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# Degranulation Cancer Immunotherapy: Harnessing the Allergy Cascade to Induce Tumor Apoptosis

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## Abstract

Cancer immunotherapy has focused on adaptive T-cell–based strategies, such as checkpoint inhibitors and CAR-T cells. However, effector cells of the allergy cascade—basophils, eosinophils, mast cells, and neutrophils—remain underexplored as cytotoxic agents within the tumor microenvironment. These cells survive and function in nutrient-deprived tumors through metabolic reprogramming, a glycolytic switch (i.e., Warburg effect) which enables sustained activity despite hypoxia and glucose competition. *Degranulation cancer immunotherapy* (DCI) is proposed, in which forced atopy is induced to enrich tumor-resident effector cells with allergen-specific immunoglobulin. Then, intratumoral administration of the sensitizing allergen triggers targeted degranulation, releasing cytotoxic mediators, and inducing apoptosis of adjacent tumor cells. This review integrates immunometabolism, IgE biology, and tumor immunology to provide a mechanistic rationale, outlines a potential therapeutic protocol, and proposes frontier research directions. DCI may represent a low-cost, innate immunity–based alternative or complement to current immunotherapies, with applicability across a broad range of solid tumors.

**Keywords:** Allergy cascade; Degranulation; Forced atopy; IgE, immunometabolism; Tumor microenvironment; Warburg effect; Cancer immunotherapy

## 1. Introduction

Modern cancer immunotherapy has transformed patient outcomes, yet significant challenges persist, including immune "cold" tumors, treatment resistance, prohibitive costs, and toxicities [1]. Most current strategies focus on T-cell–centric approaches, overlooking other immune effector mechanisms capable of direct cytotoxicity.

The allergy cascade—traditionally considered pathological—mobilizes potent effector cells armed with high-affinity IgE receptors (FcεRI) and preformed cytotoxic granules. While these responses can damage tissue in allergic diseases, they hold potential for repurposing as a targeted anti-tumor strategy in cancer treatment. Epidemiological studies suggest an inverse correlation between allergic disease prevalence and cancer incidence, hinting at shared and potentially protective immunological mechanisms [2].

In this review, a mechanistic framework is proposed for degranulation cancer immunotherapy (DCI). This approach involves metabolically priming allergen-sensitizing tumor-resident FcεRI+ cells to release cytotoxins directly into the tumor microenvironment (TME), thereby triggering apoptosis.

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## 2. Description

### 2.1. Effector Cells in the Tumor Microenvironment

Basophils (<1% of leukocytes in circulation) infiltrate certain tumors and can release granzyme B, TNF-α, and IL-4 upon activation, influencing both tumor cytotoxicity and immune recruitment [3].

Eosinophils (1–4% of leukocytes in circulation) secrete major basic protein, eosinophil peroxidase, and other granule toxins having direct tumoricidal capacity [4].

Mast cells (tissue-resident) store histamine, proteases, and cytokines that can disrupt tumor vasculature and recruit NK cells [5].

Neutrophils (50–70% of leukocytes in circulation) can generate ROS, proteases, and extracellular traps, damaging tumor cells directly [6].

### 2.2. Immunometabolic Advantage

Effector cells in tumors utilize the glycolytic switch (i.e., aerobic glycolysis) even in oxygen-rich conditions. This metabolic adaptation parallels cancer cell metabolism, allowing effector cells to:

- Function in hypoxic, nutrient-deprived TMEs [7].
- Rapidly generate ATP for degranulation [8].
- Sustain cytokine production through HIF-1α–driven glycolysis.

### 2.3. Forced Atopy and IgE Enrichment

Forced atopy is induced via repeated topical or transdermal exposure to allergenic formulations (e.g., patented topical hyperallergenic compositions) [9]. This elevates systemic allergen-specific IgE and increases FcεRI+ effector cells in solid tumors.

### 2.4. Degranulation of Mast Cells in the TME

The patient is exposed to allergens, leading to an exaggerated immune response characterized by the overproduction of allergen-specific IgE. These allergen-specific IgE infiltrate into the TME and bind to high-affinity IgE receptors (FcεRI) [10].

The patient is re-exposed to the sensitized allergens intratumorally [11]. No systematic program has yet combined allergen sensitization with targeted intratumoral allergen delivery.

Allergens specifically bind to mast cells that have been sensitized by FcεRI and allergen-specific IgE, initiating degranulation. This process leads to the release of cytotoxic inflammatory molecules, including leukotrienes and cytokines. The swift release of cytotoxins into the tumor microenvironment may then lead to apoptosis. Allergic inflammation can attract additional immune cells, which may help transform “cold” tumors into “hot” tumors [12]

## 3. Therapeutic Strategy

### 3.1. Step 1 – Sensitization Phase

- Topical or transdermal hyperallergenic composition applied over several weeks.
- Monitor IgE titers specific to chosen allergens.

### 3.2. Step 2 – Tumor Infiltration

- Natural immune trafficking delivers FcεRI+ cells to the TME.

### 3.3. Step 3 – Trigger Phase

- Topical application of allergens [13], direct intratumoral injection of an allergen solution [14], or nanoparticle formulation [15].

