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The effect of canonical and non-canonical pyroptosis in apical periodontitis

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Aim

- To investigate whether caspase-1 and caspase-4/-5/-11 are involved in the progression of apical periodontitis.
- To investigate whether caspase-1 and caspase-4/-5/-11 induce pyroptosis of macrophages in apical periodontitis.

Methods

Label-free proteomics and double quantum dots (QDs) labelling staining were used to detected the proteins related to pyroptosis in human apical periodontitis tissues and experimental apical periodontitis rat model. In addition, VX765(a caspase-1 inhibitor) and Wedelolactone (a caspase-11 inhibitor) were used in an experimental apical periodontitis rat model. Micro-CT was used to access the bone loss. THP-1 derived macrophages were stimulated with *Porphyromonas gingivalis* lipopolysaccharide *in vitro* for 6 h with or without caspase-1/-4/-5 inhibitor, Ac-FLTD-CMK. LDH release and Western blot was applied to evaluate the cell pyroptosis.

Results

1 Caspase-1 and PYCARD were expressed in human apical periodontitis tissue.

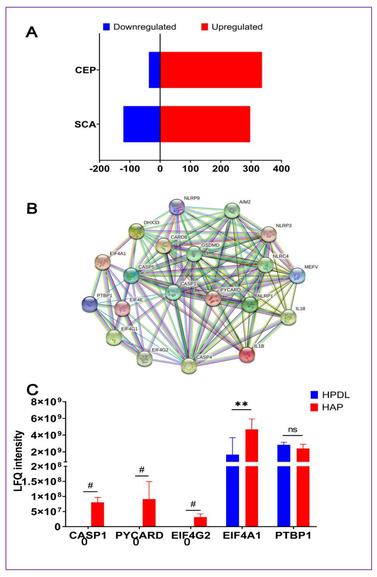

Fig 1. Label free proteomics showed caspase-1 and PYCARD were expressed in human apical periodontitis, but not in periodontitis. A: Quantitative difference analysis of proteins. CEP, consistent presence/absence profile; SCA, significantly changing in abundance. B: The PPI containing proteins that related to caspase-1/-4/-5(string). C: LFQ intensity of proteins expressing in our study. (#, consistent presence/absence profile;** P<0.001).

2 Caspase-1/-4/-5 in human apical periodontitis tissue.

Results

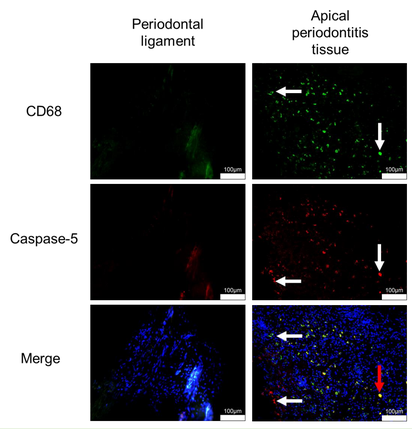

Fig 2. The expressions of caspase-1 and caspase-4/-5 in human apical periodontitis tissue. Few caspase-4+ cells underwent cell death, while most caspase-5+ cells underwent cell death. CD68+ macrophages mainly expressed caspase-5. Bar, 100μm

