Review of: "TLR2 Activation by Porphyromonas gingivalis Requires Both PPAD Activity and Fimbriae"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

The manuscript investigated the effects of PPAD activity and fimbriae on TLR2-dependent host cell responses to P. gingivalis. The authors found that PPAD activity was required for TLR2 activation by P. gingivalis cells and OMVs. They concluded that both PPAD activity and type I fimbriae are important for TLR2-dependent cell responses to P. gingivalis infection. The story is interesting. The data is novel. And the evidence provided can support the conclusion.
However, there are 2 major questions in the manuscript.
1. It was identified that type I FimA, which is present in the laboratory strain P. gingivalis ATCC 33277, could be linked specifically to TLR2 signaling. However, it is reported that most of the tested clinical strains of P. gingivalis carry type II and IV FimA. That is to say, the conclusions of this study are only applicable to standard strains of P. gingivalis in the laboratory, but not the clinical strains carried by periodontitis patients in the clinic. So how do we interpret the meaning of the experiment? How could the results play a role in the development of new therapeutic strategies for periodontitis and associated comorbidities?
2. To explore the subcellular location of the putative signaling ligand, the authors compared the responses of U251 MG-hTLR2 cells to intact P. gingivalis, bacteria sonicates lysed by sonication, and isolated OMVs produced by the parental strain and the PPAD-deficient mutants. They found there is no difference in TLR2 activation elicited by intact bacteria or bacterial sonicates. Would you tell the readers where PPAD is located in bacteria? Does the activity of PPAD changed by sonication?