IDO1 activity in selected immune cells controls antibody responses

1)Scalisi G. 2)Gargaro M. 3)Turco A. 4)Iorio A. 5)Puccetti P. 6)Matino D. 7)Fallarino F.

University of Perugia

Indoleamine 2,3-dioxygenase 1 (IDO1) is an enzyme involved in the initial step of tryptophan degradation along the kynurenine pathway. It has immunosuppressive effects, linked to enzymic and non-enzymic regulatory functions. IDO1 is also crucial for sustaining the function of T regulatory cells (Treg), which are involved in the establishment of peripheral tolerance.

We recently found that defective IDO1 induction is associated to anti-FVIII antibody production in patients with severe Hemophilia A (Matino D. et al., 2015). In hemophilic mice, CpG- rich oligodeoxynucleotides (CpG-ODN) administration induced IDO1 expression in dendritic cells (DCs) that control FVIII antibody response.

Recently we discovered that CpG-ODN selectively induced IDO1 in a subset of conventional DCs (cDCs). IDO1 was found to be highly expressed in gut CD11C+CD103+ DCs, which are required for establishment of oral tolerance (Matteoli G. et al., 2010). Based on these data we analyzed the impact of IDO1 deficiency in controlling antibody responses, in two different experimental models (FVIII and ovalbumin, OVA, immunization). Interestingly, IDO1 deficiency resulted in a significant increase of FVIII-specific antibody production relative to wild type controls. Similarly, IDO KO mice showed a significant immunoglobulin production in a model of OVA-induced oral tolerance.

These data suggest the regulatory role of IDO1 in controlling antibody responses to self and non-self antigens.

Matino D. et al. J Clin Invest. 1;125 (10):3766-81 (2015)

Matteoli G. et al. Gut. 59:595–604(2010)