

Review

Rubber Elongation Factor and Natural Allergy-Oncology

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Summary

The natural allergy-oncology perspective described herein explores how forced immunity to allergens from the rubber tree *Hevea brasiliensis* may inhibit tumor growth and metastasizing. The over expression of mast cells and proteins from the Rho family of GTPases has been shown to manifest in multiple types of cancer. Rubber elongation factor (Hev-b 1) is an allergen from *H.brasiliensis* that has structure homology with members of the Rho family of GTPases. Forced immunity to Hev-b 1 may provide immunoglobulin E (IgE) primed mast cells that cross-react with members of the Rho family of GTPases, based on structure homology, and affect angiogenesis in tumors. Research efforts should be directed at exploring if forced immunity to *H.brasiliensis* allergens can be used as a supplementary-treatment to inhibit tumor growth and metastasizing.

Abstract

Natural allergy therapy is a non-conventional medical approach that utilizes natural allergens to treat cancer. The term “natural allergy” is created from “natura” (Latin root for birth) and “allergy” an idea created by Clemens von Pirquet (1874-1929) in the understanding that the function of the immune system should be rationalized not in terms of exemption of disease but in terms of change of reactivity. The natural allergy-oncology perspective explores how forced immunity to allergens from the rubber tree *H. brasiliensis* may inhibit tumor growth and metastasizing. The over expression of mast cells and proteins from the Rho family of GTPases has been shown to manifest in multiple types of cancer. Rubber elongation factor (Hev-b 1) is an allergen from *Hevea brasiliensis* that has structure homology with members of the Rho family of GTPases. Forced immunity to Hev-b 1 may provide IgE-primed mast cells that cross-react with members of the Rho family of GTPases and affect angiogenesis in tumors. Research efforts should be directed at exploring if forced immunity to *H.brasiliensis* allergens can be used as a supplementary-treatment to inhibit tumor growth and metastasizing.

Key Words: Hev-b 1; IgE; Natural allergy Therapy

Introduction

Natural allergy therapy is a non-conventional medical approach that utilizes natural allergens to treat cancer. The term “natural allergy” is created from “natura” (Latin root for birth) and “allergy” an idea created by Clemens von Pirquet (1874-1929) in the understanding that the function of the immune system should be rationalized not in terms of exemption of disease but in terms of change of

reactivity. In an article from the International Journal of Green Pharmacy titled, *Plant latex: a natural source of pharmaceuticals and pesticides*, author Ravi K.. Upadhyay writes, “In recent times use of plant natural products has increased tremendously, and there is a very high demand of herbal products for therapeutic, clinical, agricultural purposes. Plant latex is a rich source of pharmaceuticals, pesticides and immune allergens. It also contains important biomolecules such as glycosides, tannins, phytosterols, flavonoids, acetogenins and saponins, which show diverse biological activities against bacteria, fungi, viruses, protozoans, nematodes, insects, and cancer and tumors”[1].

The objective of natural allergy-oncology is to reveal the function of IgE-mediated immune responses against cancer cells in order to enhance the understanding of its biology and to develop novel IgE-based treatment options against malignant diseases. In a research article from Allergy titled, *Allergo-oncology: the role of IgE-mediated allergy in cancer* the researchers state, “IgE antibodies may not only act in natural tumor surveillance, but could possibly also be exploited for tumor control in active and passive immunotherapy settings”[2].

Research has shown that an elevated expression of IgE antibodies may reduce the risk of cancer. In an article from the Journal of the National Cancer Institute titled, *Association between Prediagnostic IgE Levels and Risk of Glioma*, the researchers concluded, “An inverse association between IgE levels and risk of glioma was detected; the association was present at least 20 years before tumor diagnosis”[3].

Cancer suppression is suspected with IgE antibodies in that they are extremely biologically active despite low concentration in the blood stream, approximately one-thousandth of a percent. IgE bind to high affinity receptors on the surface of effector cells (e.g., mast cells, basophiles, and eosinophils) to provide IgE-primed effector cells, making them very sensitive to allergens. In an article from

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Sub Date: November 10, 2016, **Acc Date:** November 11, 2016, **Pub Date:** November 13, 2016.

Citation: Michael J Dochniak (2016) Rubber Elongation Factor and Natural Allergy-Oncology. BAOJ Cancer Res Ther 2: 027.

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the Journal of Allergy and Clinical Immunology titled, *IgE, Mast Cells, Basophils, and Eosinophils*, the researchers state, "Total IgE levels are also influenced by genetic makeup, race, immune status and environmental factors"[4].

