# TLR9 Mediates Periodontal Aging by Fostering Senescence and Inflammaging

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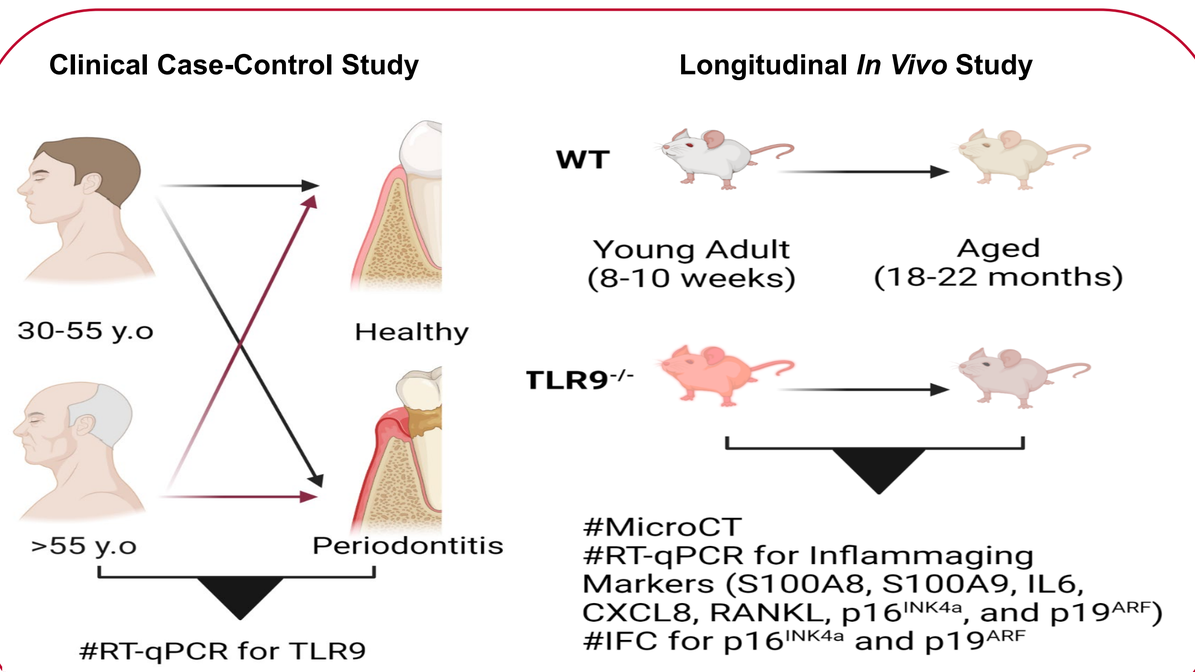
## INTRODUCTION

- The prevalence of periodontitis increases with age, yet the pathophysiological mechanism in which periodontal tissue age is poorly understood.
- TLR9 is a nucleic acid innate sensing receptor that is triggered by MAMPs/DAMPs, (e.g., nucleic acids released by dead cells, bacterial by-products and S100 proteins) and is, in part, responsible for periodontitis and periodontitis-associated comorbidities; however, the role of TLR9 in periodontal aging is unknown.
- Senescent cells are a hallmark of aging, and their mediators contribute to a pro-inflammatory environment termed inflammaging, which is associated with the development of age-related pathologies like periodontitis.
- A characteristics of cellular senescence includes increased expression of the protein p16$^{INK4a}$ over p19$^{ARF}$ (favoring cell cycle arrest).
- We hypothesize that TLR9 fosters premature senescence, inflammaging, and ultimately periodontal lesions.

