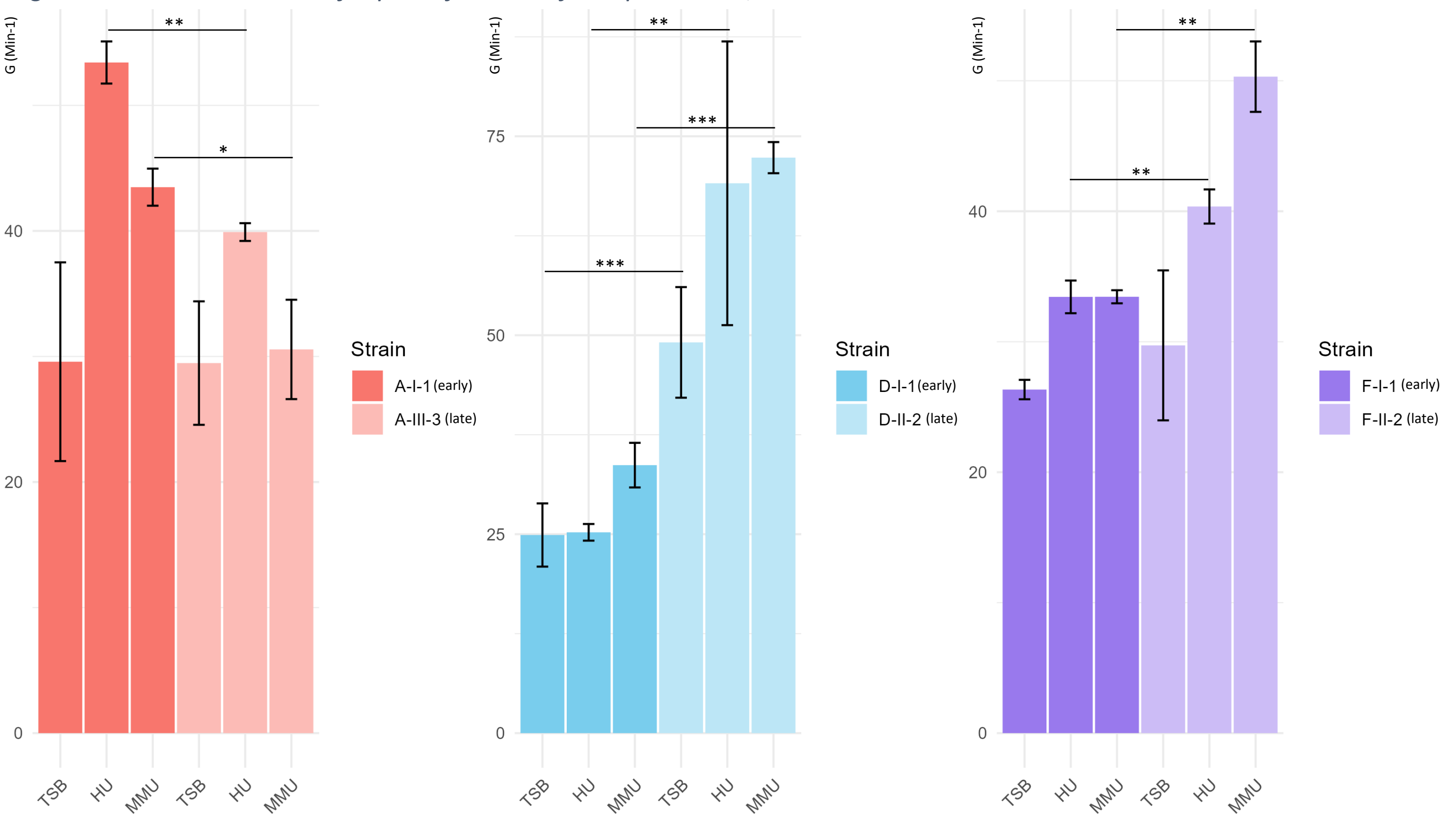
Study flowchart of the *P. aeruginosa* isolates



