

The Impact Of Gingipain From *P. gingivalis* On Microglia:Connecting Chronic Periodontitis And Alzheimer's Disease Risk

Poster
#11900

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Gingipain from *Porphyromonas gingivalis* disrupts microglial homeostasis and may promote Alzheimer's-like pathology via the oral-brain axis.

INTRODUCTION

- *Porphyromonas gingivalis* (*P. gingivalis*) is a keystone pathogen in chronic periodontitis¹. its gingipain proteases are increasingly implicated in Alzheimer's disease (AD)^{2,3}.
- However, the precise molecular mechanisms by which these proteases impair brain cell functions remain elusive.
- This study investigates the impact of gingipains on microglia, the brain's immune cells, aiming to elucidate a potential link between chronic periodontitis and neurodegeneration.

METHODS

- **Cells:** human microglia (HMC3), mouse microglia (MG6)
- **Treatment:** recombinant gingipains (rGingipain), culture supernatants from *P. gingivalis* wild-type(ATCC33277; WT) and gingipain-deficient(KDP136; Mut) strains
- **Readouts:** RT-qPCR phagocytic activity (pHrodo and DQ-BSA fluorogenic assays) Western blot
- **Statistics:** Mean ± SD (technical triplicates, one representative experiment). Student's t-test, *P < 0.05, **P < 0.01, ***P < 0.001. Biological replicates ongoing.

