

Placenta Extract as a Novel Immunosuppressor of Autoimmune Diseases

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Pregnancy is known to modulate many autoimmune diseases. For example, autoimmune thyroiditis improves during late pregnancy while autoimmune hypophysitis typically presents during this period. The mechanisms underlying the effect of pregnancy on autoimmunity remain unknown; however, the placenta contains several immunoregulatory factors. To determine whether placental proteins influence autoimmunity, we employed two mouse models of endocrine diseases: experimental autoimmune thyroiditis and hypophysitis (EAH). In the hypophysitis model, addition of mouse placenta to the immunogen, mouse pituitary, significantly decreased disease incidence and severity ($p=0.02$). This decrease was accompanied by a significant decline in antibody titers ($p=0.001$). Disease suppression was also specific to the placenta; addition of mouse liver ($p=0.79$) or muscle ($p=0.80$) to the immunogen was incapable of suppressing disease. In the thyroiditis model, addition of placenta to thyroglobulin similarly decreased disease incidence ($p=0.002$) and antibody titers ($p=0.03$). Mouse placenta was found to contain significantly higher levels of soluble TNF receptor one (sTNFR1) when compared by cytokine array to skeletal muscle. Addition of TNFR1^{-/-} placenta to pituitary decreased disease incidence and severity ($p=0.007$); suggesting that sTNFR1 is not responsible for suppressing EAH. Suppression of EAH is dependent on the route of administration of placenta; placenta given in IFA ($p=0.681$) or in a soluble form ($p=0.071$) does not suppress EAH. Furthermore, immunization with pituitary proteins during early ($p=0.53$) and late ($p=0.32$) pregnancy has no effect on EAH. These results suggest that a placenta factor is capable of dampening the immune response to a co-injected immunogen and if identified could serve as a potential therapeutic.