**Indoleamine 2,3-dioxygenase (IDO)**

Indoleamine 2,3-dioxygenase (IDO; indoleamine-pyrrole 2,3-dioxygenase; EC 1.13.11.42) [1-3] is the rate limiting enzyme in tryptophan (Trp) catabolism. It catalyzes the oxidative degradation of L-tryptophan to N-formylkynurenine. Because of this catabolic activity it has been postulated that one possible role of IDO is to inhibit the proliferation of intracellular pathogens [4, 5] or tumor cells [6] by depriving them of essential tryptophan.

**IDO2 - a new enzyme in the kynurenine pathway**

IDO2, like IDO catabolizes tryptophan but differs in the selectivity for some inhibitors. The selective inhibition of IDO2 by 1-methyl-D-tryptophan (Prod. No. ALX-106-041) suggests that IDO2 activity may have a role in the inhibition of immune responses to tumors [7, 8]. IDO2 expression is more restricted than IDO and has been found in mouse kidney, liver and sexual reproductive system as well as in dendritic cells.

**Immunoregulatory functions of IDO**

The immunoregulatory potency of IDO became clear in 1998 when D. H. Munn, et al. demonstrated that IDO is a crucial component of the mechanism by which the allogeneic fetus protects itself from rejection by the maternal immune system [9]. IDO contributes to the protection against autoimmunity [10, 11], allergy [12], and the control of inflammatory pathology [13, 14]. Inhibition of the immune response is thought to be caused by the effect of IDO on T cells. T cells undergoing antigen-dependent activation are exquisitely sensitive to local tryptophan catabolism, which causes them to arrest in G1, become anergic, or die [15-17]. Dendritic cells (DC) are suspected to be a crucial source of IDO. The protein is detectable and active in mouse [18, 19] as well as human [20] DCs. In mouse DCs cytotoxic T-lymphocyte antigen-4-immunoglobulin (CTLA-4-ig; CD152-ig) up-regulates IDO by ligation to B7 molecules upon induction of interferon-γ (IFN-γ) synthesis [21, 22]. A controversially discussed subpopulation of human DCs that constitutively expresses IDO and exhibits T cell suppressive properties has been identified [23, 24]. In addition, Platten, et al. showed that certain T cell responses can be prevented by altered peptide ligand (APL)-based induction of IDO. Naturally occurring metabolites of the IDO pathway and synthetic derivatives inhibited T cell proliferation and activation of antigen-presenting cells. Notably, the synthetic derivative N-(3',4'-dimethoxycinnamoyl) anthranilic acid (tranilast; 3,4-DAA) reversed paralysis in a mouse model of autoimmune encephalomyelitis [25]. In local tumor environment tryptophan degradation impairs the effector function of antigen-specific T cells and reduces the immunemediated control of tumor growth [26].

**For Literature References see backpage**

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**Figure 1: Mechanisms of IDO-Induced Tumoral Immune Escape.**

IDO expression in local immune stroma (1) and directly in tumor cells (2) has been implicated in promoting immune tolerance.

1. IDO is upregulated in antigen-presenting dendritic cells (DC) by autocrine IFN-γ released as a result of Treg cell–induced CTLA-4/CD152/B7-1 (CD80)-dependent cell-cell signaling. Local tryptophan (Trp) catabolism limits the proliferation and survival of T cells that would otherwise be activated by tumor antigens on the APC. This mechanism may operate in tumor-draining lymph nodes.

2. In tumor cells, attenuation of Myc box-dependent-interacting protein 1 (Bin1) leads to up-regulation of IDO expression by IFN-γ, directly suppressing activation of T cells in the local tumor environment.

Blocking IDO activity systemically with small molecule inhibitors (e.g. 1-methyl-tryptophan) reverses T cell suppression that occurs as a result of tryptophan catabolism in both settings.
IDO/IDO2 Inhibitors

Indoleamine 2,3-dioxygenase (IDO) and IDO2 catalyze the first and rate-limiting step of the kynurenine pathway along the major route of tryptophan catabolism. The scientific interest in this enzymes has been growing since the observations of the involvement of IDO and IDO2 in the mechanisms of immune tolerance and in the tumor immunomodulating process. Preclinical studies of small molecule inhibitors of the enzyme have indicated the feasibility to thwart the immunomodulating process and to enhance the efficacy of current chemotherapeutic agents, supporting the notion that IDO is a novel target in cancer disease.

