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Title	The effect of macrophage migration inhibitory factor on the development of preimplantation mouse embryos
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Citation	Japanese Journal of Veterinary Research, 46(2-3), 154-154
Issue Date	1998-11-30
Doc URL	https://hdl.handle.net/2115/2705
Type	departmental bulletin paper
File Information	KJ00003408038.pdf



The effect of macrophage migration inhibitory factor
on the development of preimplantation mouse embryos

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Cytokines proved to play an important role in the establishment of pregnancy. In this study, the role of macrophage migration inhibitory factor (MIF), one of the cytokines playing a critical role in inflammatory and immune responses, in the preimplantation development of mouse embryos was investigated.

In the first experiment, the effect of exogenous MIF on the *in vitro* development of mouse embryos was examined. One-cell mouse embryos were cultured with different concentrations of recombinant rat MIF (0.1, 1.0 and 10 $\mu\text{g/ml}$). MIF had no effect on the development of one-cell mouse embryos up to the morula stage; however, MIF at the concentration of 10 $\mu\text{g/ml}$ inhibited further development of embryos to blastocysts.

The next experiment determined the effect of embryonic MIF in the preimplantation development of mouse embryos. In this experiment, one-cell mouse embryos were cultured with anti-MIF antibody. Anti-MIF antibody had no effect on the preimplantation development of mouse embryos.

To investigate the changes in the maternal availability of MIF in the uterus, MIF concentrations in the uterus and circulation were deter-

mined in mice during the preimplantation period and the normal estrous cycle. Uterine MIF concentration of pregnant mice determined by Western blot analysis increased from day 0 (proestrus) to day 1 (the day of vaginal plug) and decreased on day 2, and the decreased concentration was maintained until day 4. In cycling mice, uterine MIF concentrations were at the same levels throughout the study. Serum MIF concentration determined by enzyme-linked immunosorbent assay did not change during the period of investigation in both pregnant and cycling mice. The increase in the concentration of MIF in the uterus on day 1 of pregnancy suggest that MIF is involved in the inflammation-like cellular response which is known to occur in the uterus following mating. The decline in MIF concentration in the uterus found from day 2 to day 4 of pregnancy may be one of the mechanisms to prevent the inhibition of embryonic development by MIF in the uterus, since a high concentration of MIF suppressed embryonic development to blastocysts.

In conclusion, MIF may be one of the cytokines regulating the preimplantation development of mouse embryos.