Research indicates that mast cells and Rho GTPases may play an important role in tumor cell survival and propagation. In an article from *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease* titled, *Mast cells, angiogenesis, and tumour growth*, the authors write, "These cells actively take part to innate and acquired immune reactions as well as to a series of fundamental functions such as angiogenesis, tissue repair, and tissue remodeling [5]. Furthermore, proteins from the Rho family of GTPases have been shown to be over expressed in multiple types of cancer. In an article from the journal *Biochemistry & Molecular Biology* titled, *Overexpression of RhoA promotes the proliferation and migration of cervical cancer cells*, the authors write, "We found a positive correlation among RhoA with the progression of cervical cancer by *in vivo* and *in vitro* evidences. A high RhoA expression in cervical cancer may predict a high metastatic potential of cervical cancer"[6].

There continues to be a need for a supplementary-treatment that inhibits tumor growth and metastasizing. Rubber elongation factor (Hev-b 1) is an allergen from *H. brasiliensis* that has structure homology with members of the Rho family of GTPases. Forced immunity to Hev-b 1 may provide IgE-primed mast cells that cross-react with members of the Rho family of GTPases and affect angiogenesis in tumors. Therefore, natural allergy-oncology research efforts should explore if Hev-b 1 can be used as a supplementary-treatment to inhibit tumor growth and metastasizing.

Discussion

In the present medical hypothesis, it is speculated that forced immunity to the allergen rubber -elongation-factor (Hev-b 1) may provide IgE-primed mast cells that may cross-react, based on β -sheet structure homology, with members of the Rho family of GTPases to inhibit tumor growth and metastasizing. *H. brasiliensis* natural rubber latex contains about 2-5% protein by weight. Analysis indicates about 200 dissimilar proteins therein and about 50-60 are suspected allergens which may induce Type-I hypersensitivity called latex allergy. The World Health Organization International Union of Immunological Societies has assigned names to thirteen allergenic proteins Hev-b 1-13.

The Hev-b1 allergen is a water-insoluble protein with a molecular weight of 14.6 Kda [7]. Research has shown that the Hev-b1 allergen shows all the characteristic of an amyloid protein with high aggregation properties. The researchers believe that this is the first report of an amyloid protein observed in the plant kingdom. A study has shown that Hev-b1, a major allergen component in *H. brasiliensis* natural rubber latex has amyloid (β -sheet) properties [8].

Members of the Rho family of GTPases are often over expressed in many malignant tumors that metastasize. The Rho family of

GTPases is a family of small (~21 Kda) signalling G-protein and is a subfamily of the Ras super family. Rho proteins are structurally comprised of six-stranded β -sheets and five α -helices [9].

Forced immunity to Hev-b1 may be induced in cancer patients using the natural allergen (nHev-b) or an effective combination of the natural allergen and recombinant allergen (rHev-b1). The rHev-b1 fusion protein has been shown to exhibit a corresponding IgE-binding reactivity to nHev-b1 [10]. Mixtures of Hev-b allergen in the presence of immunologic adjuvants are also contemplated to increase the prevalence of IgE primed mast cells that may cross react with the Rho family of GTPases.

Preferably, forced immunity to the Hev-b1 allergen is accomplished through intracutaneous (IC) exposure and/or intraperitoneal (IP) exposure. Research has shown that IC and IP latex exposure can induce a striking increase in specific immunoglobulin E (IgE) levels along with the induction of T-helper type 2 (Th2) cytokines and β -chemokines [11].

An allergy blood test or skin prick test may be used to determine if members of the Rho family of GTPases cross-react with IgE-primed mast cells induced by natural allergy therapy.

Effective cancer immunotherapy, cross-reacting IgE-primed mast cells with members of the Rho family of GTPases, may depend heavily on secondary structure (β -sheet) homology. Research has disclosed that it is expected that similarity in short stretches of the linear amino-acid sequence is unlikely to result in relevant cross-reactivity between two proteins unless there is similarity in the protein fold [12].

A contraindication is a medical condition or medical factor that serves as a reason to withhold treatment. Forced immunity to *H. brasiliensis* natural rubber latex (e.g., Hev-b 1) is a relative contraindication in that the risks of complications from latex allergy often do not outweigh the serious condition of a tumor metastasizing and growing.

In a communication from the Centers for Disease Control and Prevention (CDC) titled, *Leading Causes of Death*, statistics showed that cancer was the second leading cause of death in the year 2014 [13].

Alternatively, the American Latex Allergy Association writes that latex allergy symptoms can range from mild to severe, and can include one or more of the following: Hives or welts; Swelling of affected area; Runny nose; Sneezing; Headache; Reddened, itchy or teary eyes; Sore throat, hoarse voice; Abdominal cramps; Chest tightness, wheezing, or shortness of breath (asthma period).