Results

Growth of early and late isolates in 3 media

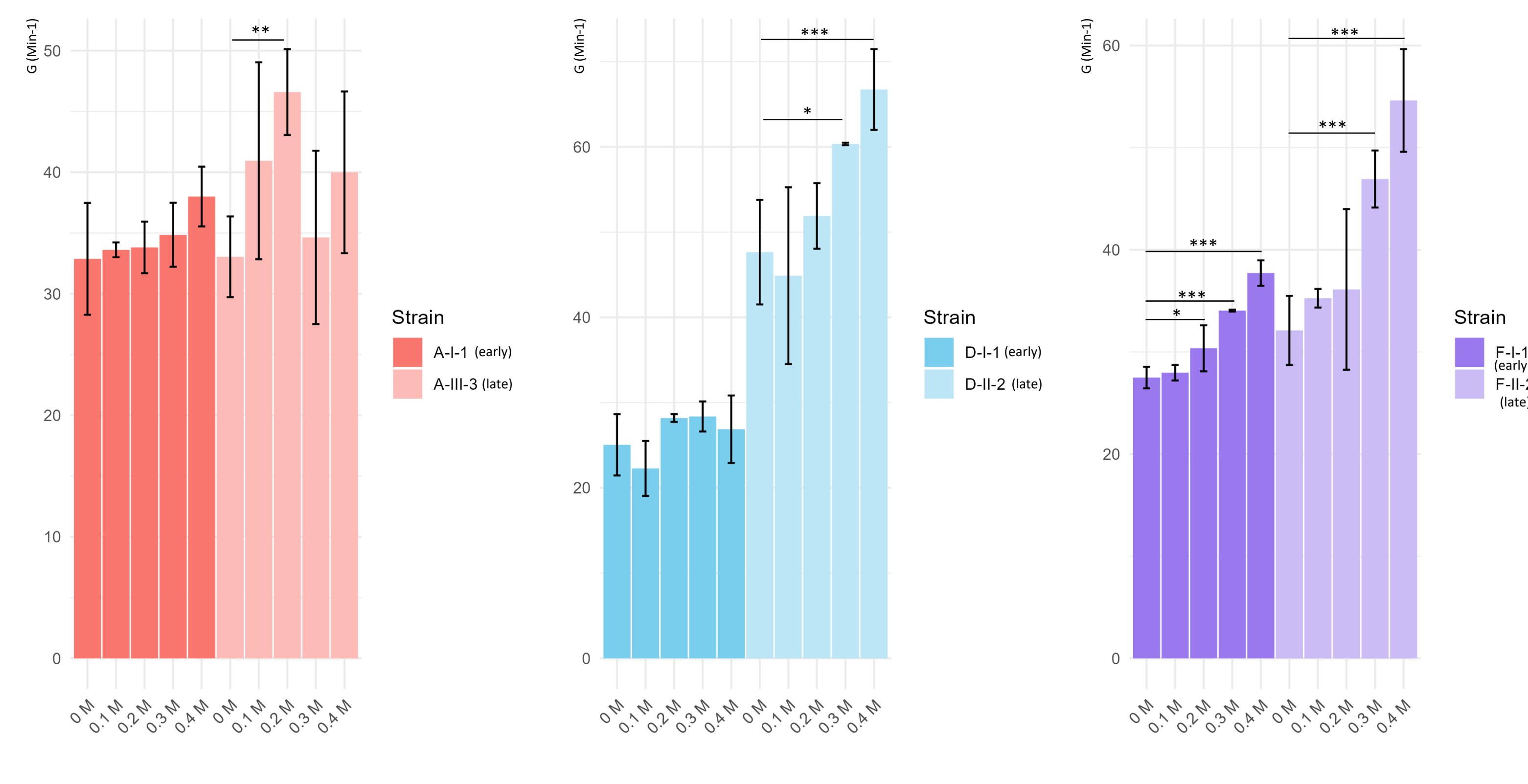
Figure 1. Generation time of a pair of isolates from patients A, D and F in 3 media



G of late isolates from patients D and F significantly increased in the 3 media (MMU, HU, TSB) Patient A's late isolates with a shorter G compared to EI in HU