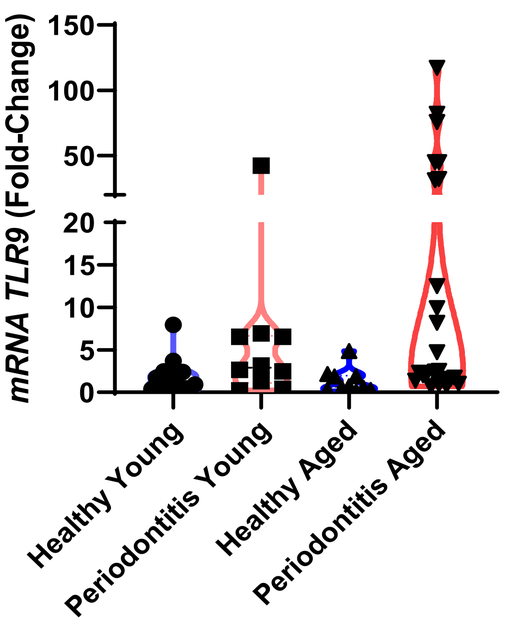
## METHODS & MATERIAL



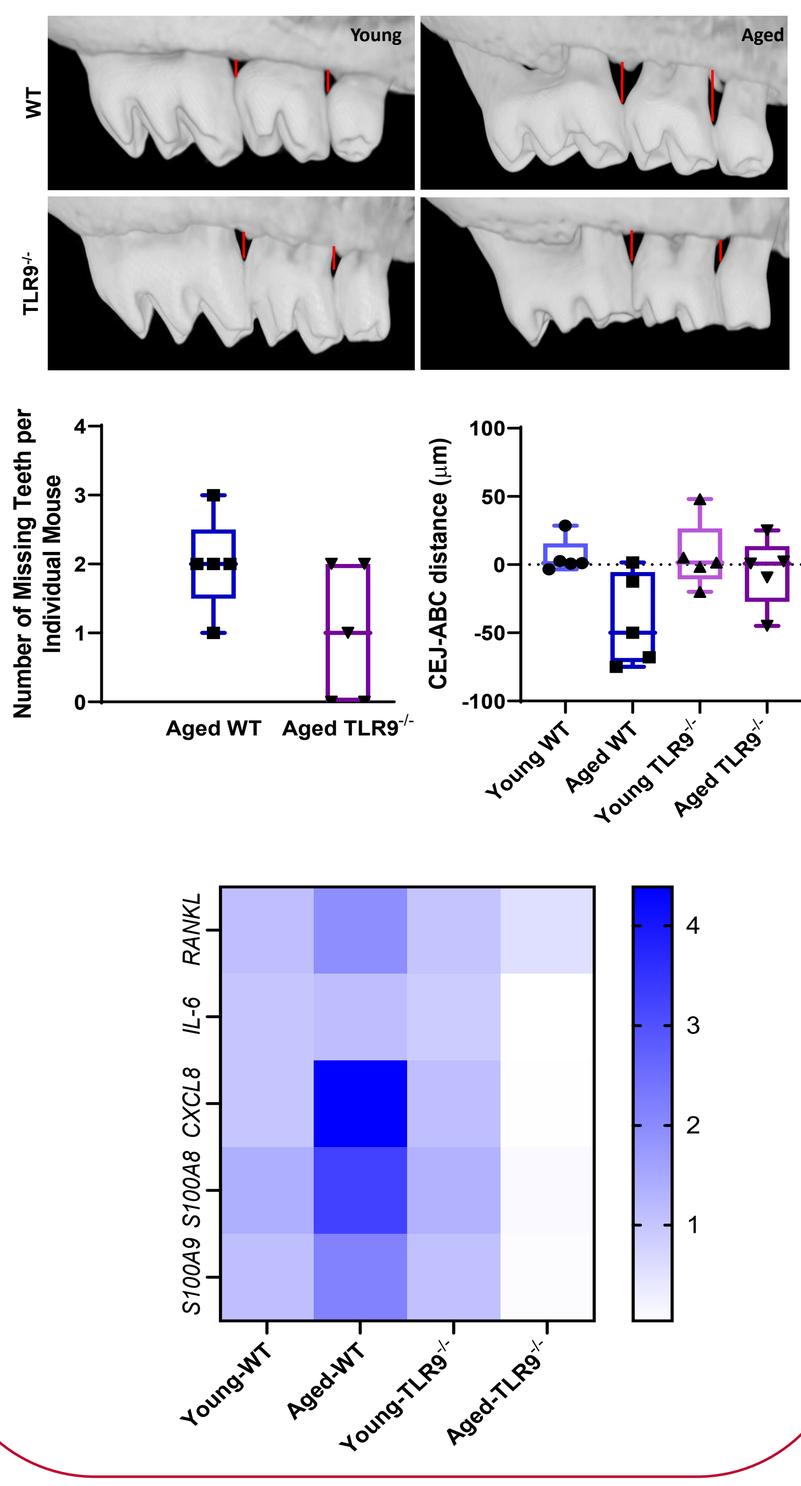

## RESULTS

### Increased Gingival TLR9 Expression was a Hallmark of Periodontitis in Aged Individuals

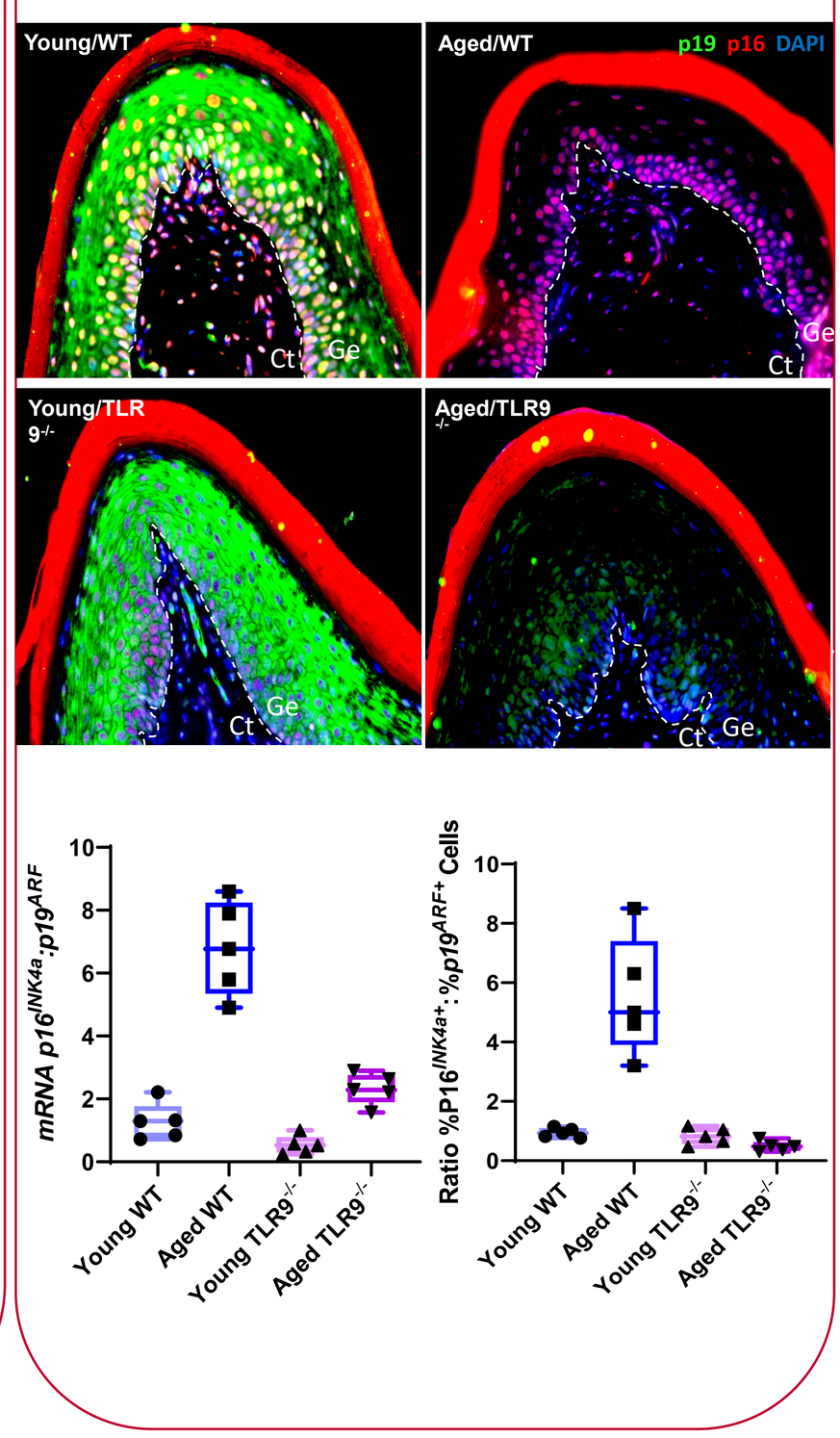
| Study Population | Young Healthy (YH) | Young Periodontitis (YP) | Aged Healthy (AH) | Aged Periodontitis (AP) |
|---|---|---|---|---|
| Gender [Male/Female] | 6/11 | 5/5 | 4/6 | 14/11 |
| Race | Caucasian | Caucasian | Caucasian | Caucasian |
| Smoker | N | N | N | N |
| Diabetes | N | N | N | N |
| Hypertension | N | N | N | N |
| Mean Age [in Years] (SD) | 40.05 (9.05) | 45.75 (8.33) | 66.12 (8.00) | 65.33 (6.96) |
| Mean PPD [in mm for sampled sites] | 2.25 (0.42) | 4.90 (1.10) | 2.55 (0.26) | 4.69 (1.18) |
| Mean CAL [in mm for sampled sites] | 2.42 (0.58) | 5.09 (1.48) | 2.84 (0.30) | 4.97 (1.60) |




