УДК: 616.344-002.44:577.175.342

Mamatova I.Y.
Doctor of Chemical Sciences, Professor
Head of the Department of Biological Chemistry
Andijan State Medical Institute
Muminova G.A.
Doctor of Chemical Sciences,
Associate Professor of the Department of Biological Chemistry
Andijan State Medical Institute

THE INFLUENCE OF P1 PURINERGIC RECEPTORS (ADENOSINE RECEPTORS) ON CROHN'S DISEASE

Abstract: This article analyzes the role of P1 purinergic receptors, also known as adenosine receptors (A1, A2A, A2B, A3), in the pathogenesis of Crohn's disease (CD), a chronic inflammatory bowel disease. It examines the impact of adenosine and its interaction with P1 receptor subtypes on the complex interplay of immune dysregulation and inflammation characteristic of CD. Particular emphasis is placed on the predominantly immunomodulatory and anti-inflammatory effects of A2A and A2B receptors in the context of intestinal inflammation. The potential of targeting P1 receptors with agonists as a therapeutic strategy for Crohn's disease is also discussed.

Keywords: Crohn's disease, P1 purinergic receptors, adenosine receptors, adenosine, inflammatory bowel disease, immune regulation, therapeutic targets.

Маматова И.Ю.
доктор химических наук, профессор
Заведующий кафедрой биологической химии
Андижанский государственный медицинский институт

Муминова Г.А.
доктор химических наук,
Доцент кафедры биологической химии
Андижанский государственный медицинский институт

ЗНАЧЕНИЕ P1 ПУРИНЕРГИЧЕСКИХ РЕЦЕПТОРОВ (АДЕНОЗИНОВЫХ РЕЦЕПТОРОВ) ПРИ ПСОРИАЗЕ

Аннотация: Данная статья посвящена анализу роли P1 пуринергических рецепторов (аденозиновых рецепторов A1, A2A, A2B, A3) в патогенезе псориаза – хронического воспалительного заболевания кожи. Рассматривается значение аденозина и его взаимодействия с P1 рецепторами в контексте иммунной дисрегуляции, воспаления, пролиферации кератиноцитов и ангиогенеза, характерных для псориаза. Особое внимание уделяется преимущественно противовоспалительным и иммуномодулирующим свойствам подтипов A2A и A2B. Обсуждается потенциал агонистов P1 рецепторов в качестве перспективных терапевтических средств для лечения псориаза.

Ключевые слова: псориаз, пуринергические рецепторы P1, аденозиновые рецепторы, аденозин, воспаление, иммунная система, терапевтические мишени.

Introduction. Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) characterized by relapsing inflammation of various parts of the gastrointestinal tract. The pathogenesis of CD is complex and involves genetic predisposition, dysbiosis of the gut microbiota, and dysregulation of the immune system [5]. In recent years, the role of the purinergic system in the development and progression of IBD has been actively investigated. This article focuses on

analyzing the influence of P1 purinergic receptors, also known as adenosine receptors (A1, A2A, A2B, A3), on the pathogenesis of Crohn's disease.

Purinergic signaling plays a crucial role in regulating various physiological processes in the gastrointestinal tract, including motility, secretion, and immune responses [1]. Extracellular adenosine, the primary ligand for P1 receptors, is generated in inflammatory sites as a result of the degradation of released ATP. In contrast to the pro-inflammatory effects of ATP mediated by P2 receptors, adenosine and P1 receptors typically exert immunomodulatory and anti-inflammatory actions, making their study particularly relevant in the context of chronic inflammatory diseases such as Crohn's disease.

Anti-inflammatory Effects of P1 Receptors in Crohn's Disease. Activation of P1 receptors, particularly the A2A and A2B subtypes, can contribute to the resolution of inflammation in Crohn's disease. The binding of adenosine to these receptors leads to the activation of adenylyl cyclase and an increase in intracellular cyclic adenosine monophosphate (cAMP) levels [3]. Elevated cAMP in immune cells, such as macrophages and T lymphocytes, can inhibit their activation and reduce the production of pro-inflammatory cytokines, including TNF-α, IL-6, and IL-12, which play key roles in the pathogenesis of CD.

Role of Different P1 Receptor Subtypes in Crohn's Disease. Different subtypes of adenosine receptors can exert specific influences on the course of Crohn's disease:

- **A1 Receptor:** Expressed on various cells in the intestine, including epithelial cells and neurons. Its activation can affect gut motility and the transmission of pain signals. Some studies suggest its involvement in regulating the inflammatory response, but its precise role in CD requires further investigation [4].
- **A2A Receptor:** Widely represented on immune cells in the intestinal mucosa. Activation of the A2A receptor exerts a pronounced anti-inflammatory effect by suppressing the activity of pro-inflammatory T cells (Th1 and Th17) and

macrophages, and by promoting the function of regulatory T cells (Treg), which play a crucial role in dampening excessive inflammation in CD. A2A receptor agonists are being considered as potential therapeutic agents for IBD.

- **A2B Receptor:** Expressed on intestinal epithelial cells, fibroblasts, and immune cells. Its role in CD is more complex and may depend on adenosine concentration and the microenvironment. In some cases, the A2B receptor can contribute to the release of pro-inflammatory mediators, but it can also exert protective effects, such as maintaining the barrier function of the intestinal epithelium [2].
- **A3 Receptor:** Expressed on immune cells and intestinal epithelial cells. Some studies indicate that activation of the A3 receptor can have both pro-inflammatory and anti-inflammatory effects in IBD depending on the model and stage of the disease. Its precise role in Crohn's disease warrants further clarification.

P1 Receptors as Potential Therapeutic Targets in Crohn's Disease. Given the predominantly anti-inflammatory and immunomodulatory actions of certain P1 receptor subtypes, particularly A2A, the development of agonists for these receptors represents a promising avenue for the treatment of Crohn's disease. Activation of the A2A receptor can help reduce inflammation in the intestinal mucosa and restore immune homeostasis. Preclinical studies in IBD models have shown the efficacy of A2A receptor agonists in reducing inflammation and intestinal damage. Clinical trials to evaluate the efficacy and safety of these compounds in patients with Crohn's disease are in various stages.

Conclusion. P1 purinergic receptors, especially the A2A and potentially A2B subtypes, play an important role in regulating inflammatory processes in Crohn's disease. Activation of the A2A receptor demonstrates significant anti-inflammatory potential and represents a promising therapeutic strategy for the treatment of this chronic bowel disease. Further research aimed at elucidating the

specific roles of each P1 receptor subtype and developing selective agonists may lead to the emergence of new effective therapies for Crohn's disease.

References:

1. Burnstock, G. (2017). Purinergic signalling: past, present and future. *Neuropharmacology*, *112*(Pt B), 4-21.
2. Chen, Y., Corridoni, R., Kwok, M., et al. (2013). The A2B adenosine receptor promotes intestinal inflammation. *Gastroenterology*, *144* (4), 822-832.e1-2.
3. Haskó, G., & Cronstein, B. N. (2004). Adenosine: an endogenous regulator of inflammation. *Pharmacological Reviews*, *56* (3), 443-474.
4. Linden, J. (2001). Adenosine receptors and gastrointestinal function. *Current Opinion in Pharmacology*, *1* (6), 597-602.
5. Neurath, M.F. (2019). Understanding the pathogenesis of inflammatory bowel diseases. *Nature Reviews Immunology*, *19* (6), 349-362.