RESULTS

pro-inflammatory genes upregulated by rGingipain/WT supernatant

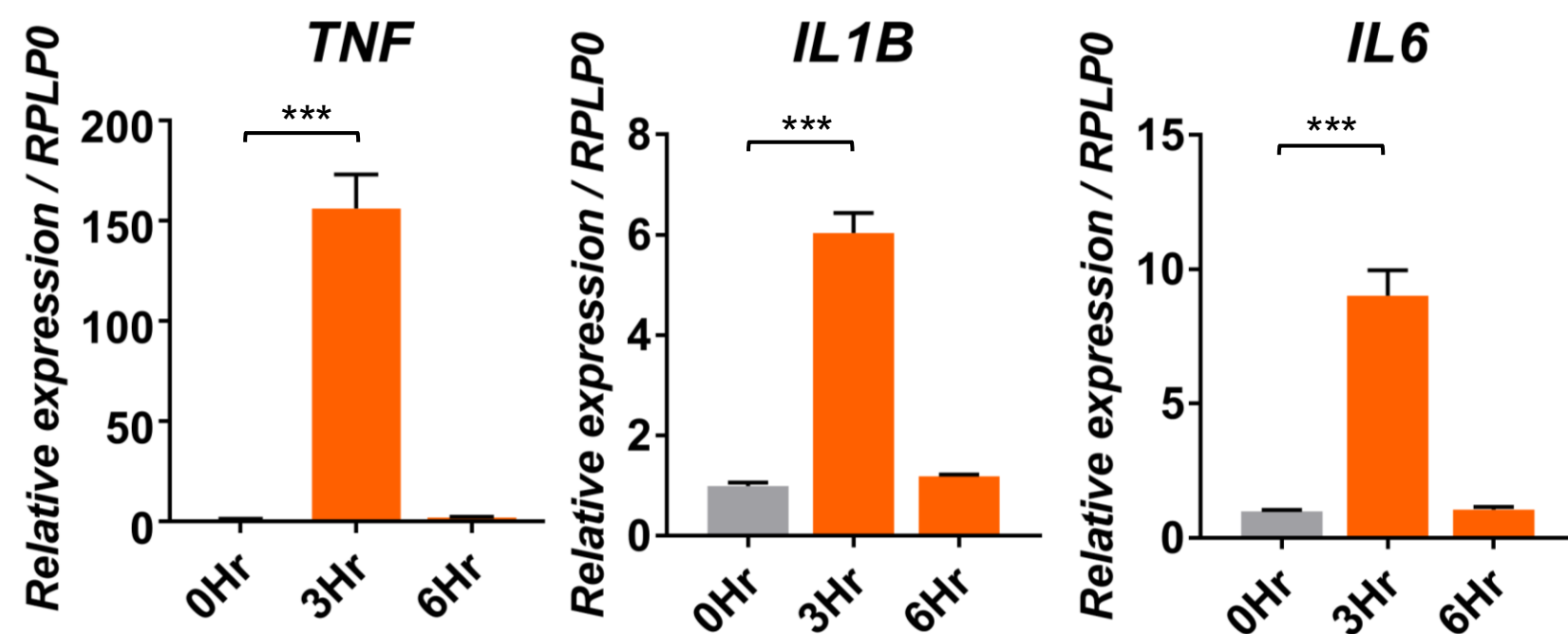
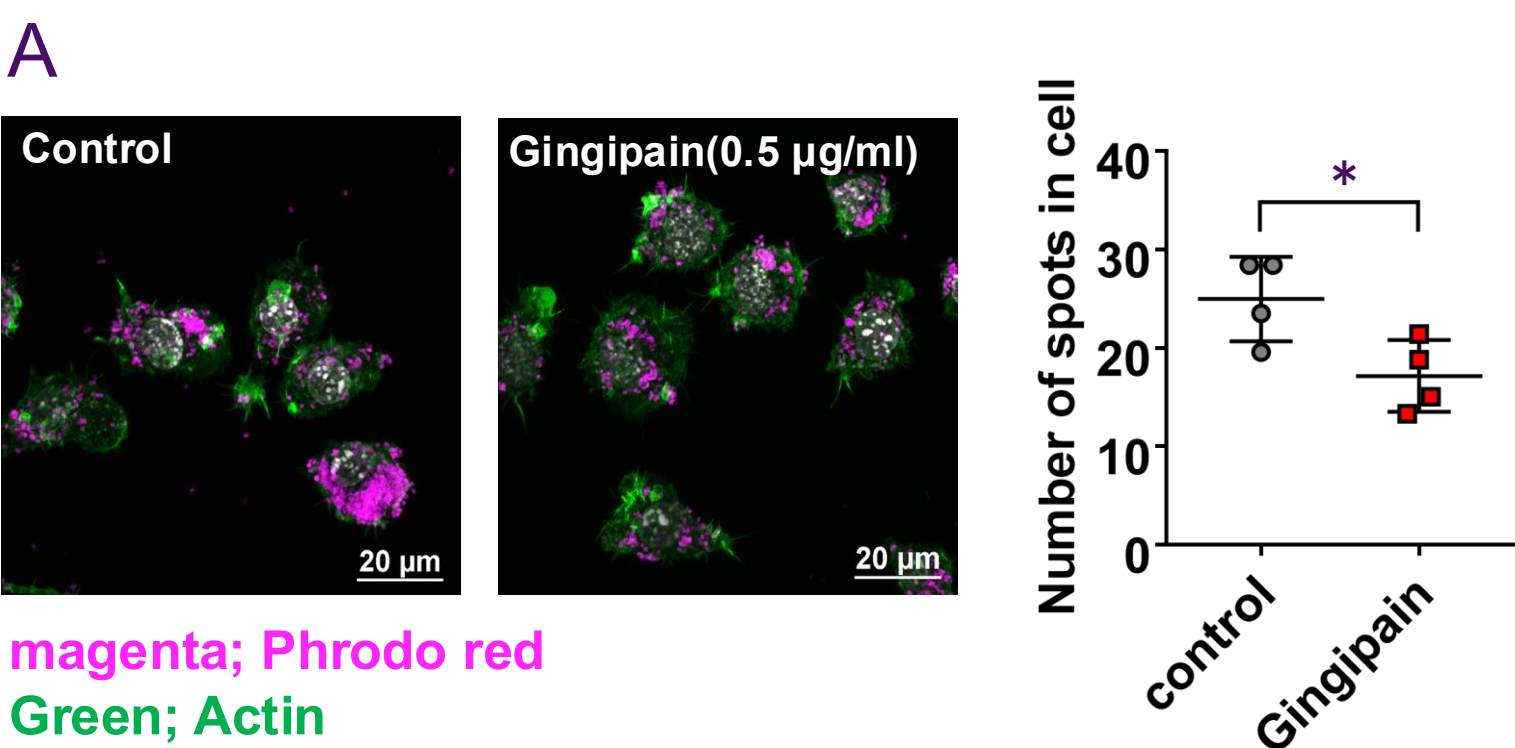


Figure 1. rGingipain upregulates pro-inflammatory genes in HMC3 microglia. HMC3 (1×10⁵ cells/well), 6well-plate. qPCR of TNF, IL1B, and IL6 (normalized to RPLP0) at 0, 3, and 6 hr after rGingipain stimulation (10μM)

