Abstract

Effect of *Porphyromonas gingivalis*- Lipopolysaccharide
on gene expression in mouse pancreas

2019
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Objectives:

Chronic pancreatitis and environmental factors such as alcohol consumption, smoking, diabetes, and obesity have been identified as potential risk factors for pancreatic cancer. Although epidemiological studies have shown the relationship between periodontal disease and pancreatic cancer, the molecular mechanisms involved have not been elucidated so far. In this study, the effects of systemic administration of *Porphyromonas gingivalis* lipopolysaccharide (PG-LPS) on gene expression was comprehensively explored in mouse pancreas that did not demonstrate any signs of inflammation.

Methods:

PG-LPS was prepared in physiological saline and intraperitoneally administered to male C57BL/6J mice (8-10 weeks of age) at a dosage of 5 mg/kg every 3 days for a period of 1 month. Physiological saline without PG-LPS was administrated as control. After extracting total RNA from the excised mice pancreas, a comprehensive DNA microarray analysis of gene expression was performed. The genes identified with the highest levels of expression were analyzed by using qRT-PCR. Expression levels of IL-6, IL-8 and TNF-a were confirmed by qRT-PCR. Tissue specimens were also subjected to hematoxylin-eosin staining and immunohistochemistry using anti- Regenerating islet-derived 3A and G (Reg3A/G) antibody. ImageJ software was used to quantify the area of Reg3A/G positive cells in pancreatic islets by binarizing image date followed by area extraction. The results were compared using Mann-Whitney U test. Data are presented as mean ± standard deviation (SD) with $p < 0.05$ considered as significant.

Results:

Reg3G, a gene related to pancreatic cancer, was one of the 10 genes with the highest levels of expression in the pancreas stimulated with PG-LPS. The comprehensive analysis revealed a 73-fold increase Reg3G expression level in the PG-LPS group when compared with the control group; in addition, the expression level of Reg3A was increased by 11-fold in the PG-LPS group. The increased expressions of Reg3A/G were

confirmed by qRT-PCR ($p<0.05$). Image analysis showed that the ratio of Reg3A/G positive cells was higher in the PG-LPS group than the control ($p<0.05$). Immunostaining showed the presence of Reg3A/G-positive cells in the alpha-cell equivalent areas around the islets of Langerhans in the PG-LPS group. No inflammatory changes were confirmed by morphological observation and expression levels of IL-6, IL-8 and TNF-a.

Conclusions:

PG-LPS may be involved in pancreatic cancer via Reg3A/G expression.