PROGESTERONE DRIVES EXPANSION OF THE CD4^CD25^FOXP3^REGULATORY T (TREG) CELLS DURING EARLY PREGNANCY OF MICE AND HUMAN

J. Ma, R. Ma
Obstetrics and Gynecology Department, First Affiliated Hospital of Kunming Medical University, China

Pregnancy is a physiological state of tolerance of the immune system of the maternal body to genetically foreign fetus. This temporary state of the maternal immune system stems from an increased expansion of regulatory T cells (Treg cells), which are characterized by the ability to suppress proliferation of effector cells by direct contact or excreting regulatory cytokines. It has been shown that the number of Treg cells increases during pregnancy. Little is known, however, regarding the relationship between progesterone and immune tolerance during early pregnancy, an important period, characterized by increased level of progesterone from non-pregnant state. We demonstrate that early-pregnant dose of progesterone is capable of augmenting Treg cells proliferation and its Foxp3 expression in vivo. Treatment of ovariectomized mice with progesterone not only increases the proportion of systemic and local uterine Treg cells and their Foxp3 expression, but also enhances their suppressive function by increasing galectin-1 expression on Treg cells and IL-10 excretion. Moreover, the effect of progesterone is inhibited in vivo by the nuclear progesterone receptors antagonist RU486 in progesterone-treated ovariectomized mice models, suggesting that progesterone expands Treg populations via nuclear progesterone receptors. Furthermore, we find that the abortion-prone patients with progesterone insufficiency show a lower proportion of systemic Treg cells than normal pregnancy. Regular progesterone therapy (20mg, im., Qd*5d) induces the proliferation of Treg cells and its Foxp3 expression, suggesting that high progesterone levels during pregnancy may help to maintain fetal tolerance. In summary, our data suggest progesterone promotes tolerance by expanding the regulatory T cell compartment.