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The mouse epididymis: A site of strong and constitutive expression of the tryptophan metabolizing enzyme indoleamine 2,3-dioxygenase (IDO)

Shigenobu Toné [a], Aurore Britan [c], Aicha Jrad [b], Violette Maffre [b], Joël R. Drevet [b,*]

[a] *Department of Biochemistry, Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama 701-0192, Japan*
[b] *CNRS UMR 6547 GEEM, Université Blaise Pascal, 24, avenue des Landais, 63177 Aubière cedex, France*
[c] *Department of Cell Physiology and Metabolism, University of Geneva, School of Medicine, Genève, Switzerland*

Abstract. Some twenty-five years ago it was reported for the first time that indoleamine 2,3-dioxygenase (IDO) activity was particularly important in rodent epididymis protein extracts. Several years ago, it was also shown that the epididymal expression of IDO was constitutive and not driven by the interferon-gamma, inflammatory cytokine, as is the case in most of the other tissues tested. Since then, the epididymal expression of IDO has not been investigated further. Recently, we have reported a more detailed study showing that indeed the mouse epididymis expresses both IDO transcript and protein at a high level while this is not the case for the other tryptophan-catabolizing enzyme, TDO. On the basis of the different functions that have been assigned to IDO we discuss here the putative roles of IDO expression as well as tryptophan metabolism on the physiology of the mammalian epididymis. © 2007 Published by Elsevier B.V.

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* Corresponding author.
E-mail address: joel.drevet@univ-bpclermont.fr (J.R. Drevet).

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1. Introduction

In earlier studies, Yoshida et al. (1980) [1] reported that rodent epididymis protein extracts had a high indoleamine 2,3-dioxygenase (IDO) activity. Later on, Takikawa et al. (1999) [2] established that the epididymal expression of IDO was constitutive and independent of the control exerted by the inflammatory interferon-gamma cytokine, its major inducer in most tissues. Very recently, two reports confirmed that the mammalian epididymis is indeed the site of constitutive and intense expression of the IDO mRNA [3,4].

IDO (EC 1.13.11.42) is an enzyme that regulates the intracellular level of tryptophan and is the rate-limiting and first enzyme in the kynurenine pathway. To recycle tryptophan, the least abundant of the essential amino acids for mammals, IDO uses oxygen and superoxide anion [5,6] and it has been reported that superoxide dismutase (SOD) inhibited partially, *in vitro*, the activity of IDO [7–9]. Because of these characteristics it was proposed that IDO could act as an anti-oxidant scavenger [10]. However, in the presence of oxygen, the active ferrous form of IDO is easily oxidized to its inactive ferric form, thus resulting in the release of superoxide anion [6]. In addition, IDO does not decompose superoxide anion as SOD does and therefore should not be strictly considered as an anti-oxidant scavenger [11]. The anti-oxidant potential of IDO could, however, reside in the downstream-products generated by the catabolism of tryptophan along the kynurenine pathway or in its impact on the biosynthesis of serotonin and melatonin. However, it is not really clear whether several of the kynurenines are anti-oxidant or pro-oxidant molecules (for a review see: [12]). In this report we bring precisions regarding the expression/distribution of IDO mRNA and protein in the mouse epididymis. We then discuss what could be the role of IDO in the physiology of the mammalian epididymis.

2. Materials and methods

2.1. Animals and materials

Tissues were obtained from male mice of the Swiss strain CD1 (Charles River, Cléon, France) raised in the laboratory under constant conditions of temperature (20 °C ± 1 °C), daylight, and feeding. Animals were manipulated according to the French guidelines of the "Use and Care of Laboratory Animals". They were sacrificed at 80 days old by cervical dislocation. Tissues of interest were dissected, washed in PBS and processed immediately or frozen in liquid nitrogen and stored at −80 °C before use. Alpha^{32}P-dCTP (3000 Ci/mmol) used for northern analyses was from Amersham (Les Ulis, France).

2.2. RNA Master blot

Positively charged nylon membrane onto which polyA^{+} RNAs from several mouse tissues were immobilized (RNA Master blot™, Clontech Laboratories, Palo Alto, CA, USA) was hybridized overnight at 65 °C with a ^{32}P-dCTP random-labeled IDO cDNA fragment in ExpressHyb hybridization solution (Clontech) as recommended by the manufacturer. After washing (2X SSC-1% SDS, 65 °C, 20 min; 0.1X SSC-0.5% SDS, twice 20 min), blots were exposed to a phosphorimager apparatus (Personal Molecular

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