### 3.4. Step 4 – Immune Cascade Amplification

- Combination immunotherapy with immune checkpoint inhibitors to stimulate humoral immunity and sustain T-cell–mediated tumor control [16].

### 3.5. Metabolic Modulation

Pre-treat with agents that boost glycolysis in effector cells (e.g., HIF-1α stabilizers) to maximize degranulation capacity [17].

### 3.6. Biomarker Development

- Identify patient subgroups with low IgE or "immune cold" tumors as optimal candidates.
- Develop histamine, tryptase, and cytokine monitoring tools for safety and efficacy tracking.

## 4. Conclusion

Degranulation cancer immunotherapy reframes allergic inflammation as a precision immuno-oncology tool. By deliberately enriching tumors with allergen-specific effector cells and triggering localized degranulation, DCI could offer a low-cost, broad-spectrum alternative or complement to existing treatments. Patient selection criteria, right-to-try validation, and safety optimization are essential next steps.

## Compliance with ethical standards

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*Disclosure of conflict of interest*

No conflict of interest to be disclosed.

*Author Profile*

Michael John Dochniak has authored several books on Alzheimer's disease, Artificial Intelligence, Autism Spectrum Disorders, and Climate Change through Cambridge Scholars Publishing and Nova Science Publishers.

## References

[1] Emens LA, Romero PJ, Anderson AC, Bruno TC, Capitini CM, Collyar D, Gulley JL, Hwu P, Posey AD Jr, Silk AW, Wargo JA. Challenges and opportunities in cancer immunotherapy: a Society for Immunotherapy of Cancer (SITC) strategic vision. J Immunother Cancer. 2024 Jun 19;12(6): e009063.

[2] Yang K, Zhao H, Wang L, Cai C, Lv P, Wang B. Correlation between allergic diseases and lung cancer: a systematic review and meta-analysis. Front Med (Lausanne). 2025 Jul 16;12: 1560000.

[3] Chauhan J, Stavraka C, Grandits M, Palhares LCGF, Josephs DH, Lacy KE, Spicer J, Bax HJ, Karagiannis SN. Clinical and Translational Significance of Basophils in Patients with Cancer. Cells. 2022 Jan 27;11(3):438.

[4] Grisaru-Tal S, Jacobsen EA, Munitz A. Evolving role for eosinophils in cancer: from bench to bedside. Trends Cancer. 2025 Jun 12: S2405-8033(25)00131-1.

[5] Lichterman JN, Reddy SM. Mast Cells: A New Frontier for Cancer Immunotherapy. Cells. 2021 May 21;10(6):1270.

[6] Huang X, Nepovimova E, Adam V, Sivak L, Heger Z, Valko M, Wu Q, Kuca K. Neutrophils in Cancer immunotherapy: friends or foes? Mol Cancer. 2024 May 18;23(1):107.

[7] Xiao C, Tian H, Zheng Y, Yang Z, Li S, Fan T, Xu J, Bai G, Liu J, Deng Z, Li C, He J. Glycolysis in tumor microenvironment as a target to improve cancer immunotherapy. Front Cell Dev Biol. 2022 Sep 19;10: 1013885.

[8] Zhang H, Li S, Wang D, Liu S, Xiao T, Gu W, Yang H, Wang H, Yang M, Chen P. Metabolic reprogramming and immune evasion: the interplay in the tumor microenvironment. Biomark Res. 2024 Sep 3;12(1):96.

[9] Dochniak MJ. Topical hyper-allergenic composition and method of treating using the same. United States Patent 11,911,463. 02/27/2024.

[10] Dochniak MJ, Bensen CA. Allergo oncology: Targeted degranulation. Open Access Research Journal of Science and Technology. 2023; 08(01): 011–013.

[11] Plattner K, Bachmann MF, Vogel M. On the complexity of IgE: The role of structural flexibility and glycosylation for binding its receptors. Front Allergy. 2023 Mar 28; 4:1117611.

[12] Lu C, Liu Y, Ali NM, Zhang B, Cui X. The role of innate immune cells in the tumor microenvironment and research progress in anti-tumor therapy. Front Immunol. 2023 Jan 19;13: 1039260.

[13] Dochniak MJ. Topical hyper-allergenic composition and method of treating using the same. United States Patent 11,911,463. 02/27/2024.

[14] Dochniak MJ, Bensen CA. Allergo oncology: Targeted degranulation. Open Access Research Journal of Science and Technology. 2023; 08(01): 011–013.

[15] Lu Q, Kou D, Lou S, Ashrafizadeh M, Aref AR, Canadas I, Tian Y, Niu X, Wang Y, Torabian P, Wang L, Sethi G, Tergaonkar V, Tay F, Yuan Z, Han P. Nanoparticles in tumor microenvironment remodeling and cancer immunotherapy. J Hematol Oncol. 2024 Apr 2;17(1):16.

[16] Dochniak MJ. Combinational cancer immunotherapy: Allergy-assisted immunotherapy and immune checkpoint inhibitors GSC Biological and Pharmaceutical Sciences. 2025, 31(01), 131-133.

[17] Kierans SJ, Taylor CT. Regulation of glycolysis by the hypoxia-inducible factor (HIF): implications for cellular physiology. J Physiol. 2021 Jan;599(1):23-37.