SNU MEDICINE

# Genetic Tool Development and Metabolic Characterization of *Selenomonas sputigena* in Relation to Human Lung Colonization


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## Abstract

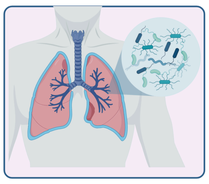

***Selenomonas sputigena*** **is an anaerobic mucosa-associated bacterium with contrasting roles in human health, acting as a pathobiont in periodontal disease while demonstrating protective effects against allergic airway inflammation. Despite these clinically relevant associations, the physiological and metabolic foundations of *S. sputigena*'s niche adaptation and immune-modulatory mechanisms remain largely unexplored. The absence of genetic tools for this organism has severely limited our understanding of its molecular mechanisms and therapeutic potential.**

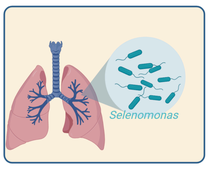
**We constructed a shuttle vector carrying the Rep191 replication protein from *Selenomonas ruminantium* and systematically optimized transformation conditions. Through careful systematic optimization of key parameters, we achieved a 22.5-fold improvement in transformation efficiency (Nguyen et al. 2025a). The broad applicability of our system was demonstrated by the successful transformation of multiple Selenomonas species, and its functionality was validated by achieving stable GFP expression in *S. sputigena*, representing the first demonstration of ectopic protein expression in this organism.**

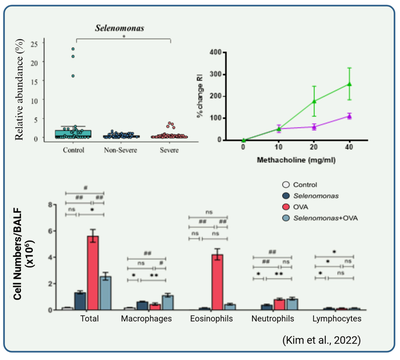
**Then, we systematically characterized *S. sputigena*'s metabolic capacity and developed genetic tools for functional studies by generating native promoter constructs and validating their capacity to drive GFP reporter expression under anaerobic conditions (Nguyen et al. 2025b). The GFP-expressing strains would be used to assess colonization potential in the lung in a mouse model.**

**We next investigate the potential of mucin degradation in this bacterium to maintain lung homeostasis and alleviate asthma symptoms.**


## Background






(Kim et al., 2022)

1. Basic characteristics of *Selenomonas sputigena*: genetic toolbox? Metabolic pathways?
2. Colonization potential of *S. sputigena* on lung using mouse model (using GFP-tagging strains)?
3. Host immune responses with recombinant *S. sputigena* strain(s)?
4. Molecular mechanisms of regulation to promote the lung health.

## Results

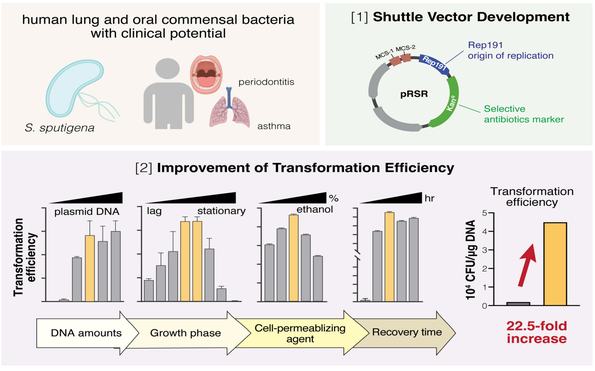
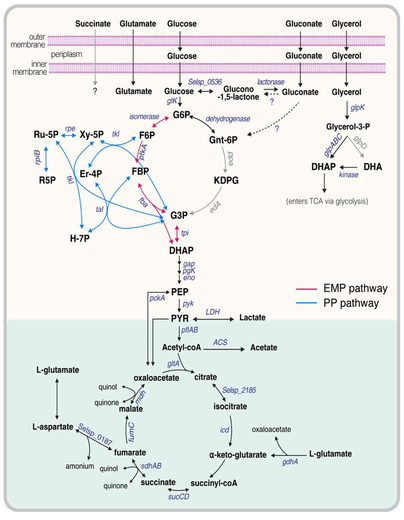



