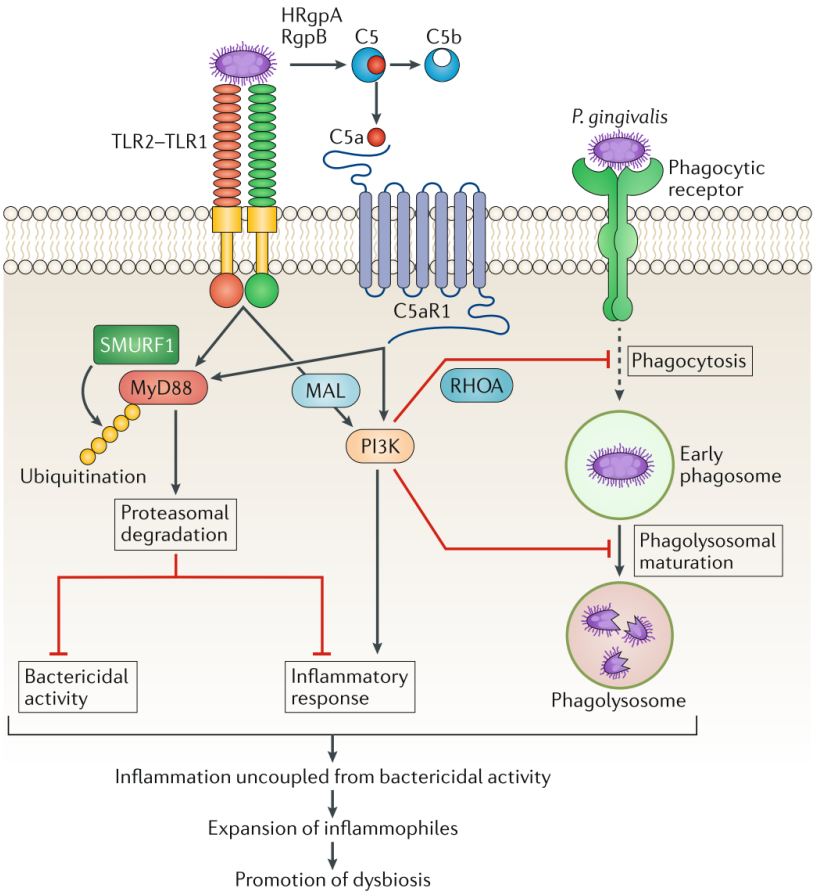
口腔微生物群：动态群落和宿主的相互作用

The oral microbiota: dynamic communities and host interactions【6】



牙龈卟啉单胞菌通过同时损害宿主固有防御系统和促进吞噬细胞中的炎症反应诱导生态失调。

牙龈卟啉单胞菌因此可以在吞噬细胞如中性粒细胞（neutrophils）和巨噬细胞（macrophages）中同时激活 C5aR1 和 TLR2 。牙龈卟啉单胞菌（*Porphyromonas gingivalis*）表达细胞表面分子，激活 Toll 样受体 2 - Toll 样受体 1（TLR1-TLR2）复合物并分泌作用于补体成分 C5 的酶（HRgpA和RgpB gingipains），以产生局部高浓度的 C5a，C5a 是补体 C5a 受体 1（C5aR1）的配体。在中性粒细胞和巨噬细胞这两种骨髓细胞类型中，牙龈卟啉单胞菌可以避开 MyD88，从而防止相关的杀菌作用[1,2]。在中性粒细胞中，MyD88 的失活和 E3 泛素连接酶 SMURF1的泛素化和随后的蛋白酶体降解有关。虽然牙龈卟啉单胞菌阻断了 MyD88 依赖的炎症，但是它在中性粒细胞和巨噬细胞中却能够诱导 PI3K 依赖的炎症细胞因子。牙龈卟啉单胞菌诱导的 PI3K 活化能够抑制两种细胞的吞噬作用[1,3]。在中性粒细胞中， PI3K 可以抑制 RhoA GTP酶 （RhoA GTPase） 和肌动蛋白聚合从而阻止吞噬作用的发生[1]。有意思的是，即使吞噬牙龈卟啉单胞菌被巨噬细胞吞噬，PI3K 信号也能够抑制了巨噬细胞内的吞噬 - 溶酶体成熟，从而阻止了病原体的破坏[3]。这些事件会损害宿主的固有免疫力并促进炎症，从而导致炎症性疾病的选择性扩张。与之相反，在小鼠实验中抑制 C5aR1，TLR2 或 PI3K 可以逆转失调的炎症和牙周炎[1,4]。

TIPs：
Ubiquitination: 泛素化
Proteasomal degradation: 蛋白酶体降解
Phagolysosome: 吞噬溶酶体

1. Maekawa, T. et al. Porphyromonas gingivalis manipulates complement and TLR signaling to uncouple bacterial clearance from inflammation and promote dysbiosis. Cell Host Microbe 15, 768–778 (2014). This study shows that a keystone periodontal pathogen manipulates complement–TLR crosstalk to block bactericidal mechanisms while fostering a nutritionally favourable inflammatory response; this uncoupling of immune bacterial clearance from inflammation promotes dysbiosis and periodontitis . 117
2. Burns, E., Eliyahu, T., Uematsu, S., Akira, S. & Nussbaum, G. TLR2-dependent inflammatory response to Porphyromonas gingivalis is MyD88 independent, whereas MyD88 is required to clear infection. J. Immunol. 184, 1455–1462 (2010). 161
3. Makkawi, H. et al. Porphyromonas gingivalis stimulates TLR2-PI3K signaling to escape immune clearance and induce bon resorption independently of MyD88. Front. Cell. Infect. Microbiol. 7, 359 (2017). 118
4. Hajishengallis, G. et al. Low-abundance biofilm species orchestrates inflammatory periodontal disease through the commensal microbiota and complement. Cell Host Microbe 10, 497–506 (2011). This study substantiates the concept of a keystone pathogen by providing in vivo evidence that a specific microorganism instigates quantitative and qualitative alterations to the commensal microbiota, which is thereby remodelled into a dysbiotic community driving periodontitis. 102