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EXPRESSION OF CYP27A1, CYP2R1 AND VDR IN EQUINE CRYPTORCHID TESTIS

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A functional vitamin D (VitD) requires a double step bioactivation by six cytochrome P450 (CYP) isoforms. The first step happens in the liver by four D-25-hydroxylase enzymes, among them the most active are CY27A1 and CYP2R1; the activation pathway ends in the kidney by a 1-α-hydroxylase [1]. The biological activity of VitD requires binding to the cytosolic VitD receptor (VDR), which translocate to the nucleus and act as a factor regulating the transcription of more than 200 genes modulating normal and cancer cell growth, differentiation, apoptosis, angiogenesis and metastatic potential [2]. VitD deficiency has been suggested as a risk factor for cancer because it impairs the anti-proliferative properties of vitamin D receptor (VDR) [3], and it adds to cryptorchidism as a cause of testicular cancer [4]. In the horse cryptorchidism is one of the male developmental defect that affects more than 9% of the subjects. Male reproductive tract expresses VDR and the enzymes involved in vitamin D activation through 25-hydroxilation [5]. Therefore, this study examined whether equine testis expresses CYP27A1 and/or CYP2R1 and VDR proteins and whether cryptorchidism may impair their expression thus enhancing the risk of developing testicular cancer. By western blot and immunohistochemistry, CYP27A1, CYP2R1 and VDR proteins were quantified and localized. Results demonstrated that all the three proteins were expressed in equine testis, moreover the expression level of CYP27A1 and VDR were significantly lower ($P<0.01$ and $P<0.05$ respectively) in the retained testis in respect to the contralateral scrotal testis. CYP2R1 protein resulted expressed at the same level both in the undescended and in the scrotal testis. This study showed that also in the horse testes play a role in the vitamin D metabolism.

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[2] Bergadà et al., Role of local bioactivation of vitamin D by CYP27A1 and CYP2R1 in the control of cell growth in normal endometrium and endometrial carcinoma. Laboratory investigation, 94:608-22, 2014.

[3] Yabushita et al. Vitamin D receptor in endometrial carcinoma and the differentiation inducing effect of 1,25-dihydroxyvitamin D3 on endometrial carcinoma cell lines. J Obstet Gynaecol Res 22: 529-39, 1996.

[4] Schepisi et al. Vitamin D status among long-term survivors of testicular cancer. Oncotarget 8(22):36780-6, 2017.

[5] Blomberg et al. Vitamin D receptor and vitamin D metabolizing enzymes are expressed in the human male reproductive tract. Human Reprod 25:1303-11, 2010.