

Metagenome-Massive Reservoir of Antifungal Peptides to Treat Emerging Infectious Diseases

“Metagenomics for antifungal drug discovery”

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COLUMN ARTICLE

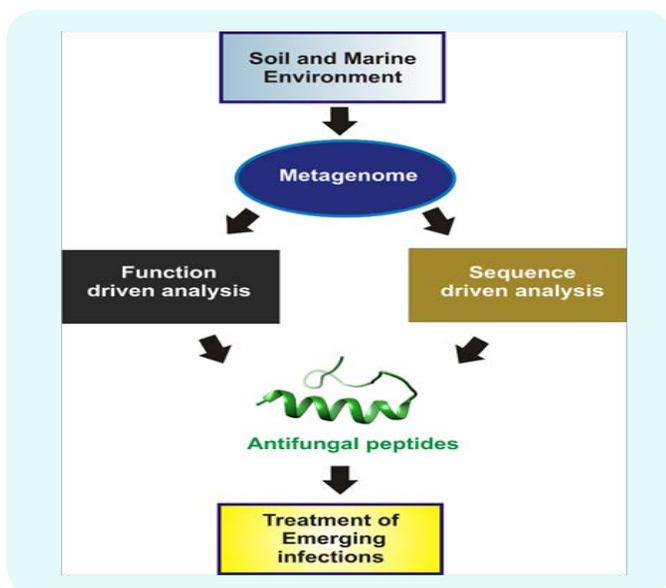
Opportunistic fungal infections such as Candidiasis and Aspergillosis brings in therapeutic challenges especially in high risk immunocompromised patients with AIDS, cancer and other medical conditions. The incidence and diversity of invasive mycosis have been increasing worldwide in recent years and the radiant of emerging resistance to conventional antibiotics invites new antifungal drugs and innovative approaches [1]. Candidiasis is caused by *Candida* spp., which encompasses infections that range from superficial to systemic and potentially life threatening diseases. *Candida* infection also known to cause leakage of intestinal permeability in humans, a condition called as leaky gut syndrome [2]. Aspergillosis is caused by filamentous fungi *Aspergillus* spp. that comprises of large number of diseases involving both infections and allergic responses [3]. Besides these, other saprophytic fungi were also been shown to be associated with human pathology [4]. Thus, the increase in the number of immune compromised patients at risk for invasive fungal infections tend to increase the need for new antifungal agents.

Currently, there is a considerable interest in antimicrobial peptides (AMPs) as a choice of therapeutic drug due to their versatile biological properties, broad range of activity, lesser toxicity, and lower resistance development by pathogens [5,6]. The peptide-based antifungal therapy receives greater attention in recent years due to technological advancement

in peptide engineering, solid-phase peptide synthesis and the potential to select peptides as an efficient antifungal drug with acceptable toxicity profiles [7]. A wide variety of antifungal drugs with diverse structures and mechanisms of actions have been identified from different sources such as plants, animals, mammals and microorganisms [5,8]. It is well documented that less than 1% of the microorganisms in environment can be cultured by conventional microbiological methods which have been exhaustively utilized for the isolation and identification of bioactive compounds [9]. Thus large fractions of the diverse group of microbes in the soil and marine environments defy cultivation. Metagenomic approaches (Figure 1) provide access to the genetic resources of the total microbial community (metagenome) present in different environments and has uncovered a diverse group of novel antimicrobial genes involved in antibiotic productions [10-12]. Novel antimicrobial compounds with various bio-activities such as terragines, violacein, indirubin, turbomycins, patellamide and MMGP1 have been reported from soil and marine metagenomes [13,14,10]. In this regard, over the last decade metagenomics approaches have allowed insight into the diversity of antifungal peptides from different environments, which may serve as a reliable alternative strategy to reveal the reservoir of potential antifungal peptides in uncultivable and unexplored microbial community that inhabits soil and marine environments.

Bioprospecting Metagenome For novel Antifungal Peptides

Metagenomic strategy involves function-based and sequence-based screening of genes encoding antifungal peptides. In activity based screening, the genes encoding antifungal peptides are identified based on antimicrobial function. In sequence based screening, the genes of interest are screened based on the known genes sequences.



BIBLIOGRAPHY

1. Kourkoumpetis Themistoklis., *et al.* "Candida infection and colonization among non-trauma emergency surgery patients". *Virulence* 1.5 (2010): 359-366.
2. Pushpanathan M. "Leaky Gut Syndrome: Mystery Illness Triggered by *Candida albicans*". *Journal of Nutritional Health & Food Engineering* 4(2016): 00133.
3. Kradin Richard L and Eugene J Mark. "The pathology of pulmonary disorders due to *Aspergillus* spp". *Archives of pathology & laboratory medicine* 132.4 (2008): 606-614.
4. Walsh TJ and AH Groll. "Emerging fungal pathogens: evolving challenges to immunocompromised patients for the twenty-first century". *Transplant infectious disease* 1.4 (1999): 247-261.
5. Pushpanathan Muthuirulan., *et al.* "Antimicrobial peptides:

versatile biological properties". *International journal of peptides* 2013 (2013).

6. Hancock Robert EW., *et al.* "Host defense peptides from invertebrates—emerging antimicrobial strategies". *Immunobiology* 211.4 (2006): 315-322.
7. Matejuk A., *et al.* "Peptide-based antifungal therapies against emerging infections". *Drugs of the Future* 35.3 (2010): 197.
8. De Lucca Anthony J and Thomas J Walsh. "Antifungal peptides: origin, activity, and therapeutic potential". *Revista Iberoamericana de Micología* 17.4 (2000): 116-120.
9. Handelsman Jo. "Metagenomics: application of genomics to uncultured microorganisms". *Microbiology and molecular biology reviews* 68.4 (2004): 669-685.
10. Pushpanathan Muthuirulan., *et al.* "Identification of a novel antifungal peptide with chitin-binding property from marine metagenome". *Protein and peptide letters* 19.12 (2012): 1289-1296.
11. Pushpanathan M., *et al.* "Microbial Bioremediation: A Metagenomic Approach". *Microbial Biodegradation and Bioremediation* (2014): 407-419.
12. Rajendhran J and P Gunasekaran. "Strategies for accessing soil metagenome for desired applications". *Biotechnology advances* 26.6 (2008): 576-590.
13. Li Xiang and Ling Qin. "Metagenomics-based drug discovery and marine microbial diversity". *Trends in Biotechnology* 23.11 (2005): 539-543.
14. Long Paul F., *et al.* "Shotgun cloning and heterologous expression of the patellamide gene cluster as a strategy to achieving sustained metabolite production". *ChemBioChem* 6.10 (2005): 1760-1765.

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