Response to osmotic stress

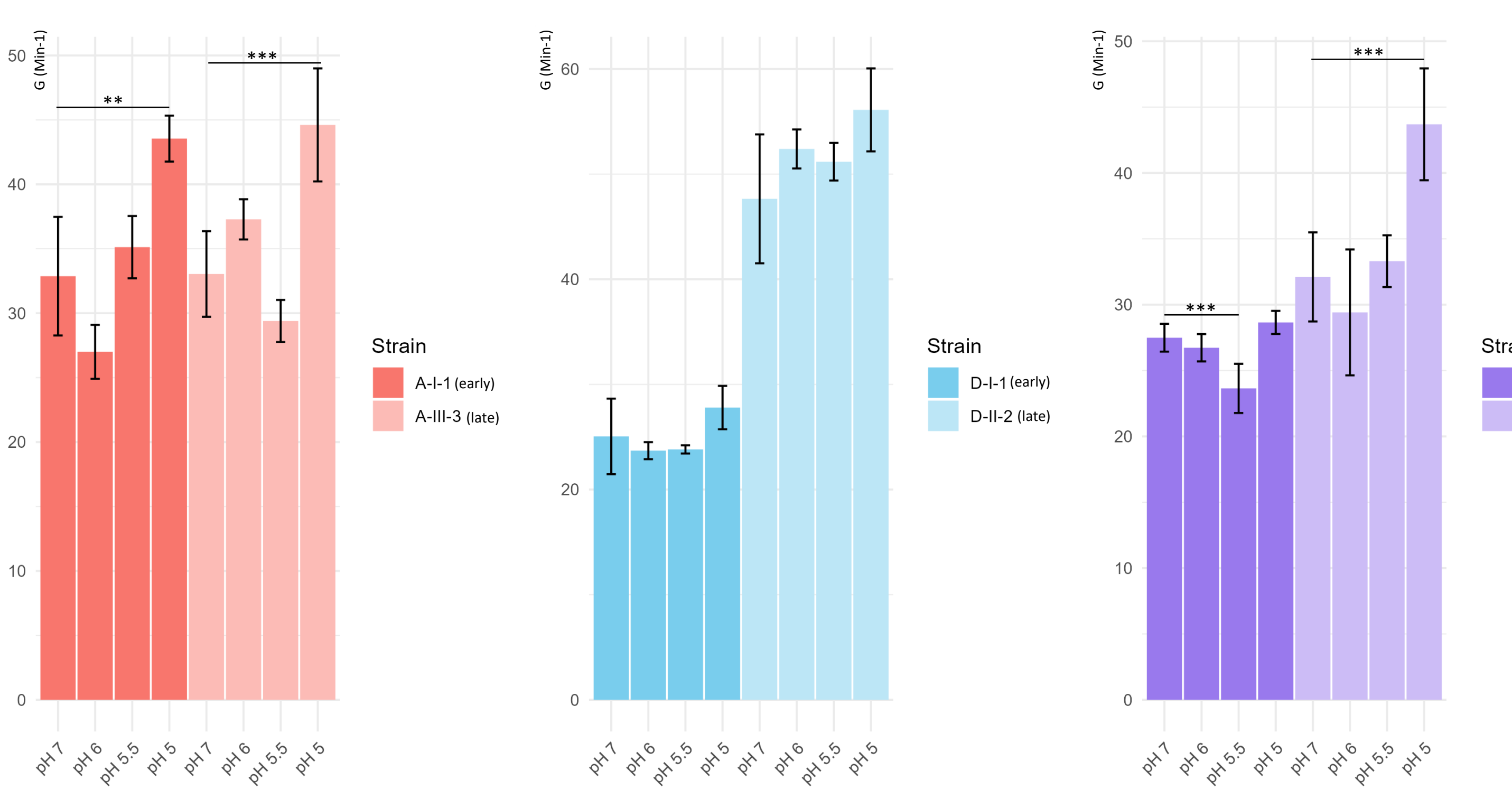
Figure 2. Generation time of a pair of isolates from patients A, D and F at different NaCl concentrations



Late isolates from the 3 patients significantly more affected by osmotic stress than early isolates

