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Non-Ribosomal Peptide Synthetase: A Virulence Factor in Fungal Plant Pathogens

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SUMMARY

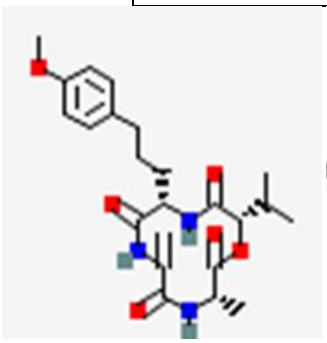
Proteins play an essential role in all living organisms and are responsible for several metabolic processes in organisms. Non ribosomal peptides (NRPs) are some special proteins which are produced by non ribosomal peptides synthetase gene. NRPSs are found almost exclusively in bacteria and fungi except for a few NRPS-like enzymes reported in other organisms. Non ribosomal peptides play an important role in plant pathogenic fungi as many of them are virulence determinants.

INTRODUCTION

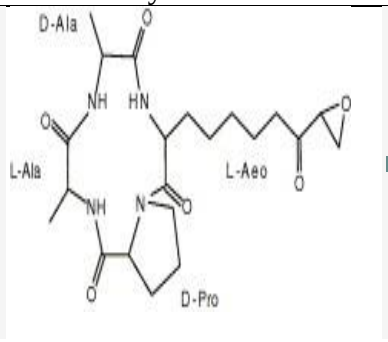
Ribosomes play a vital role in biosynthesis of proteins which is very important for every living organism. Other than ribosomal protein synthesis there exist ribosome independent mechanisms of amide bond formation in nature. Most prominent among these is nonribosomal peptide (NRP) synthesis by large multienzyme complexes called nonribosomal peptide synthetases (NRPSs). NRPSs are found almost exclusively in bacteria and fungi. Each nonribosomal peptide synthetase can synthesize only one type of peptide. Nonribosomal peptides often have cyclic and/or branched structures, can contain non-proteinogenic amino acids including D-amino acids, carry modifications like *N*-methyl and *N*-formyl groups, or are glycosylated, acylated, halogenated, or hydroxylated. Cyclization of amino acids against the peptide "backbone" is often performed, resulting in oxazolines and thiazolines; these can be further oxidized or reduced. Nonribosomal peptides are often dimers or trimers of identical sequences chained together or cyclized, or even branched. Nonribosomal peptides belong to diverse family of natural products performing wide range of biological activities and may have pharmacological properties. They are often toxins, siderophores, or pigments. Nonribosomal peptide antibiotics, cytostatics, and immunosuppressants have been utilised commercially.

Table 1: Examples of NRPs

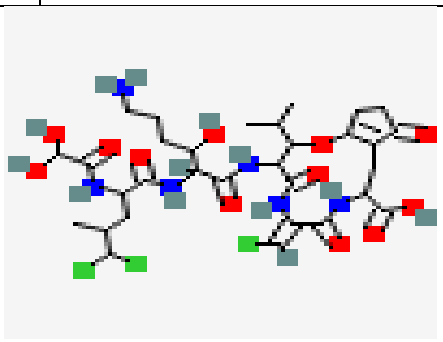
NRPs	Produced by (Organsim)
HC toxin	*Cochliobolus carbonum*
AM toxin	*Alternaria alternate*
Enniatin	*Fusarium spp.*
Victorin	*Cochliobolus victoriae*
Bacitracin	*Bacillus subtilis*
Pyoverdins	*Pseudomonads*
Zwittermycin	*Bacillus cereus*



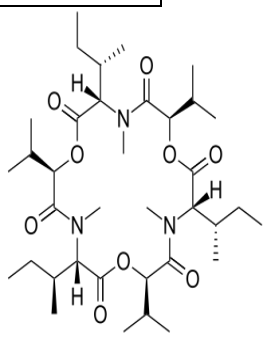
AM Toxin



HC Toxin



Victorin



Enniatin

Biosynthesis of Non ribosomal peptides:

Nonribosomal peptides are synthesized by one or more specialized nonribosomal peptide-synthetase (NRPS) enzymes. The NRPS genes for a certain peptide are usually organized in one operon in bacteria and in gene clusters in eukaryotes. However the first fungal NRP to be found was ciclosporin. It is synthesized by a

single 1.6MDa NRPS. The enzymes are organized in modules that are responsible for the introduction of one additional amino acid. Each module consists of several domains with defined functions, separated by short spacer regions of about 15 amino acids. The biosynthesis of nonribosomal peptides shares characteristics with the polyketide and fatty acid biosynthesis. Due to these structural and mechanistic similarities, some nonribosomal peptide synthetases contain polyketide synthase modules for the insertion of acetate or propionate-derived subunits into the peptide chain. Some NRPS modules deviate from the standard domain structure, and some extra domains have been described. There are also NRPS enzymes that serve as a scaffold for other modifications to the substrate to incorporate unusual amino acids.Many NRPS gene have been reported to synthesise some peptides responsible for virulence in plant pathogenic fungi and bacteria. NPS6 gene in *Cochliobolus heterostrophus* is involved in virulence and oxidative stress in this plant pathogenic fungus.NPS1 and NPS2, were found to be related to genes involved in NPS hydroxamate siderophore biosynthesis and chemical analysis of a *F. graminearum*. NPS2 deletion mutant showed that this gene encodes the NPS responsible for the biosynthesis of ferricrocin. VdNPS, a non ribosomal peptide synthetase has been reported to regulate the virulence in *Verticillium dahlia,* and the deletion of NPS gene lead to the reduction in formation of conidia and microslerotia and minimised pathogenecity.

Determinants of virulence

Cytotoxic Non Ribosomal Peptides produced by pathogenic fungi are considered as potential virulence factors. The phytopathogenic fungus *Leptosphaeria maculans* (Sowerby) P. Karst is known to produce sirodesmin toxin. The toxin on application to leaves of different host plants of *L. maculans*, causes chlorotic and collapsed lesions. Host-selective toxins (HSTs) produced by certain phytopathogenic fungi are active specifically against limited species or cultivars of plants. The ability to produce host specific toxins is often a prerequisite for the producing fungi to infect the toxin-sensitive plants, and loss of HST production usually turns the fungi nonpathogenic. They are the most important weapons of pathogenic fungi. HSTs include structurally diverse metabolites, including NRPs, polyketides, and proteins. A cyclic depsipeptide AM-toxin produced by the apple pathotype of *Alternaria alternate* is an example of HSTs synthesized by Non Ribosomal Peptide Synthetase. HC-toxin is a cyclic tetrapeptide HST produced by race 1 of *Cochliobolus carbonum*. In contrast to AM-toxin, HC-toxin is a virulence determinant.

CONCLUSION

Non ribosomal pepetides are known to play several roles (signalling molecules, virulence factor, siderophores etc.) in an organism. Their role in plant pathogenic organism as a virulence factor is of immense importance as absence of that particular peptide may prevent the appearance of disease in host plants. Some of the NRPs are well recognised but their exact function might not be very clear, further studies may help to get the insights of the mechanism involved in host pathogen interactions.

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