**Fig. 1. Shuttle vector construction and systematic optimization of transformation efficiency in *Selenomonas sputigena* ATCC 35185 [1].**



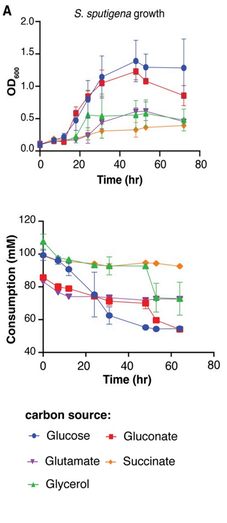




**Fig. 2. *In silico* reconstruction of central carbon metabolism and growth kinetics, substrate utilization, and fermentation profiles of *S. sputigena* across five carbon sources [2].**

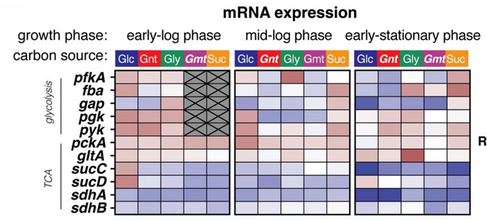



**Fig. 3. Substrate-dependent transcriptional regulation of central metabolic genes in *S. sputigena* [2].**

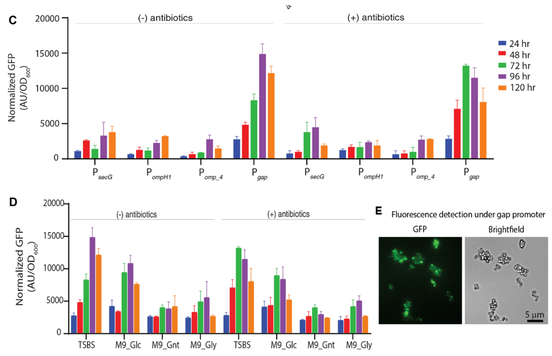



**Fig. 4. Development and validation of native promoter tools for heterologous gene expression in *S. sputigena* [2].**

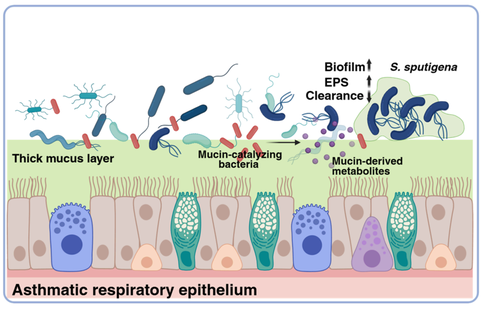



**Fig. 5. Prediction of regulation on maintaining lung homeostasis by *S. sputigena*.**

## Conclusion

- **Development of the first shuttle vector in *Selenomonas sputigena* carrying the Rep191 from *Selenomonas ruminantium* and systematically optimized the transformation conditions.**
- **Reconstruction of the central carbon metabolism of *S. sputigena* and confirmation of the preferred carbon substrate with the comparison of gene expression at mRNA levels and the growth consumption rates.**
- **Prediction of the regulation by *S. sputigena* on the lung homeostasis and alleviation of asthma symptoms.**

## References


**[1] Nguyen, Trinh Thi et al. 2025. "Development of the First Shuttle Vector System and Optimization of Transformation in Selenomonas Sputigena" Journal of Microbiology and Biotechnology 35(4): 1–9. http://jmb.or.kr/journal/view.html?doi=10.4014/jmb.2501.01011.**

**[2] Nguyen TT, Kim YK, Nguyen TVT, Kwon J, Bang YJ. Metabolic profiling and genetic tool development in the mucosal bacterium Selenomonas sputigena. Genes Genomics. 2025 Aug 20. doi: 10.1007/s13258-025-01668-1. Epub ahead of print. PMID: 40835787.**

**[3] Y. C. Kim et al., "Selenomonas: A marker of asthma severity with the potential therapeutic effect," Allergy: European Journal of Allergy and Clinical Immunology, vol. 77, no. 1. John Wiley & Sons, Ltd, pp. 317–320, Jan. 2022. doi: 10.1111/all.15114.**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