Response to acidic stress

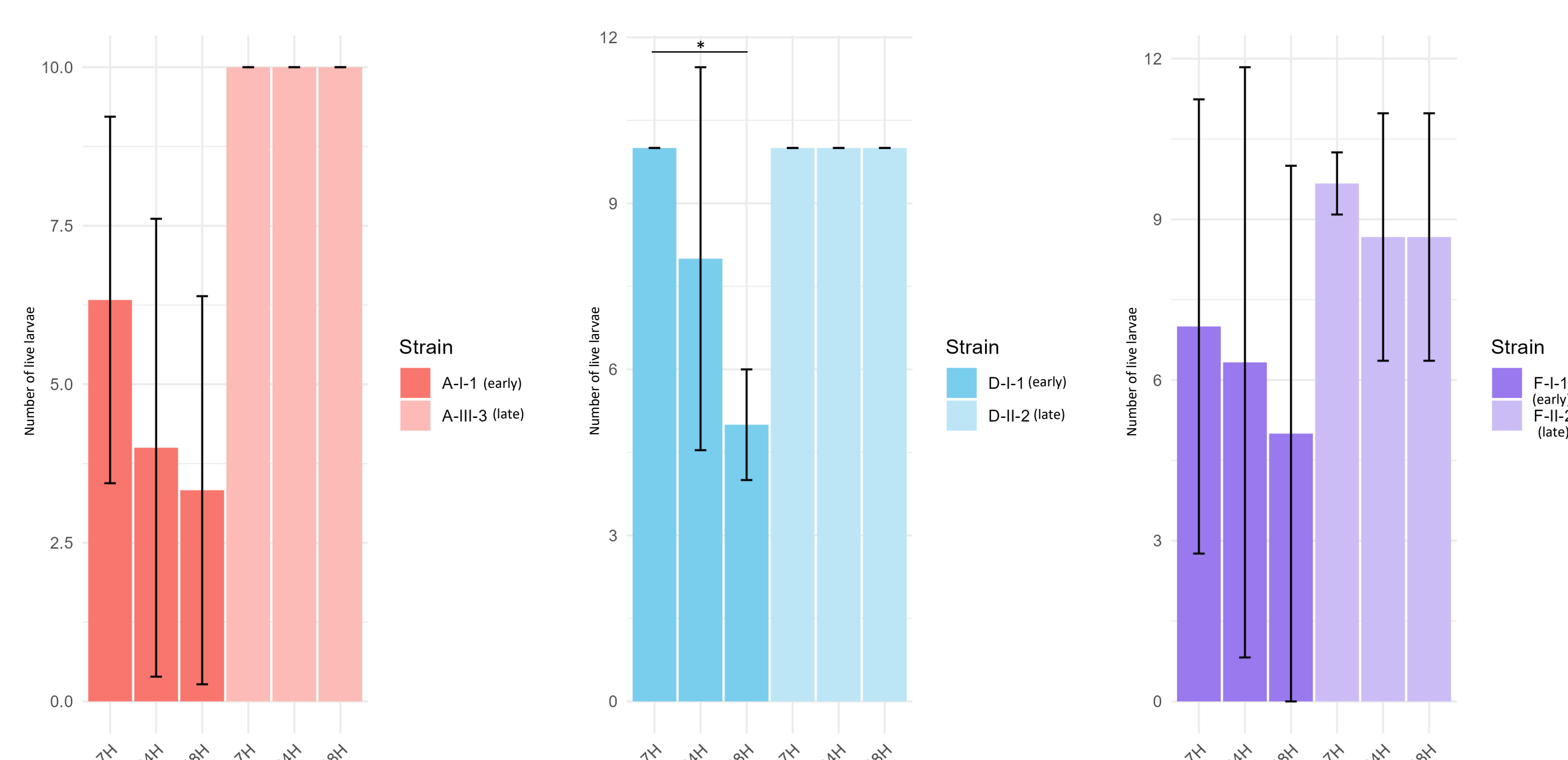
Figure 3. Generation time of a pair of isolates from patients A,D and F at different pH levels



Late isolates of patients A and F significantly more affected by pH stress than those of patient D

Virulence of early and late isolates

Figure 4. Virulence of a pair of isolates from patients, A, D and F at 3 different times in the Galleria mellonella model



Tendency to reduced virulence of late isolates from the 3 patients

Conclusion

This work provided evidence that the **genomic adaptation** of *P. aeruginosa* to urine can lead to phenotypic changes more oriented towards **colonization** than towards increased virulence⁽³⁾ and activation of the stress response. This needs to be confirmed by **transcriptomic** (in progress), **proteomic** and **metabolomic** studies to identify the regulatory and metabolic pathways underlying the evolutionary adaptation of this species to the urinary tract.

1. Cottalorda, A. et al. Within-Host Microevolution of *Pseudomonas aeruginosa* Urinary Isolates: A Seven-Patient Longitudinal Genomic and Phenotypic Study. *Front. Microbiol.* 11, 611246 (2021).
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3. Harmer, C. et al. Modulation of gene expression by *Pseudomonas aeruginosa* during chronic infection in the adult cystic fibrosis lung. *Microbiology* 159, 2354-2363 (2013).