**Background:**

Toll-like receptors (TLRs) play a role in the innate immune response to microbes in the sinonasal cavity. The aim of this study was to evaluate whether nasal polyp-derived fibroblasts (NPDFs) and organ-cultured nasal polyps can synthesize pro-inflammatory cytokines and matrix metalloproteinases (MMPs) after exposure to lipopolysaccharide (LPS).

**Methods:**

The mRNA and protein expression levels of TLRs, cytokines, and MMPs were determined using a gene expression microarray, real-time RT-PCR, western blot analysis, ELISA, and immunofluorescence staining. The enzymatic activities of MMPs were analyzed using collagen or gelatin zymography.

**Results:**

LPS induced mRNA expression of TLR4, IL-6, IL-8, and MMP-1 and activated MAPK signaling in NPDFs. LPS promoted the release of interleukin (IL)-6 through extracellular signal-related kinase (ERK) and IL-8 through ERK and c-Jun N-terminal kinases (JNK). Production of IL-6 and IL-8 was induced by PI3K/Akt signaling in LPS-stimulated NPDFs. LPS increased the transcript and protein expression levels of MMP-1 and induced collagenase activity of MMP-1 via ERK and p38. Rhodobacter sphaeroides (LPS-RS) inhibited the stimulatory effects of LPS in NPDFs as well as in organ culture of nasal polyp.

**Conclusion:**

LPS triggers immune response via TLR 4 and activates MAPK and PI3K/Akt signaling pathway, which is involved in remodeling of nasal polyps.

**Abstract**

We showed that LPS induces production and expression of IL-6, IL-8, and MMP-1 via the TLR4, MAPK and PI3K/Akt signaling pathways in NPDFs. We found that expression of IL-6, IL-8, and MMP-1 is stimulated by LPS via TLR4 in nasal polyp organ cultures. Thus, LPS exposure may be involved in the pathogenesis in the remodeling of nasal polyposis.

**Materials and Methods**

NPDFs and organ-cultured nasal polyps were isolated from nasal polyps of 8 patients and exposed to LPS. Cells used for experiments were obtained from the fourth cell passage. Microarray analysis were performed using a DNA microarray scanner and quantified using Feature Extraction Software. Ex vivo organ culture were performed by following protocols. The rinsed tissue fragments were placed on gelatin sponge with the mucosa side facing up and the submucosa side facing down. Tissue fragments were placed into 6-well plates and filled with 1.5 mL of culture medium per well such that the mucosa was above the liquid phase. Statistically significant differences between groups were assessed by one-way ANOVA for factorial comparisons and Tukey’s test for multiple comparisons. A value of $p < 0.05$ was accepted as significant.

**Results**

![Fig. 1. Expression of MMP-1 in inferior turbinate and nasal polyps.](image1.png)

![Fig. 2. Effect of LPS on TLR4 expression in NPDFs.](image2.png)

![Fig. 3. Effect of LPS on pro-inflammatory cytokines expression in NPDFs.](image3.png)

![Fig. 4. Effect of LPS on MMP expressions in NPDFs.](image4.png)

![Fig. 5. Inhibitory effect of TLR4 antagonist on pro-inflammatory cytokines and MMP-1 production in NPDFs.](image5.png)

![Fig. 6. Inhibitory effect of TLR4 antagonist on pro-inflammatory cytokines and MMP-1 Production in nasal polyp organ cultures.](image6.png)

**Conclusions**

We showed that LPS induces production and expression of IL-6, IL-8, and MMP-1 via the TLR4, MAPK and PI3K/Akt signaling pathways in NPDFs. We found that expression of IL-6, IL-8, and MMP-1 is stimulated by LPS via TLR4 in nasal polyp organ cultures. Thus, LPS exposure may be involved in the pathogenesis in the remodeling of nasal polyposis.

**References**