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Review Article

Allergenic Ribosomal P Proteins

Abstract

Allergenic ribosomal P proteins have been isolated almost exclusively from allergenic mold species with the exception of one from almond. Presently, nine cloned ribosomal P proteins are listed as allergens in Allergen Nomenclature, WHO/IUIS database. They belong to either P1 or P2 protein families.

Introduction

Characteristics of ribosomal P proteins

Ribosomal P proteins are small molecules (10-11 kDa) that form the ribosomal stalk structure which plays a key role in the elongation step of protein translation [1]. Ribosomal P proteins have an isoelectric point in a very acidic range (pI 3-4), and are phosphorylated. For these reasons, they are also called acidic ribosomal P proteins. In addition to ribosome-bound P proteins, they are also found in a free-state in cytoplasm and an exchange occurs between the nucleus and cytoplasmic sites [2]. Free ribosomal proteins are contained in the nuclear sap and participate in the assembly of ribosome subunits that takes place in the nucleolus. Ribosomal proteins are ubiquitous and abundant in the cell. They are prime candidates for recruitment towards extraribosomal functions that are often related to overall cellular health, such as balancing the synthesis of the RNA and protein components of the ribosome and involving in apoptosis [3].

Based on sequence homology, mammals and yeast have two types of acidic ribosomal P proteins: P1 and P2 [4], and plants also have a third type P3 [5]. Both P1 and P2 have unique N-terminal domains and highly conserved C-terminal domains which contain a phosphorylated serine residue [4]. Both P1 and P2 proteins form heterodimers and bind to a neutral phosphoprotein, P0 through their N-terminal domain to form the pentameric stalk structure in the 60S ribosomal subunit [6]. Eukaryotic P0, P1/P2 stalk proteins are analogous to bacterial L10, L12 and archaeal P0, P1 stalk proteins, respectively [7]. They interact with elongation factors EF1 and EF2, and their level of phosphorylation regulates the overall rate of translation [8].

Ribosomal P proteins show strong sequence homology, probably reflective of their common evolutionary origin. The C-terminal domains of all three proteins, P1, P2 and P0 show significant sequence homology [1]. The C-terminal domains of ribosomal P proteins are involved in specific recognition of elongation factors [9,10]. They also bind some eukaryote-specific ribosome-inactivating proteins (RIP), such as ricin, trichosanthin, maize RIP, pokeweed antiviral proteins, shiga and shiga-like toxins [7]. The ribosomal P proteins also share a common C-terminal epitope, which is recognized by the same autoantibodies in the sera of individuals with autoimmune diseases such as systemic lupus erythematosus [11,12], protozoan infections [13], and Chagas' heart disease [14]. In addition to the common C-terminus epitope, ribosomal P proteins may contain epitopes in their N-terminal domains [15]. Ribosomal P proteins found in a free-state in the cytoplasm will most likely bind to toxic RIPs, autoantibodies and also play a role in their antigenic and allergenic properties since they are readily available unlike ribosome-bound P proteins. They are also readily isolated in the cytoplasmic fraction during protein isolation. Therefore, extra ribosomal functions of the isolated ribosomal P proteins are most likely manifested in autoimmune diseases, allergic reactions and toxicity of RIPs. The purpose of this article is to review the ribosomal P proteins that are reported to be allergenic in the literature.

Allergenic ribosomal P proteins

Allergen definition rules for a protein to be considered in the Allergen Nomenclature is set by the World Health Organisation/International Union of Immunological Societies (WHO/IUIS) which recognizes a protein as an allergen if the protein binds to IgE antibodies in atopic sera from a minimum of five different individuals [16]. Presently, most allergenic extracts are produced using recombinant DNA technology. In the past, preparation of allergen extracts were not only tedious but also contained large portion of cross-reactive impurities which interfered with test results. The advent of recombinant DNA technology made it easier to clone allergenic proteins, and produce allergen extracts in large-scale and exceptional purity.

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Allergen extracts prepared from cloned recombinant allergens are more useful than the extracts produced by the traditional methods. This is important, since allergen extracts are used as standards for diagnostic reagents as well as potential vaccines for desensitization of mold-allergic patients.

Several ribosomal P proteins have been cloned, expressed in large-scale and purified. Table 1 shows the current list of the cloned ribosomal P proteins that are determined to be allergenic in WHO/IUIS database [17]. So far, all isolated allergenic ribosomal P proteins belong to either P1 or P2 protein families. Furthermore, almost all of these allergenic ribosomal P proteins with the exception of Pru du 5 of almond appear to be of fungal origin, and play a role in mold allergy.

Alternaria sp., *Cladosporium* sp., *Penicillium* sp., *Aspergillus* sp., and *Fusarium* sp. are all rich sources of mold allergens. These mold species together with other common indoor allergens including house dust mite, cockroach and animal dander play a role in asthma and other airborne respiratory diseases [27,28]. At present, WHO/IUIS database lists about 80 mold allergens from various protein families. Ribosomal P proteins (n=8) ranks second after proteases (n=18), followed by enolases (n=5), dehydrogenases (n=4), and others.

Ribosomal P proteins are the predominant allergens of some mold species listed in Table 1. These proteins were also described as cross-reactive fungal allergens [29]. Perhaps, this may account for their role in autoimmunity.

Future directions

Among the listed ribosomal P proteins, Pen cr 26 appears to be a naturally-occurring hypoallergen [22]. Pen cr 26 has a strong sequence homology to Pen b 26, and unlike Pen b 26, has weak IgE- and strong IgG-binding capacity. This characteristic of Pen cr 26 is useful for allergen-specific immunotherapy to desensitize patients against Pen b 26-like ribosomal P proteins without producing anaphylactic shock while promoting the production of neutralizing IgG antibodies. Further research is required to test the hypoallergenic characteristics of Pen cr 26 against other ribosomal P protein allergens since all share strong sequence homology and probably have common epitopes. So far, nine of the cloned ribosomal P proteins have been reported to be allergenic. This number is expected to rise in the future.

Table 1: Allergenic ribosomal P proteins currently listed in Allergen Nomenclature, WHO/IUIS database [17].

Protein family	Allergen designation	Source species	GenBank accession no.	Allergen Nomenclature entry date	References
P1	Alt a 12	*Alternaria alternata*	X84216	2009	[18,19]
	Cla h 12	*Cladosporium herbarum*	X85180	2009	[19,20]
	Pen b 26	*Penicillium brevicompactum*	AY786077	2006	[21]
	Pen cr 26	*Penicillium crustosum*	JN791438	2014	[22]
P2	Alt a 5	*A. alternata*	X78222	2009	[23]
	Cla h 5	*C. herbarum*	X78223	2009	[24]
	Asp f 8	*Aspergillus fumigatus*	AJ224333	2003	[19]
	Fus c 1	*Fusarium culmorum*	AY077706	2003	[25]
	Pru du 5	*Prunus dulcis* (almonds)	DQ836316	2007	[26]

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