**Introduction:** The causes of loosening are mainly divided into two major categories. One is the septic loosening caused by implant infection and the other one is the so-called aseptic loosening caused by foreign body inflammation against adhesive and abrasive wear debris. It has lately become apparent that even dead microbes, not able to divide, can provoke inflammation as ligands for Toll-like receptors (TLRs). TLRs are transmembrane proteins of inflammatory cells, which recognize infectious threats, so called danger signals. Microbial components can provoke inflammation as ligands for TLRs (1). Recently, it also becomes evident that TLRs can also recognize the molecule of self-components (2), which may induce production of osteolytic inflammatory cytokines found in aseptic loose interfacial membrane.

As inflammatory molecules play important roles in not only innate immune responses to microorganisms, but also foreign body reactions, this work was performed to assess the eventual presence of TLRs in the aseptic and septic loosening of total hip joints.

**Materials and Methods:** 1) Immunohistochemistry: Aseptic synovial-like membranes in the regenerated capsular tissues of loose hip prostheses were obtained at revision total hip arthroplasty (n=12). Synovial-like membranes from septic regenerated capsular tissues of the hip implants (n=3) and ostearthritic synovial tissues were used for comparison (n=4). The samples were processed for immunopathologic analysis on tissue co-localization of TLRs with CD68 (monocytes/macrophages) and/or CD15 (granulocytes/myeloids) to be examined using Alexa fluorescent system (Molecular Probes Inc., OR, USA). 2) mRNA analysis: Total RNA was isolated from frozen tissues and converted into cDNA. Enzymatic amplification of the specific cDNA sequences was performed on Light Cycler system (Rosch, Germany). TLR2, TLR4, TLR5 and TLR9 were amplified using Light Cycler Software and beta-actin as a control.

**Results:** 1) Immunostaining: Immunofluorescent staining showed co-localization of TLR2, TLR4, TLR5, and TLR9 with CD68 in the focal monocyte/macrophage aggregates in the aseptic synovial-like membrane in the loose total hip joints [Figure 1]. TLR2, TLR4, TLR5, and TLR9 co-localized with CD15 mainly in polymorphonuclear leukocytes and CD68 positive mononuclear cells of the septic synovial-like membrane around total hip joints. In ostearthritic synovial tissues, expression of TLRs was only found in vascular cells and mononuclear cells, but the reactivity was weak. 2) mRNA analysis: Agarose gel electrophoresis showed moderate to marked presence of TLR2, TLR4, TLR5 and TLR9 both in aseptic and septic synovial-like tissues around total hip joints. The presence of TLR2, TLR4, TLR5 and TLR9 were absent and/or weak in ostearthritic synovium when compared to aseptic and septic synovial-like tissues.

**Discussion:** TLRs are found both in aseptic and septic synovial-like membranes around loose hip prosthesis.

TLRs were mainly found in polymorphonuclear leukocytes of septic synovial-like membranes. This indicates some of the components and one of the cascades involved in cellular host defense to microorganisms. The presence of TLRs in aseptic synovial-like tissues probably indicates enhanced responsiveness of periprosthetic tissue as a result of foreign body reaction to whatever TLR ligands might be there derived from the sterile joint prosthesis implanted in the primary operation or later absorbed from the circulation to the surface of the implant or implant-derived wear debris.