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• ORIGINAL PAPER •

Adoptive transfer of FTY720-treated immature bone marrow-derived dendritic cells (BMDCs) significantly reduced the spontaneous resorption rate in the CBA/J ×DBA/2 mouse model

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Objective *To investigate the effect of FTY720-treated immature bone marrow-derived dendritic cells (BMDCs) on the embryo resorption rate in the CBA/J × DBA/2 abortion mouse model.*

Methods *The dendritic cells (DCs) were derived from bone marrow of DBA/2 mice, and then co-cultured with FTY720. The abortion mouse models were established by mating female CBA/J mice with DBA/2 mice. Via the CBA/J × DBA/2 abortion mouse model, six groups were established, group A: normal pregnancy model; group B: abortion mouse model with no treatment; group C: abortion mouse model injected with DC culture medium (DCCM); group D: abortion mouse model injected with DC; group E: abortion mouse model injected with FTY720; group F: abortion model mouse injected with FTY720-DC. The differences were compared in the embryo resorption rates of the CBA/J × DBA/2 abortion mouse model treated with FTY720-DC or different controls observed on gestation day 12 to 14, and then the microenvironment in murine pregnancy was investigated.*

Results *The embryo resorption rate was statistically significantly decreased in group D and group E when they compared with group B and group C ($P<0.05$, respectively). Furthermore, the embryo resorption rate in group F showed a statistically significant decrease when compared with the other groups except group A ($P<0.01$). These results*

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suggest that FTY720-DCs possess a notable advantage over DCs or FTY720 in reducing the embryo resorption rate of the abortion mouse model. The percentage of Th17 (IL-17$^+$CD4$^+$T cells) in peripheral blood mononuclear cell (PBMC) in the abortion mouse model was 4.35% ± 0.34% before treated with FTY720-DC, and was 1.34% ± 0.28% after treated with FTY720-DC (P<0.01). The percentage of Tregs (CD4$^+$CD25$^+$Foxp3$^+$T cells) in PBMC was significantly increased in group F (8.35% ± 1.80%) as compared with group B (2.68% ± 0.65%)(P<0.01).

Conclusion *Adoptive transfer of FTY720-DC can statistically significantly reduce the embryo resorption rate in the CBA/J × DBA/2 abortion mouse model. The lower embryo resorption rate in the FTY720-DC treated abortion mouse model may be caused by the imbalance of Treg/Th17.*

Key words: embryo resorption rate; FTY720; tolerance; adoptive transfer; spontaneous abortion; dendritic cell (DC)

In reproductive immunology, the embryo is considered a semihomograft that is not rejected by maternal immune system in normal pregnancy. The maternal immune system expresses a special type of immune tolerance to the fetus. If this immune tolerance is destroyed, pathological pregnancy will occur, such as recurrent spontaneous abortion.

FTY720, a sphingosine 1 phosphate (S1P) receptor modulator, is a potent immunosuppressant that can prolong allograft survival[1], prevent the development of graft-versus-host disease[2], autoimmune type I diabetes, rheumatoid arthritis and multiple sclerosis[3]. Most previous studies[4,5] have been focused on Treg cells and dendritic cell (DC) to elucidate the mechanisms and possible target cells of the immunosuppressive effects of FTY720. There is a large body of evidence indicating that DC plays a certain regulatory role in the process of inducing immune tolerance. Possible mechanisms include allogeneic microchimerism, immature DCs or specialized tolerogenic DCs subsets inducing apoptosis or anergy of recipient T cells, while shifting naïve T cells towards a regulatory phenotype and expanding existing Treg. Some pioneered researches found[4,5] that FTY720-DCs showed potent capacity to prolong allograft survival. Their role in inducing pregnancy immune tolerance has drawn more attention from researchers recently. Our study will observe the influence of adoptive transfer of FTY720-DCs on the spontaneous resorption rate in the CBA/J × DBA/2 mouse model. Here we report that the adoptive transfer of FTY720-treated immature bone marrow-derived dendritic cells (BMDCs) could notably reduce the spontaneous resorption rate in the CBA/J × DBA/2 mouse model. It may provide an alternative therapeutic method based on allogeneic DCs vaccination in the future.