Microglial phagocytosis impaired by rGingipain/WT supernatant



proteolytic activity

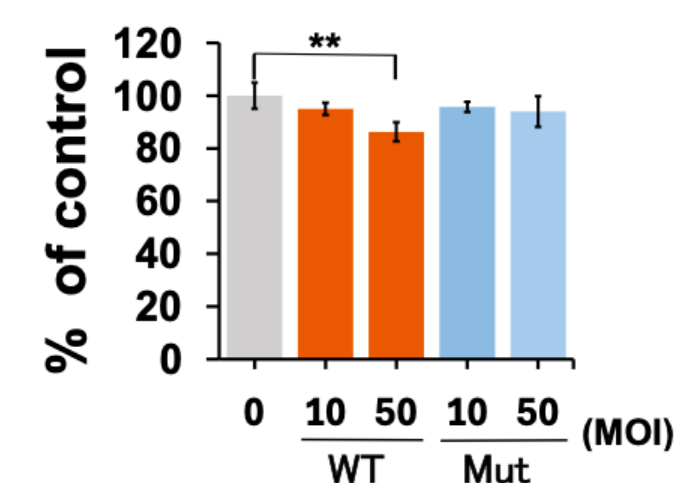


Figure 2. rGingipain impairs phagocytosis and lysosomal degradation. (A) MG6 (1×10⁴ cells/well, 8-well slide chamber), ± rGingipain, 24 h. Confocal images of MG6 (B) MG6 (3×10⁴ cells/well, 96-well plate), culture supernatants from *P. gingivalis*, 12 hr. DQ-BSA degradation, 2 hr

