Microbial Toxins-a Mini Review

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Abstract- A toxin is a poisonous substance produced within living cells or organisms. Toxins can be small molecules, peptides, or proteins that are capable of causing disease on contact with or absorption by body tissues interacting with biological macromolecules such as enzymes or cellular receptors. Microbial toxins include toxins produced by micro-organisms, including bacteria and fungi. Microbial toxins promote infection and disease by directly damaging host tissues and by disabling the immune system.

Introduction

Microbial toxins are toxins produced by micro-organisms, including bacteria and fungi. Microbial toxins promote infection and disease by directly damaging host tissues and by disabling the immune system. Some bacterial toxins, such as Botulinum neurotoxins, are the most potent natural toxins known. However, microbial toxins also have important uses in medical science and research. Potential applications of toxin research include combating microbial virulence, the development of novel anticancer drugs and other medicines, and the use of toxins as tools in neurobiology and cellular biology(1)

Microbially produced toxins, which appear to lack a role in microbial survival, may be antimicrobial compounds of significance to the producers. These toxin/antibiotics may act against cell metabolism shared by man or animals and other microorganisms. Protein toxin/antibiotics are produced by single species of bacteria. Those from fungi and algae are nonprotein secondary metabolites and several microorganisms may make the same or similar toxin/antibiotics

Discussion

Bacterial toxins

Many bacterial toxins are proteins, encoded by the bacterial chromosomal genes, plasmids or phages. Lysogenic phages form part of the chromosome. The toxins are usually liberated from the organism by lysis, but some are shed with outer membrane proteins in outer membrane vesicles. An important non-protein toxin is lipopolysaccharide or endotoxin, which is a constituent of the cell wall of gram negative bacteria. Toxins may damage the eukaryotic cell membrane by combining with some structural component, or otherwise alter its function. Many toxins combine with specific receptors on the surface membrane, frequently glycoproteins or gangliosides, and penetrate the cell to reach their intracellular target. A common mechanism of entry is absorptive endocytosis. Many protein toxins have an A-B structure, B being a polypeptide which binds to the receptor and A being an enzyme. Many toxins are activated, either when produced by the bacterium or when bound to the membrane receptor, by proteases (nicking). An enzymatic process common to many toxins is adenosine diphosphate (ADP)-ribosylation of the adenylatecyclase regulatory proteins, leading to an increase in intracellular cyclic adenosine monophosphate (cAMP). This is the mechanism of action of cholera toxin. Diphtheria toxin catalyzes the transfer of ADP-ribose to elongation factor-2, inhibiting protein synthesis. Most toxins act on the target cells to which they bind, but tetanus toxin, and, to a lesser degree, botulinum toxin, ascend axons and affect

more distant structures. Although many toxin effects caused by bacteria have been described, only a few toxins have been identified, characterized, and their mode of action determined at the molecular level.(2,3)

Fungal toxins

Most fungi are aerobic (use oxygen) and are found almost everywhere in extremely small quantities due to the minute size of their spores. They consume organic matter wherever humidity and temperature are sufficient. Where conditions are right, fungi proliferate into colonies and mycotoxin levels become high. The reason for the production of mycotoxins is not yet known; they are not necessary for the growth or the development of the fungi.[7] Because mycotoxins weaken the receiving host, the fungus may use them as a strategy to better the environment for further fungal proliferation. The production of toxins depends on the surrounding intrinsic and extrinsic environments and these substances vary greatly in their toxicity, depending on the organism infected and its susceptibility, metabolism, and defense mechanisms(4,5)

Types of fungal toxins

Aflatoxins are a type of mycotoxin produced by Aspergillus species of fungi, such as A. flavus and A. parasiticus.[9] The umbrella term aflatoxin refers to four different types of mycotoxins produced, which are B1, B2, G1, and G2.[10] Aflatoxin B1, the most toxic, is a potent carcinogen and has been directly correlated to adverse health effects, such as liver cancer, in many animal species.[9] Aflatoxins are largely associated with commodities produced in the tropics and subtropics, such as cotton, peanuts, spices, pistachios, and maize.[9][10]

