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Editorial

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The Importance of Arginine Deiminase

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Cancer is a global problem, and despite the efforts made in the past, research is still continuing worldwide to find medicines that are effective to solve this problem [1]. Arginine is a non-essential amino acid synthesized from citrate by urea cycle enzymes arginine ossuccinate synthetase and argininosuccinate lyase. Enzyme deprivation was effective in other malignancies. A well-known example is pegylated asparaginase, which is approved for the treatment of acute lymphoblastic leukemia [2].

Arginine plays an important role in the nutritional requirements of cancer cells. Some cancers may be oxotrophic for a particular amino acid, and amino acid deprivation is a method for treating these tumors [3]. It makes some cancer cells unable to synthesize (or not synthesize) these nutrients (amino acids) and depend on their external sources for their nutrition. Arginine, in particular, is one of them and is an effective source of nitrogen used by cancer cells for nucleic acid and protein synthesis [1].

The enzymatic degradation strategy of amino acids to deprive malignant cells of important nutrients is an established component of induction Therapy of various tumor cells [3]. L-Arginine deiminase (EC 3.5.3.6) is a therapeutic enzyme that catalyzes the irreversible hydrolysis of arginine to citrulline and ammonia. Mycoplasma, Pseudomonas aeruginosa and some Enterococcus species are commonly expressed in bacteria. L - arginine has started with the discovery of anti-cancer properties, such as deimase, and has been continuing its extensive research on microbial L-arginine ever since [1].

Arginine deiminase (ADI); It is an important arginine-washing enzyme, with broad applications as an anti-cancer agent for the treatment of arginine-oxotrophic tumors in particular. Arginine deiminase (E.C: 3.5.3.6) catalyzes the hydrolysis of arginine to citrulline and ammonia by deamination of the guanidino group. In general, the hydrolysis of arginine with ADI is considered the first step of the ADI system consisting of two reactions: conversion of citrulline to ornithine and reduction of carboamyl phosphate to ammonia and CO2 by carbamyl phosphate and carbamate kinase catalyzed by ornithine transcarbamylase (OTC) [4]. Pseudomonas aeruginosa (PaADI) L-Arginine deiminase catalyzes the hydrolysis of arginine to citrulline and ammonia [5]. It has been shown that arginine catabolism through arginine deiminase (ADI) allows it to resist in acidic environments and to avoid defense mechanisms. The ADI route consists of three enzymes: arginine deiminase, ornithine carbamoyl transferase and carbamate kinase; respectively arcA, arcB and arcC encoded by. These three proteins convert arginine into ornithine, ammonia and carbon dioxide. The ammonia produced increases the local pH and protects the bacteria from the surrounding acidic environment [6].

Arginine deiminase (ADI) has a high affinity for arginine and catalyzes arginine to citrulline and ammonia. Citrullin can be recycled to arginine in normal cells expressing arginine osuccinate synthetase (ASS), whereas ASS (-) tumor cells cannot. ASS expression loss; although it is described in other types of tumors, including pancreatic cancer, leukemia, prostate cancer and renal cell carcinoma, it is most commonly associated with melanoma and hepatocellular carcinoma [3].

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Vibrio alginolyticus and some other microorganisms use ADS (Arginine Deaminase System) for energy production and survival under extremely acidic conditions. It has been shown that the metabolism of arginine via ADS produces enough energy's maintain the growth of various bacteria, such as Enterococcus faecalis. In addition to the natural role of energy production, arginine was found to be effective in the treatment of arginino succinate synthetase (ASS) negative tumors. These tumors are oxotropic in nature and are exposed to food starvation in the presence of arginine-disrupting enzymes such as ADI or 1-arginase. Therefore, these enzymes can be used to stop the growth of certain cancer cells. The beneficial effects of ADI administration have also been demonstrated in the treatment of certain cancers. Although the presence of ADI is shown in many microorganisms, the yield obtained from them is quite low [7].

The relationship between arginine and cancer has been known for many years. Generally, the de novo biosynthesis of arginine is, in turn, the precursor argininosuccinate produced from citrulline. This is facilitated by, respectively, arginine oscillinate lyase (ASL) and ASS enzymes. ASS is a biosynthetic enzyme that limits the rate of intracellular arginine synthesis in different cells. These ASS-negative tumor cells are oxotrophic for arginine (due to extracellular arginine uptake) and therefore very sensitive to arginine withdrawal. The clinical significance of arginine metabolism in cancers has been demonstrated by a more aggressive clinical behavior relationship with decreased ASS and pancreatic cancer. As a result, arginine deprivation by arginine degrading enzymes is used as a treatment for selective tumor cell death, although it does not damage normal cells [8].

Because the bacterial enzyme is highly immunogenic in humans, therapeutic preparations of ADI have to be conjugated with polyethylene glycol, which reduces the immunogenicity of the enzyme while greatly improving the pharmacokinetic half-life of the serum [3].

Unfortunately, ADI is highly immunogenic because it is not a natural human enzyme. The addition of polyethylene glycol (PEG) to the ADI enzyme allows a formulation that has a less antigenic, longer circulating half-life and results in a generally more effective anticancer agent [2].

In addition, ADI shows an antitumor activity in vivo with apparently minimal side effects, and is expressed to inhibit proliferation of human leukemia cells more strongly than asparaginase, the only amino-acid-disrupting enzyme regularly used in cancer chemotherapy [9].

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