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Defensive Effect of 30kDa Protein from Silkworm, Bombyxmori against Apoptosis Induced Diseases

Nattar Singam Jothi[1], Veeranarayanan Surya Aathmanathan[1] and Muthukalingan Krishnan[2]*

[1]*Department of Environmental Biotechnology, Bharathidasan University, India*

[2]*Department of Biochemistry, Central University of Rajasthan, India*

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***Corresponding author:** Muthukalingan Krishnan, Department of Biochemistry, Central University of Rajasthan, Ajmer, Rajasthan, India, Tel: 9443998251; Email: profmkrish@curaj.ac.in

Abstract

During embryonic development of the domesticated silkworm, Bombyx mori, 30kDa proteins comprise about 35% of the total embryo yolk proteins and function as storage proteins. In the early and midpupal developmental phase 30kDa proteins is one among the most abundant components of hemolymph. Albeit, the 30kDa family proteins are important anti-apoptotic molecules in silkworm hemolymph, the underlying mechanism remains to be investigated. This article reviews 30kDa protein as a novel anti-apoptotic protein from silkworm, which also protects from Reactive Oxygen Species (ROS) generation.

Keywords: 30kDa protein; Anti- apoptosis; ROS generation; Cardiovascular diseases

Abbreviations: ROS: Reactive Oxygen Species; FB: Fat Body; MW: Molecular Weight

Introduction

Cell death is categorized as either apoptotic or necrotic. Apoptosis is an important characteristic feature of normal tissue. It is a naturally controlled by cell deletion process which is visible in distinct morphological and biochemical patterns. It is characterized by autophagy which includes condensed cytosol, marginalized chromatin and nuclear fragmentation, formation of apoptotic bodies that are ultimately engulfed by surrounding cells or macrophagesand lysosomal degradation of intracellular components [1-3].

It is essential for embryogenesis and for the development of the immune system and maintenance of tissues homeostasis [4], it is not surprising that inconsistent apoptosis-either excessive or deficient is the direct cause of serious diseases. Extensive studies have been undertaken on apoptosis in model animals such as fruit flies, nematodes and Bombyxmori [5,6]. Thereby, research on B. mori, an organism very important for sericulture, has been considered complimentary to that of the widely used experimental organism Drosophila.

30kDa protein from Silkworm, *Bombyx mori*

Lepidoptera are the most successful groups of insect family. They are found on all continents, except Antarctica. It consist of 126 families and nearly 1,74,000 species [7]. It consists of moths and butterflies which includes both monophagous and polyphagous insect. Among the lepidopteran family, *Bombyx mori* is the only monophagous domesticated insect species, thereby it is act as an outstanding model animal. Transgenic *B. mori* is used as an effective bioreactor for production of recombinant proteins. Nowadays, *B. mori* is used for the screening of drug and safety test; more over they are the instrumental for fundamental findings on pheromones, hormones, brain structure and physiology [8].

The insect fat body is a functional analogue of the vertebrate liver [2] serving as a protein factory which is responsible for the production of virtually all hemolymph proteins that are directed to their destination by its signal peptides. In early and middle pupal stages of *B. mori,* hemolymph comprises 21%~25% of body weight, which is involved in nutrient and hormone transportation [9]. The group of 30kDa proteins is synthesized in fat body (FB) of both sexes and secreted into hemolymph and other organs through specific receptors, which are expressed in a time dependent manner [10,11].

30kDa proteins has multiple functions in lepidopteran insects such as antiapototic properties [12] and in embryogenesis [13]. In mature female moths, 30kDa proteins are transported into yolk granules, where they become the second major yolk

protein of the eggs after vitellin [14,15]. The amount of 30kDa proteins were decreased in pharate adult female hemolymph for providing nutrition to the embryonic development [16]. The 30kDa proteins are enzymatically degraded in male pupa during pupal- adult development for eclosion and mating. Krishnan et al. [17] reported that the 30kDa proteins are solubilized by enzyme digestion or pH regulation in periveciral fat body tissues and transported to the respective tissues via hemolymph. In self-defense system 30kDa proteins binds to glucose and glycans [18], Due to the presence putative sugar binding domain of Bmlp7 plays a crucial role in the protection of *B. mori* against invading pathogens. It is also involved in lipid transport in the larvae of silkworm [19]. In Paecilomycestenuipes, 30kDa proteinsinhibit the hyphal growth of the entomopathogenic fungus [18]. Similarly, 30kDa proteins translocate chymotrypsin inhibitor-8 to the membrane of the midgut [20].

Therapeutic role of 30 kDa protein

The recombinant 30Kc6 prolong the growth of host cell when supplemented in medium [19]. It also inhibits the virus and chemical induced apoptosis in mammalian and insect cell culture. The 30kc6 protein inhibited nuclear fragmentation and apoptotic body formation as well as the activation of Sf-caspase-1in Sf9 cells. Most effective anti-apoptotic activity was reported for 30Kc19 recombinant protein obtained from periplasm. Rhee et al. [21] & Kim et al. [19] reported that the *B. mori* hemolymph protects the host cell against apoptosis induced by various chemicals including actinomycin D, camptothecin, and staurosporine. Anti-apoptotic property of 30kDa protein was effectively worked in insect, mammalian, and human cell systems. Kim et al. [22] have separated four most antiapoptotic components of ~30kDa from *B. mori* hemolymph. It was a nonglycosylated member (~28kDa) of the 30kDa proteins, a family of structure related major plasma proteins with a molecular weight (MW) of approximately 30kDa. The whole silkworm hemolymph was comparable with 30kDa recombinant protein for its apoptosis inhibitory activity.

Previous reports suggested that a variety of biological pathways are likely to be involved in 30K proteins, largely exemplified as providing nutrients for embryogenesis. 30K recombinant protein defending against fungal infection and effectively inhibiting apoptosis in human and insect cells induced by viral or chemicals. It also played an important role in the transport and accumulation of tryptophan metabolites during the formation of serosa [23]. 30Kc6 recombinant protein prevents hyperosmotic pressure-induced apoptosis in a CHO cell line producing a chimeric anti-human CD20 monoclonal antibody. Yu et al. [24] reported the defensive effect of 30kc6 on cells damaged by oxidized low density lipoprotein in human vascular endothelial. 30K protein prevents the cell death induced by 20-hydroxyecdysone in the Bm5 silkworm ovarian cell line. It protects by blocking the binding of ultraspiracle to ecdysone receptor–B1 through the formation of a 30K and EcR-B1 complex [25-32].

Conclusion

Apoptosis is essential for growth and survival of multicellular organism. The dysregulation of apoptosis is the direct cause for various diseases. Increased cell death due to increased apoptosis leads to neurological disorders, cardiovascular disorders and auto immune diseases. For this, the scientists are introducing anti -apoptotic genes for treating neurodegenerative diseases. The recombinant 30K protein may act as apotential therapeutic agent for various human diseases related to apoptosis.

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