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Prolonged estrus suppression by ectopic transplantation of invasive equine trophoblast

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1. Introduction

Previous studies from our laboratory have demonstrated that invasive trophoblast cells of the equine chorionic girdle have the capacity to differentiate and survive after transplantation to ectopic sites in fully allogeneic, non-pregnant mares. The lifespan of the transplanted cells was not determined, and no functional outcome was described.

2. Material and methods

Previously described methods were used for chorionic girdle recovery and transplantation to the vulvar mucosa in non-pregnant recipient mares (de Mestre et al., 2008, Placenta 29:158–169). Seven mares received day 34 chorionic girdle. Three mares received transplants of day 34 allantochorion membranes, and one non-treated mare was followed as an additional control. The mares were teased twice weekly with a stallion and estrous behavior recorded. Blood samples were taken twice weekly and assayed for progesterone and equine Chorionic Gonadotrophin (eCG) by radio-immunoassay or ELISA. Serum samples were tested for cytotoxic antibody to the Major Histocompatibility Complex (MHC) class I antigens of the donor horses as previously described. Biopsies of the transplant sites were taken from 3 recipients at various times after transplantation and evaluated using immunohistochemistry and monoclonal antibodies to equine lymphocyte subsets and trophoblast markers.

3. Results

The transplanted trophoblasts expressed polymorphic MHC class I molecules, which induced strong cytotoxic antibody responses in the recipients against the donor MHC class I antigens. The transplants also attracted intense accumulations of T cells that persisted at the site of transplantation. Trophoblast cells resisted immunological destruction by the recipients and functioned for up to 105 days post-transplantation, as assessed by serial examination of biopsies and eCG assays. The eCG levels of 3–25 iu/ml were lower than

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usually measured in normal horse pregnancy, but still easily detectable. The eCG delivered by the cells was biologically active and induced profound changes in the reproductive physiology and behaviour of the recipients, causing secondary ovulations and corpora lutea formation that prevented the recipients from displaying signs of estrus for up to three months after a single injection of trophoblast cells. Control mares that received allantochorion transplants continued to cycle normally.

4. Discussion

It is likely that the changes in reproductive physiology and estrous behavior in the recipients was caused by sustained delivery of low levels of eCG. This form of cellular therapy may find utility as a means of extended suppression of unwanted estrous behavior in performance horses.