3 Caspase-1/-11 in experimental apical periodontitis rat model.

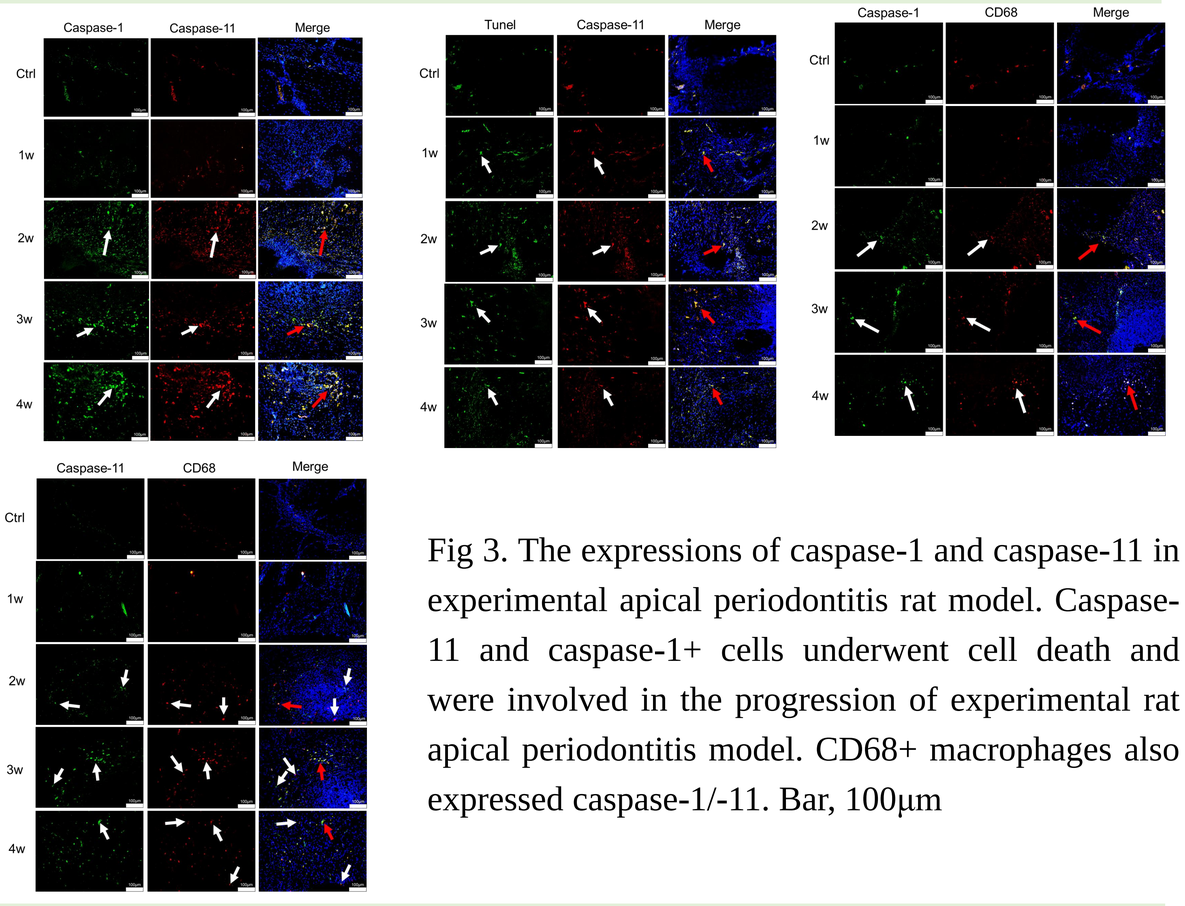

Fig 3. The expressions of caspase-1 and caspase-11 in experimental apical periodontitis rat model. Caspase-11 and caspase-1+ cells underwent cell death and were involved in the progression of experimental rat apical periodontitis model. CD68+ macrophages also expressed caspase-1/-11. Bar, 100μm

4 Bone loss in experimental apical periodontitis rat model when caspase-1/-11 were inhibited

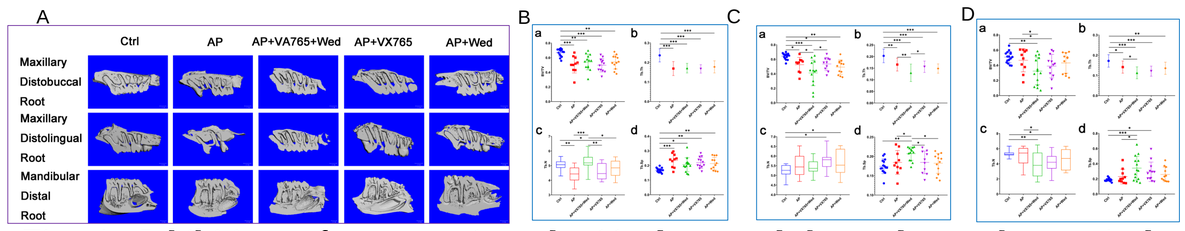

Fig 4. Inhibition of caspase-1 and -11 decreased bone loss when apical periodontitis was severe. On the contrary, bone loss was increased when apical periodontitis was mild. A: Three-dimensional reconstruction of experimental rat apical periodontitis model. B-D: Bone loss of maxillary distobuccal root, maxillary distolingual root and mandibular distal root.

5 *P.gingivalis* LPS induced pyroptosis of THP-1 macrophage

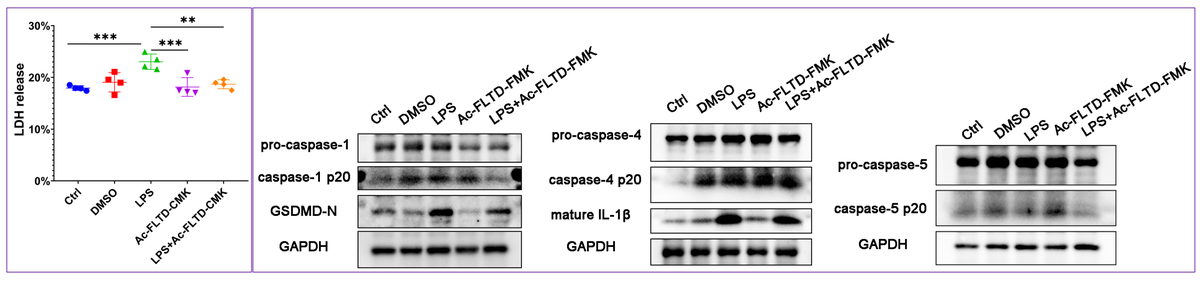

Fig 5. LDH release and the expression of pro-caspase-1, caspase-1 p20, pro caspase-4, caspase-4 p20, pro-caspase-5, caspase-5 p20, mature IL-1β and GSDMD-N increased in macrophages after LPS stimulating, but decreased treated with Ac-FLTD-CMK.

Conclusions

Pyroptosis may be induced in macrophages when bacteria invaded, which contributed to apical periodontitis.