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# Pediatric glioblastomas and passive degranulation immunotherapy

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## Abstract

Pediatric glioblastoma is among the most aggressive and deadly brain tumors, with current therapies providing limited efficacy and poor long-term survival. Recent advances in AllergoOncology have introduced targeted passive degranulation immunotherapy (TPDI), a promising approach that leverages human immunoglobulin E monoclonal antibodies (hIgE mAbs) to induce localized degranulation and stimulate anti-glioblastoma inflammation. TPDI entails the intratumoral administration of hIgE mAbs—sourced from atopic donors or produced through recombinant technology—followed by the precise delivery of the relevant allergen directly into the glioblastoma microenvironment. Of relevance are polyploid giant cancer cells (PGCCs), a highly aggressive and therapy-resistant subpopulation implicated in glioblastoma progression and recurrence. This review explores the potential of TPDI to disrupt glioblastoma-associated PGCCs to improve survival outcomes in pediatric patients.

**Keywords:** Pediatric glioblastoma; Passive degranulation immunotherapy; Immunoglobulin E monoclonal antibodies; Polyploid giant cancer cells; AllergoOncology

## 1. Introduction

AllergoOncology uses IgE antibodies to combat cancer [1]. Targeted passive degranulation immunotherapy (TPDI) and the use of human Immunoglobulin E monoclonal antibodies (hIgE mAbs) are emerging as innovative theoretical strategies in AllergoOncology to dismantle the complex, immunosuppressive microenvironment of solid tumors [2]. The approach may be used to combat pediatric glioblastoma populations by overcoming immune evasion and disrupting polyploid giant cancer cells.

### 1.1. Targeted Degranulation

By delivering hIgE mAbs intratumorally and subsequently exposing them to the corresponding allergen, researchers aim to trigger localized, intense inflammation driven by mast cells and basophils [3].

### 1.2. Overcoming Immune Evasion

Glioblastomas are notoriously "cold" tumors that actively suppress the body's immune system [4]. The localized degranulation incited by TPDI aims to break this tolerance by recruiting a robust cytotoxic immune response directly to the tumor site [5].

### 1.3. Disrupting Polyploid Giant Cancer Cells (PGCCs)

PGCCs represent a highly therapy-resistant, stress-adapted subpopulation of tumor cells implicated in cancer recurrence and progression [6]. The intense inflammatory cascade induced by TPDI is hypothesized to target and disrupt these resilient cells, preventing them from driving further glioblastoma growth [7].

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### 1.4. Clinical Implications

If successfully translated into pediatric trials, TPDI could overcome resistance mechanisms associated with standard treatments (such as surgery, radiation, and temozolomide), paving the way for significantly improved survival outcomes for children with this devastating disease [8].

## 2. Discussion

The exploration of TPDI marks a promising advance in the treatment landscape for pediatric glioblastoma—a malignancy notorious for its aggressiveness and resistance to conventional therapies. TPDI leverages the unique immunostimulatory properties of allergen-specific hIgE monoclonal antibodies to induce local inflammation, disrupt the immunosuppressive tumor microenvironment, and target therapy-resistant subpopulations such as PGCCs [9].

A central strength of TPDI is its dual mechanism of action: it not only initiates a robust inflammatory response that attracts cytotoxic immune cells to the tumor site but also directly perturbs cancer cell organelles and protein homeostasis. This duality is particularly relevant for PGCCs, which are known for their adaptability and ability to drive recurrence. By disrupting organellar integrity and proteostasis, TPDI may sensitize these resilient cells to apoptosis and inhibit their role in tumor repopulation following standard treatments.

The integration of TPDI into glioblastoma therapy introduces novel therapeutic opportunities but also raises important safety considerations. While intratumoral delivery and allergen specificity are designed to localize immune activation, the potential for systemic allergic reactions or unintended inflammation must be rigorously addressed in preclinical and clinical studies. Careful patient selection, allergen dose optimization, and emergency protocols for adverse events will be critical to translating TPDI from concept to clinic.

## 3. Conclusion

TPDI represents a novel and theoretically powerful approach for overcoming the immune evasion and therapy resistance that characterize pediatric glioblastomas. Continued research is needed to validate its efficacy, optimize its safety, and determine its place among emerging immunotherapeutic strategies. If these challenges can be addressed, TPDI has the potential to significantly improve outcomes for children afflicted by this devastating disease.

## Compliance with ethical standards

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Grammarly was used for grammar, spelling, and punctuation throughout the preparation of the review article. The tool (Grammarly, version 14.1271.0, Grammarly Inc., San Francisco, CA) was used to review and edit the entire review article for grammatical accuracy, clarity, and readability. Grammarly's AI-powered writing assistant provided suggestions on sentence structure, word choice, and tone consistency, which the author reviewed and selectively incorporated. The tool was not used to generate original scientific content, data analysis, or research conclusions. The author takes full responsibility for the integrity of all content generated and presented in this review article.

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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

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