Tranilast

[3,4-DAA]

ALX-550-409-M010 10 mg
ALX-550-409-M050 50 mg

Tranilast is a synthetic compound with structural similarity to the tryptophan (Trp) catabolites kynurenines. Trp degradation is an important mechanism in the maintenance of T cell tolerance in a variety of disease models and is mediated by the rate limiting enzyme indoleamine 2,3-dioxygenase (IDO).

For a comprehensive bibliography please visit our website.

Related Compounds

L-Tryptophan

ALX-101-051-G001 1 g

Kynurenic acid

ALX-550-052-M250 250 mg
ALX-550-052-G001 1 g

Metabolite of tryptophan. Antagonist at both the NMDA and AMPA/kainate receptors. Blocks kainic acid neurotoxicity.

Tranilast: a potential endogenous agonist for the kainate receptor.

L-Kynurenic acid

ALX-550-408-M050 50 mg

Metabolite of tryptophan. Key intermediate in the breakdown pathway of tryptophan.

Quinolinic acid

ALX-550-057-G001 1 g

Metabolite of tryptophan. Putative NMDA receptor agonist.

L-Tryptophan: a potential endogenous agonist for the NMDA receptor.

Dexamethasone

ALX-370-002-M250 250 mg
ALX-370-002-G001 1 g

Glucocorticoid with anti-inflammatory activity. Inhibits the induction of nitric oxide synthases (NOS). Activates Indoleamine 2,3-dioxygenase (IDO) in plasmacytoid dendritic cells in vivo and thus promotes tryptophan catabolism and thereby suppression of T cells.

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IDO Proteins, Antibodies & Activators

**IDO (human) (rec.) (His)**
- ALX-201-333-C050 50 µg
  - Produced in *E. coli*. Mature human IDO (indoleamine 2,3-dioxygenase) (aa 1-403) is fused at the C-terminus to a His-tag.

**IDO (mouse) (rec.) (His)**
- ALX-201-335-C050 50 µg
  - Produced in *E. coli*. Mature mouse IDO (indoleamine 2,3-dioxygenase) (aa 1-407) is fused at the C-terminus to a His-tag.

**MAb to IDO (human) (ID 177)**
- ALX-804-719-C050 50 µg
- ALX-804-719-C100 100 µg
  - CLONE: ID 177. ISO TYPE: Mouse IgG1. IMMUNOGEN: Recombinant human IDO (indoleamine 2,3-dioxygenase). SPECIFICITY: Recognizes human IDO. Detects a band of ~45kDa by Western blot. Other species not tested. APPLICATION: ELISA, WB.

**PAb to IDO (human)**
- ALX-210-429-C050 100 µg
  - From rabbit. IMMUNOGEN: Recombinant human IDO (indoleamine 2,3-dioxygenase). SPECIFICITY: Recognizes human IDO. APPLICATION: ELISA, FC, ICC, WB.

**PAb to IDO (mouse)**
- ALX-210-429-C100 100 µg
  - From rabbit. IMMUNOGEN: Recombinant mouse IDO (indoleamine 2,3-dioxygenase). SPECIFICITY: Recognizes mouse IDO. APPLICATION: ELISA, WB.

**IDO Proteins, Antibodies & Activators**

**LPS**
- Lipopolysaccharides (LPS) from *E. coli* are potent inducers of IDO in dendritic cells (DC). LPS was found to significantly augment kynurenine production and decrease tryptophan levels in supernatants of DC [1, 2].

**ODNs**
- Unmethylated CpG motifs are prevalent in bacterial in contrast to vertebrate genomic DNA. Both, microbial DNA and synthetic oligonucleotides containing unmethylated CpG motifs (CpG-oligonucleotides (CpG-ODNs)) have been found to induce innate immune responses through motif-specific activation of toll-like receptor 9 (TLR9). Recent studies indicate that CpG-ODNs not only act as immune stimulatory agents but can also induce immune suppression depending on IDO and their route of administration [1-3].

**CONTROL ODNs and BULK SIZES ARE ALSO AVAILABLE.**
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