Gingipains activate NF-κB & suppress Wnt-β-catenin

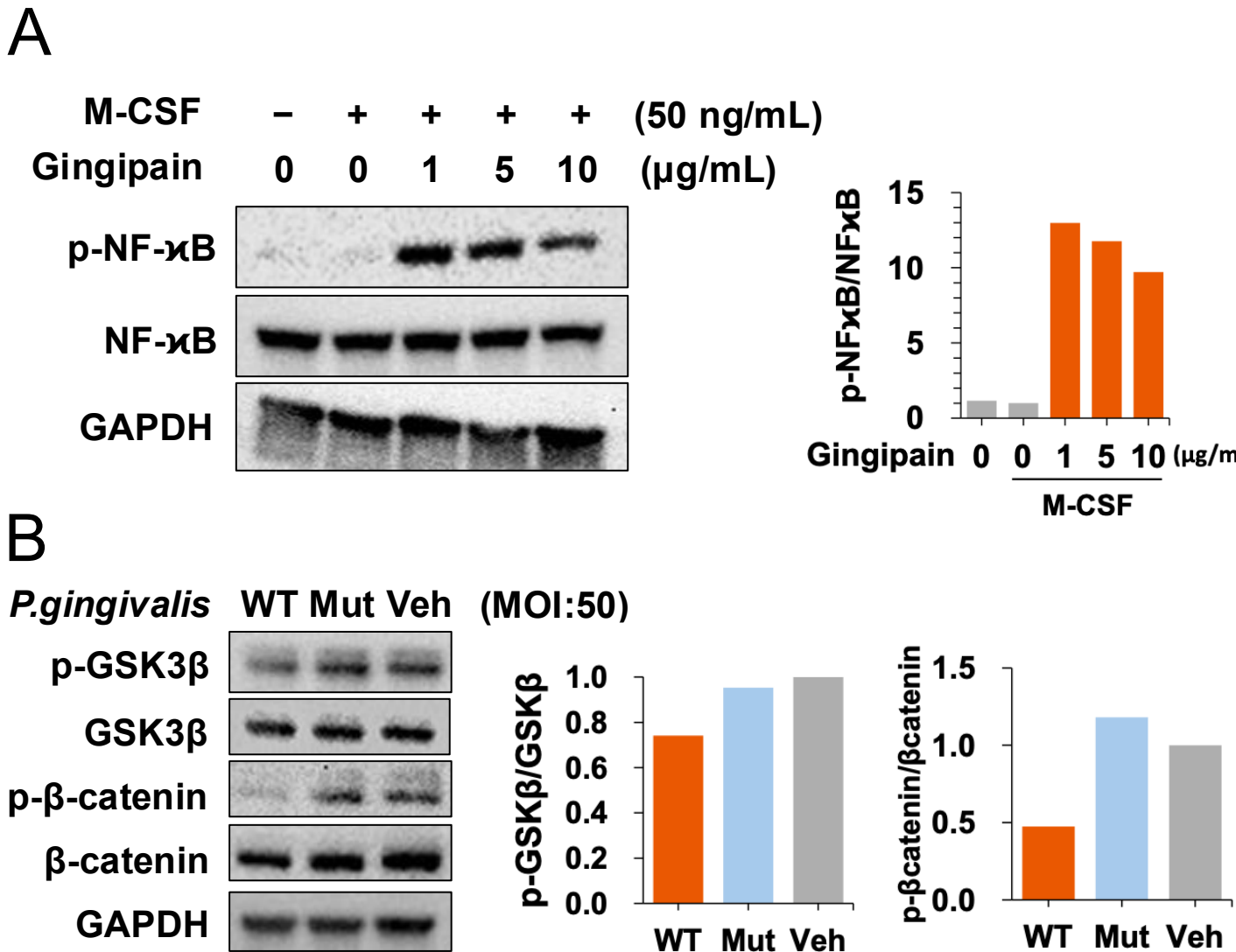
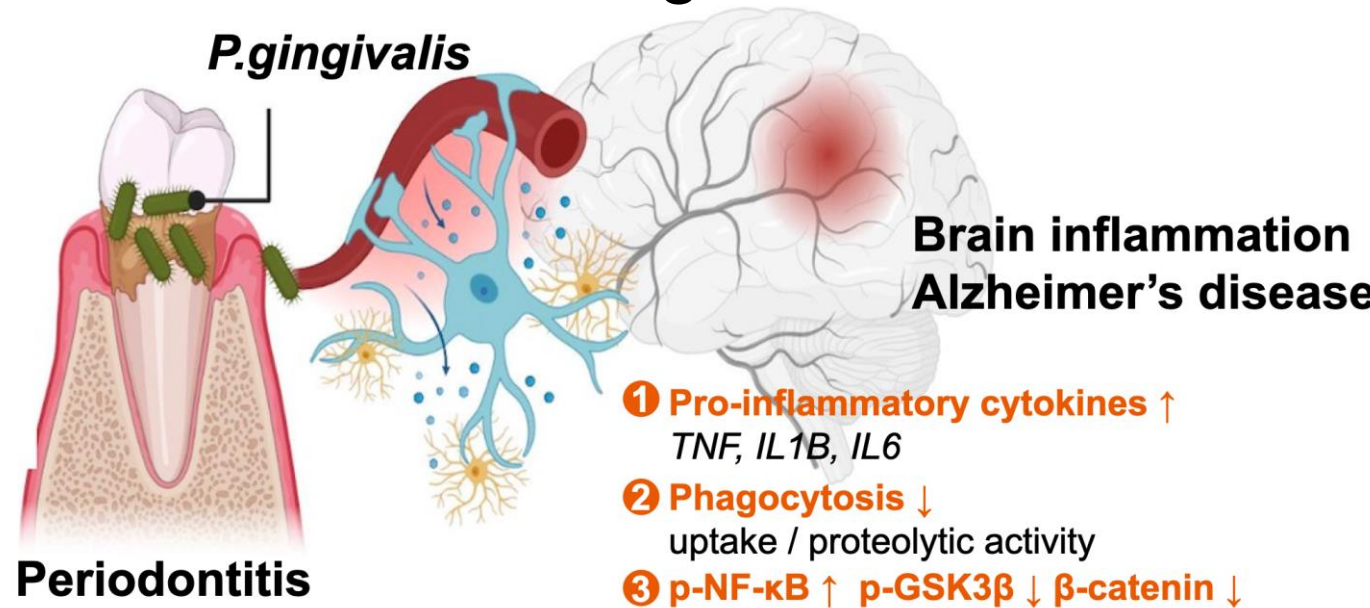


Figure 3. Gingipains activate NF-κB and suppress Wnt-β-catenin. MG6(1×10⁶ cells, 24hr incubation) (A) 6-cm dish; rGingipain (0–10 μg/mL) + M-CSF (50 ng/mL), 15 min. (B) 6-well plate; culture supernatants from *P. gingivalis* MOI 50 or vehicle (Veh), 15 min. Representative blots; densitometry at right.

CONCLUSIONS

Our findings suggest that *P. gingivalis*-derived gingipains disrupt microglial homeostasis by modulating the GSK-3β and β-catenin signaling pathway, thereby accelerating the progression of Alzheimer's disease through the oral-brain axis.



REFERENCES

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