### Lack of TLR9 Reduced Aging Associated Physiological Alveolar Bone Resorption and Gingival Expression of Inflammaging Markers

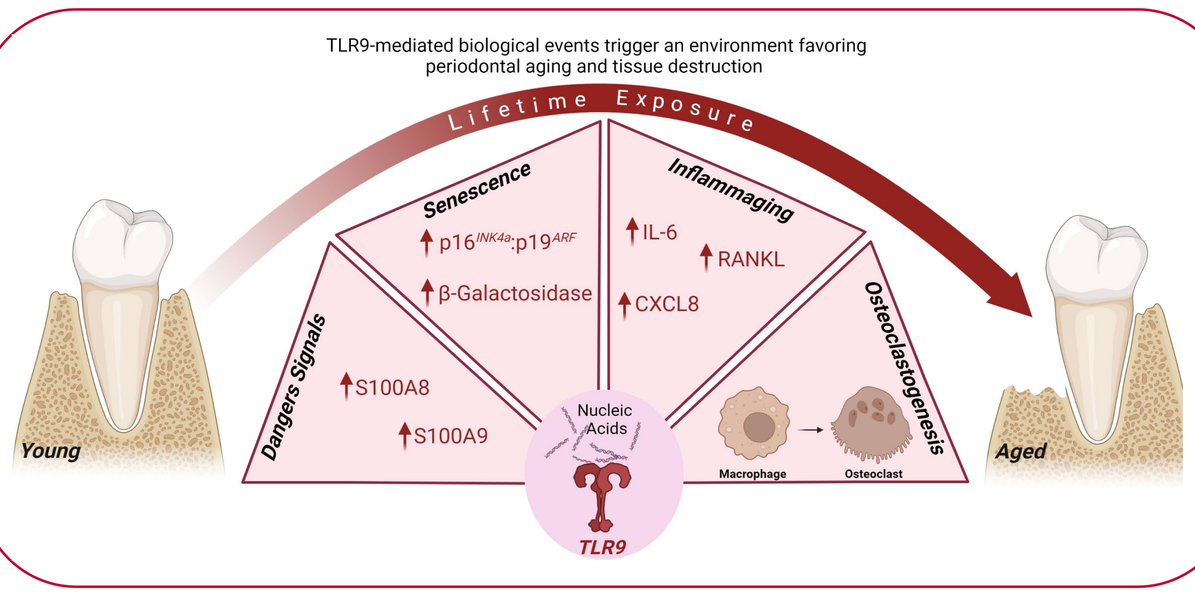



### Lack of TLR9 Improves Senescence Phenotype by Instigating a Balanced p16$^{INK4A}$:p19$^{ARF}$ Ratio in Aged Periodontal Tissues




## CONCLUSION

- Clinically, TLR9 expression increased in aged periodontitis lesions.
- *In vivo,* lack of TLR9 caused a reduction in alveolar bone loss, as well as a decrease in pro-inflammatory/osteoclastic markers IL-6, CXCL8, and RANKL and damage signals S100A8 and S100A9.
- Moreover, lack of TLR9 also caused an improved senescence phenotype by favoring a better balanced p16$^{INK4a}$:p19$^{ARF}$ senescence ratio in aged mouse periodontal tissues.
- Together, these findings highlight TLR9's involvement in promoting a deleterious pro-senescence/inflammaging environment and, consequently, periodontal disease.
- Further studies are needed to explore targeting TLR9 as a means of improving periodontal health in aged populations.

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