

## Intestinal immunomodulatory effects of a hypoallergenic buckwheat Fag e 1 prepared by Maillard-type glycation with a mannan type-polysaccharide

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Shigeru Katayama<sup>a)</sup>, Shigeru Tazawa<sup>b)</sup>, Masahiro Kasai<sup>a)</sup>, Takakazu Mitani<sup>c)</sup>, Soichiro Nakamura<sup>a, b)</sup>

a) Faculty of Agriculture, Shinshu University

b) Interdisciplinary Graduate School of Science and Technology, Shinshu University

c) Institute for Biomedical Science, Shinshu University

### Abstract

The 24 kDa protein (Fag e 1) in buckwheat is considered to be one of its major allergens. The purpose of this study is to investigate the immunomodulatory effects of hypoallergenic Fag e 1 prepared by glycation with polysaccharide on mucosal allergic responses in mice. Mannan-type-polysaccharide such as galactomannan (GalM), konjac glucomannan (KGM), and yeast glucomannan (YGM) showed attenuation of IL-4 and IL-17 production and elevation of IL-10 in cultured Peyer's patch (PP) cells. The conjugate of Fag e 1 with GalM, KGM, or YGM was prepared using naturally occurring Maillard-type glycosylation. Dietary administration with Fag e 1-YGM conjugate for 8 weeks induced a significant reduction in Fag e 1-specific IgE and IgG1 levels and elevation in IgA level in sera and PP cells. A decrease in IL-4 and IL-17 and increase in IL-10 in PP cells were observed in the group of Fag e 1-YGM conjugate. Differentiation ratio of regulatory T cells (Treg) and T follicular helper cells in PP increased by feeding with Fag e 1-YGM conjugate. These suggest that Fag e 1-YGM conjugate could be contribute to the development of an immunomodulatory hypoallergenic agent for buckwheat allergy.

**Keywords :** buckwheat, allergy, glycation, immunological tolerance, Treg

## I Introduction

Buckwheat (*Fagopyrum esculentum*) is commonly consumed in Asian countries such as Japan, China, and Korea, and it has recently become more popular in Europe<sup>1)</sup>. Buckwheat has been recognized as a common food allergen and it causes severe anaphylactic reactions by intake of even a small amount of flour or food products made from buckwheat. The prevalence of buckwheat allergy was estimated approximately 3% of all anaphylaxis in Japan<sup>2)</sup>. Among the allergenic proteins in buckwheat, proteins with molecular weight of 9 kDa, 16 kDa, 19 kDa, and 24 kDa are considered major allergens, and 24 kDa and 16 kDa proteins are named as Fag e 1 and Fag e 2, respectively<sup>3)</sup>. Fag e 1 belonging to the  $\beta$  subunit of the legumin-like storage molecule has been reported that the most important allergen responsible for the induction of the immunoglobulin E (IgE)-

mediated immediate hypersensitivity reaction in buckwheat allergy<sup>4)</sup>.

Allergen-specific immunotherapy, which entails gradual increasing exposure to allergens in the hopes of desensitization and promoting tolerance, is the most researched approaches to treat allergies<sup>5)</sup>. Currently, oral immunotherapy appears to be a more promising therapeutic approach for food allergies because subcutaneous immunotherapy resulted in unacceptably high rates of severe adverse reactions<sup>6)</sup>. However, there is still the high risk of IgE-mediated side effects, and there is thus a strong need to develop effective and safer tolerogens.

A number of attempts were made to modify allergenic proteins for use in specific immunotherapy. Maillard-type glycosylation has become recognized as effective methods for modification of molecular surface of the target protein. It has been showed that the attachment of polysaccharides