

## The immuno-modulatory properties of Progesterone

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In the presence of progesterone, activated lymphocytes synthesize an immunomodulatory protein, named the progesterone induced blocking factor (PIBF). PIBF induces Th2 biased cytokine production by binding to a PIBF receptor - IL-4 receptor alpha complex and activating the STAT6 pathway via the latter.

PIBF concentrations were determined in urine samples of 520 pregnant women. Significantly higher concentrations were found in samples from healthy pregnant women than in those of patients at risk for premature pregnancy termination. 70% of healthy pregnant women demonstrated higher than normal (non-pregnancy) values, whereas the rate of higher than normal values in risk pregnancies was less than 10%. Via inducing PIBF production, dydrogesterone treatment improves pregnancy success rates in threatened aborters by inhibiting the production of the Th1 cytokines and up-regulating the production of the Th2 cytokines.

The possibility that PIBF concentration is related to successful pregnancy was investigated in murine systems. In pregnant mice progesterone receptor block as well as neutralization of endogenous PIBF activity results in pregnancy loss. Pregnancy termination is accompanied by increased  $\geq$  IFN and reduced IL10 production, resulting in increased splenic NK activity. Both increased resorption rates and immunological alterations are corrected by simultaneous treatment of the pregnant mice with anti-NK antibodies. These data suggest PIBF exerts an anti abortive effect by altering the cytokine balance.