If exposure to latex continues, allergy symptoms may include a severe and life threatening allergic reaction called anaphylaxis [14].

The Advisory Committee on Immunization Practices from the CDC provides the following general recommendation on immunizations and latex allergy, "If a person reports a severe (anaphylactic) allergy to latex, vaccines supplied in vials or syringes that contain natural

rubber, or whose product information does not say “not made with natural rubber latex” should not be administered unless the benefit of vaccination outweighs the risk for a potential allergic reaction. In these cases, providers should be prepared to treat patients who are having an allergic reaction. For latex allergies other than anaphylactic allergies (e.g., a history of contact allergy to latex gloves), vaccines supplied in vials or syringes that contain dry natural rubber or rubber latex may be administered” [15].

A limitation of natural allergy therapy as a supplementary-treatment relates to the understanding that a number of anticancer drugs may cause impairment of antibody synthesis and cell-mediated immunity. In an article from Transplantation Proceedings titled, *Immunosuppression and Cancer*, the authors write, “While cancer chemotherapy has had some notable successes, the overall results have been rather disappointing. These have been blamed on unresponsiveness of the tumor to a particular agent, or to the subsequent development of resistance by the cancer cells, or to the toxic effects of the compounds used. Another factor, which has received relatively scant attention, is the prolonged immunosuppressive effect of the agents when administered continuously. Could this be the explanation for the observation that a better objective response and longer survival was observed when chemotherapy was given intermittently rather than continuously?” [16].

Conclusion

Although natural allergy therapy is a non-conventional medical approach, research efforts should be directed at exploring if forced immunity to *H.brasiliensis* allergens can be used as a supplementary-treatment to inhibit tumor growth and metastasizing.

References

1. Upadhyay RK (2011) Plant Latex: A natural source of pharmaceuticals and pesticides. *International Journal of Green Pharmacy* 5(3).
2. Jenson-Jarolim E, Achatz G, Turner MC, Karagiannis S, Legrand F et al. (2008) AllergoOncology: the role of IgE-mediated allergy in cancer. *Allergy* 63(10): 1255-1266.
3. Schwartzbaum J, Ding B, Johannesen TB, Liv T. N. Osnes, Linda Karavodin et al. (2012) Association between prediagnostic IgE levels and risk of glioma. *Journal of the National Cancer Institute* 104(16): 1251-1259.
4. Stone KD, Prussin C, Metcalfe DD (2010) IgE, Mast Cells, Basophils, and Eosinophils. *J Allergy Clin Immunol* 125(2 Suppl 2): 573-580.
5. Ribatti D, Crivellato E (2012) Mast cells, angiogenesis, and tumour growth. *Biochimica et Biophysica Acta (BBA) – Molecular Basis of Disease* 1822(1): 2-8.
6. Liu X, Chen D, Liu G (2014) Over expression of RhoA promotes the proliferation and migration of cervical cancer cells. *Journal of Bioscience, Biotechnology and Biochemistry* 78(11): 1895-1901.
7. Hev-b 1, (2003) IUIS Allergen Nomenclature Sub-Committee.
8. Berthlot K, Lecomte S, Estevez Y, Couлары-Salin B, Bentaleb A et al. (2012) Rubber Elongation Factor (REF), a major allergen component in *hevea brasiliensis* latex has amyloid properties. *PLOS One* 7(10): e48065.
9. Rho family of GTPases. Wikipedia, the free encyclopedia.
10. Rihs, Chen, Schumacher, Rozynek, Cremer et al. (2000) Recombinant Hev-b 1: large-scale production and immunological characterization. *Clinical & Experimental Allergy* 30(9): 1285-1292.
11. Lehto M, Haapakoski R, Wolff M, Marja-Leena M, Mika J. Mäkelä et al. (2005) Cutaneous, but not airway, latex exposure induces allergic lung inflammation and airway hyper reactivity in mice. *Journal of Investigative Dermatology* 125(5): 962-968.
12. Aalberse RC (2007) Assessment of allergen cross reactivity: Commentary. *Clinical and Molecular Allergy, Open Access* 5(2).
13. CDC (2014) National Center for Health Statistics: Leading Causes of Death.
14. American Latex Allergy Association (website) About Latex Allergy: Symptoms.
15. CDC, Appendix B-Pink Book – Latex in Vaccine Packaging.
16. Penn I, Starzl T (1973) Immunosuppression and cancer. *Transplant Proc* 5(1): 943-947.