

The immunomodulatory enzyme IDO: Expression in the uterus of mares?

IDO modulates immune responses. The enzyme indoleamine 2,3-dioxygenase 1 (IDO) degrades tryptophan. This amino acid is required for immune defences against pathogens, but also stimulates pathogen growth. Its degradation inhibits effector lymphocytes and retards pathogen proliferation. Thus, IDO reduces tissue damage associated with inflammation and infection.

IDO deficiency decreases fertility. IDO expression in the uterus of women and mice likely supports tissue integrity and proper organ function that are requirements for pregnancy and fetal development; IDO deficiency can result in abortion and premature birth.

In mares, reproductive failure can have an economic importance. In mares, reproductive problems can have an impact on the wellbeing of individual animals and can cause financial loss for the horse breeding industry. To the authors knowledge, no previous studies on the IDO expression in the equine uterus exist.

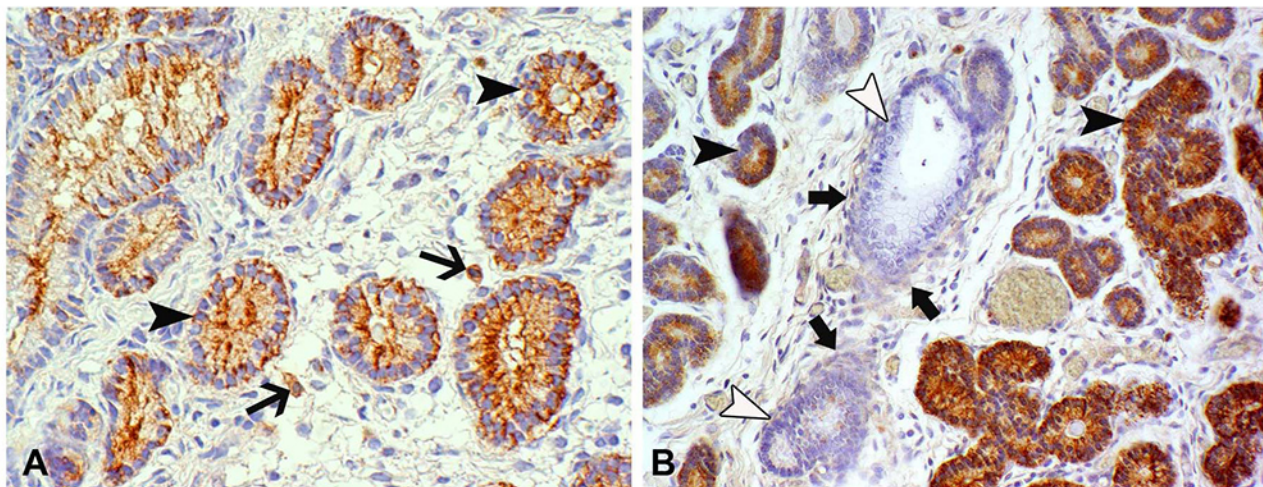


Fig. 1. Detection of IDO protein in the equine endometrium by immunohistochemistry. The presence of IDO protein corresponds to the brown chromogen. A. Equine endometrium containing healthy uterine glands. IDO is expressed in epithelial cells of healthy glands (black arrowheads) and macrophages (thin arrows). B. Equine endometrium with healthy (black arrowheads) and diseased (white arrowheads) uterine glands. Diseased glands have periglandular fibrosis (endometrosis) that is characterized by periglandular stroma cells, that are concentrically arranged around affected glands (thick arrows). In comparison to healthy glands, diseased glands lack IDO expression.

Expression of IDO in the uterus of mares? The endometrium of 25 mares is examined by immunohistochemistry. The endometrium forms the innermost lining of the uterus. It is composed of the luminal epithelium and the underlying stroma that contains uterine glands and immune cells including macrophages. Immunohistochemistry is a scientific method for the detection of IDO protein in cells.

IDO is present in the endometria of all 25 mares. Endometria of three mares are healthy, the remaining endometria show inflammatory and/or degenerative diseases, i.e. endometritis, endometrosis and/or angiosclerosis.

IDO is produced by epithelial cells and macrophages. IDO containing epithelial cells are mostly located in glands (Figure 1A) and less frequently in the luminal epithelium.

Two different patterns of IDO expression are observed. The endometrium of 21 displays a concurrent expression of IDO in epithelial cells and macrophages, whereas in 4 mares IDO is only detected in macrophages.

IDO expression differs between healthy and diseased uterine glands. In comparison to healthy glands, endometrotic glands mostly lack IDO expression (Figure 1B). The endometrium of older mares often contains diseased glands that show periglandular fibrosis together with functional alterations. This unique disease of mares is named as endometrosis. Please note that endometrios is a different disease that occurs in women, but not mares.

Identification of IDO as an immunological component of the equine endometrium. The detection of IDO in all examined endometria implies its functional importance in the equine uterus as well.

Role of IDO in breeding-induced endometritis? In mares breeding and insemination evokes an inflammatory response (breeding-induced endometritis: BIE). In most mares (referred to as "resistant mares"), BIE is a transient condition that lasts less than 72 hrs and has no impact on fertility. Some mares, however, develop long lasting inflammation that results in pregnancy failure. These mares are named as „susceptible mares“.

Individual differences between mares. The absence of IDO in epithelial cells of 4 mares suggest the presence of individual differences between mares that could possibly predispose mares to bacterial infection or BIE.

Endometrosis: paving the way for endometritis? The markedly reduced IDO expression in diseased glands suggests that endometrosis may predispose to prolonged inflammation and/or bacterial infection. Inflammation/infection of glands will impair the production of glandular secretions that provide the nutrition for the early equine conceptus.

A pilot investigation with likely clinical relevance. Results of this study are an important prerequisite

for future studies on a larger number of endometrial biopsies under consideration of clinical data, e.g. biopsy submission from a susceptible mare. Such future studies will likely provide important insights into the pathogenesis of fertility disorders in mares and may even lead to novel treatment options.

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[Expression of indoleamine 2,3-dioxygenase 1 as transcript and protein in the healthy and diseased equine endometrium.](#)

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