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Discovery of cyclic peptide natural product inhibitors of free living amoeba

Novel cyclic peptides offer a promising drug lead for highly lethal central nervous system infections caused by free-living amoeba, such as Balamuthia amoebic encephalitis, with demonstrated potent activity and minimal toxicity.

Balamuthia mandrillaris is a pathogenic free-living amoeba that causes infection of central nervous system, called Balamuthia amoebic encephalitis (BAE), as well as cutaneous and systemic diseases. Patients infected have a high mortality rate due to the lack of effective treatments. A combination of non-optimized antimicrobial drug regimen is typically recommended; however, they have poor parasite activity and can cause various severe side effects.

Cyclic peptides exhibit a broad spectrum of antimicrobial activities and lower cytotoxicity. Researchers at Purdue University have developed novel therapeutics regarding the anti-B. mandrillaris effect of cyclic peptides. The predicted natural product-43 (pNP-43), identified from the SNaPP (Synthetic Natural Product Inspired Cyclic Peptides) library, and its derivates displayed a significant inhibition for B. mandrillaris trophozoites. This technology has indicated the anti-B. mandrillaris effect of cyclic peptides, which provides a new direction for drug development.

In addition to B. mandrillaris, these cyclic peptides may by used for inhibiting or treating and infection or disease caused by other pathogenic free-living amoeba such as Acanthamoeba castellanii and Naegleria fowleri. Currently there are no effective drugs for any of these diseases as indicated by mortality rates of >90% for CNS infections. These cyclic peptides have potent activity and low toxicity making them promising drug leads.

Technology Validation: Forty-four cyclic peptides were screened from the SNaPP library for trophocidal activity at 16 ug/mL and several hits were identified for each amoeba. None of the compounds caused hemolysis at the highest concentration tested (100 ÂµM). This suggests that the cyclic peptides are likely to have minimal toxicity to humans.

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Category
Biotechnology & Life Sciences/Synthetic Biology & Genetic Engineering
Biotechnology & Life Sciences/Biomarker Discovery & Diagnostics
Pharmaceuticals/Drug Discovery & Development
Biotechnology & Life Sciences/Analytical & Diagnostic Instrumentation
Pharmaceuticals/Small Molecule Therapeutics

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Advantages:

-Promising potential for BAE therapeutics

-Can be made into tablets

Applications:

-Pharmaceuticals company

-Therapeutics

TRL: 3

Intellectual Property:

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Keywords: Balamuthia mandrillaris, BAE therapeutics, cyclic peptides, anti-amoeba drugs, Acanthamoeba castellanii, Naegleria fowleri, SNaPP library, anti-B. mandrillaris, free-living amoeba, drug development