R-19. PGE2 dowreguates LPS-induced IL-12 production via EP4 in monocytes

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PGE2 is thought to have important function in the pathogenesis of periodotnal disease. PGE2 functions via PGE2 receptors, which are classified into EP1, EP2, EP3 and EP4. To determine the roles of PGE2 in the pathogenesis of periodontal disease, we examined the effect of PGE2 and various EP agonists on production of IL-12, which plays pivotal roles in immune responces including T cell differentiation and IFN-g secretion, in monocytes stimulated with LPS from *Actinobacillus actinomycetemcomitans* (*A.a.*). Monocytes isolated from peripheral blood were stimulated with LPS and IFN-g. After 48-h incubation, the levels of IL-12 production in the media were measured by ELISA. EP receptor expression in monocytes was analyzed by RT-PCR. Indomethacin, a cyclooxygenase inhibitor, enhanced IL-12 production and addition of exogenous PGE2 completely inhibited IL-12 production. RT-PCR analysis showed that monocytes expressed mRNA of EP2, EP3 and EP4 receptors. 11-deoxy-PGE1 (an EP2/EP4 agonist) diminished IL-12 production, whereas butaprost (an EP2 agonist) and ONO-AP324 (an EP3 agonist) had no effect on IL-12 production. Dibutyryl cAMP and forskolin, cAMP elevating agents, depressed IL-12 production. From these results, we conclude that PGE2 inhibits the production of IL-12 primarily via EP4 receptors by increasing intracellular cAMP levels and may control immune responses in periodontal disease.