STRESZCZENIE W JĘZYKU ANGIELSKIM

During pregnancy, a series of anatomical and physiological changes occur in the mother's body, creating an appropriate environment for the developing fetus. The immune system must also undergo temporary modulation to simultaneously protect both the mother and the fetus from pathogens while accepting the semi-allogeneic fetus. Therefore, the proper progression of pregnancy depends on the appropriate regulation of the immune system, which is largely dependent on acquired immunity activity, particularly on the regulatory cell populations, mainly regulatory T cells (Tregs). Recently, research has also focused on B cells with suppressive properties, known as regulatory B cells (Bregs), and their role in both normal and pathological pregnancy.

B cells are an important component of the immune system, and during pregnancy, both their activity and number undergo changes. To date, their role in pregnancy has been mainly studied in the context of the humoral response. However, as antigen-presenting cells (APCs), B cells may also participate in inducing tolerance to paternal antigens.

Toll-like receptors (TLRs), including TLR9, regulate the activity of B cells as both APCs and Bregs. Research on the role of TLR9 in pregnancy has mainly focused on the activation of these receptors in later stages of pregnancy. Activation of TLR9, following the recognition of endogenous signals (cell-free mitochondrial DNA and cell-free fetal DNA), has been associated with complications such as preterm birth and preeclampsia. However, little is known about the role of TLR9 in the early stages of pregnancy and associated complications, as well as its potential involvement in shaping immunotolerance.

The overall aim of this study was to investigate the role of the TLR9 receptor in shaping the B cell phenotype and regulating immunological tolerance in the murine abortion-prone model of pregnancy (♀CBA/J x ♂DBA/J) and in women during early pregnancy.

The study demonstrated that blocking TLR9 signaling in female CBA/J mice mated with DBA/2J males increases the likelihood of losing an allogenic pregnancy but does not affect successful implantation. Additionally, reducing TLR9 signaling caused changes in the costimulatory phenotype of T and B cells and led to a decrease in Treg cell numbers and activated Th cells, but did not affect the frequency of Breg.

In the second part of the study, it was shown that peripheral blood B cells do not exhibit differences in TLR9 expression between pregnant women and those after miscarriage (7-14 weeks of pregnancy). This suggests that this receptor is not involved in the observed change in the costimulatory phenotype of these cells following a miscarriage. However, women after miscarriage showed an increased frequency of B cells with a tolerogenic phenotype ($CD19^{+}CD38^{high}CD24^{high}$), which, combined with the observed decrease in activated T cells, suggests their involvement in restoring the immunological balance disrupted by early pregnancy loss.

In summary, the studies indicate the involvement of the TLR9 receptor in shaping immunological tolerance and maintaining pregnancy in mice by influencing the B cell costimulatory phenotype and Treg frequency. In contrast, in women after miscarriage, TLR9 is likely not involved in restoring the disrupted immunological balance, where Breg $CD19^{+}CD38^{high}CD24^{high}$ play a role.