Ochratoxin is a mycotoxin that comes in three secondary metabolite forms, A, B, and C. All are produced by Penicillium and Aspergillus species. The three forms differ in that Ochratoxin B (OTB) is a nonchlorinated form of OchratoxinA (OTA) and that Ochratoxin C (OTC) is an ethyl ester form Ochratoxin A.[11] Aspergillusochraceus is found as a contaminant of a wide range of commodities including beverages such as beer and wine. Aspergilluscarbonarius is the main species found on vine fruit, which releases its toxin during the juice making process.[12] OTA has been labeled as a carcinogen and a nephrotoxin, and has been linked to tumors in the human urinary tract, although research in humans is limited by confounding factors.[11][12]

Citrinin is a toxin that was first isolated from Penicilliumcitrinum, but has been identified in over a dozen species of Penicillium and several species of Aspergillus. Some of these species are used to produce human foodstuffs such as cheese (Penicilliumcamemberti), sake, miso, and soy sauce (Aspergillusoryzae). Citrinin is associated with yellowed rice disease in Japan and acts as a nephrotoxin in all animal species tested.[13]Although it is associated with many human foods (wheat, rice, corn, barley, oats, rye, and food colored with Monascus pigment) its full significance for human health is unknown. Citrinin can also act synergistically with Ochratoxin A to depress RNA synthesis in murine kidneys.[14]

Ergot Alkaloids are compounds produced as a toxic mixture of alkaloids in the sclerotia of species of Claviceps, which are common pathogens of various grass species. The ingestion of ergot sclerotia from infected cereals, commonly in the form of bread produced from contaminated flour, cause ergotism, the human disease historically known as St. Anthony's Fire. There are two forms of ergotism: gangrenous, affecting blood supply to extremities, and convulsive, affecting the central nervous system. Modern methods of grain cleaning have significantly reduced ergotism as a human disease, however it is still an important veterinary problem. Ergot alkaloids have been used pharmaceutically.[14]

Patulin is a toxin produced by the P. expansum, Aspergillus, Penicillium, and Paecilomyces fungal species. P. expansum is especially associated with a range of moldy fruits and vegetables, in particular rotting apples and figs.[15][16] It is destroyed by the fermentation process and so is not found in apple beverages, such as cider. Although patulin has not been shown to be carcinogenic, it has been reported to damage the immune system in animals.[15] In 2004, the European Community set limits to the concentrations of patulin in food products. They currently stand at 50 μg/kg in all fruit juice concentrations, at 25 μg/kg in solid apple products used for direct consumption, and at 10 μg/kg for children's apple products, including apple juice.[15][16]

Fusarium toxins are produced by over 50 species of Fusarium and have a history of infecting the grain of developing cereals such as wheat and maize.[17][18] They include a range of mycotoxins, such as: the fumonisins, which affect the nervous systems of horses and may cause cancer in rodents; the trichothecenes, which are most strongly associated with chronic and fatal toxic effects in animals and humans; and zearalenone, which is not correlated to any fatal toxic effects in animals or humans. Some of the other major types of Fusarium toxins include: beauvercin and enniatins, butenolide, equisetin, and fusarins.(6)

Toxin-antitoxin systems

Toxin-antitoxin (TA) systems are small genetic elements found on plasmids or chromosomes of many bacteria and Archaea. Under normal growth conditions, the activity of the toxin protein or its translation is counteracted by an antitoxin protein or a non-coding antitoxin sRNA (see below for classification of TA types). Toxins are stable whereas antitoxins are metabolically unstable so that, unless the antitoxin is continuously expressed, the free toxin accumulates and exerts its toxic effect Changes in the physiological conditions, like stress conditions or viral infection can result in the degradation of the antitoxin which is highly unstable. Proteases (e.g. Lon, Clp, Hlfp) have be linked to the degradation of many antitoxins. Unleashed toxin proteins impede or alter cellular processes including translation, cell division, DNA replication, ATP synthesis, mRNA stability or cell wall synthesis and leads to dormancy. This dormant state probably enables the bacteria to survive environmentally unfavorable conditions but may also sometimes lead to cell death. The modularity of the TA systems whereby toxins and antitoxins can have more than one partner gives rise to a network of complex, interconnected families of TA systems.

The number of TA systems is variable: E.coli K12 codes for least 33 TA systems, M.tuberculosis than 60 whereas M.segmatis has only two so far.

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