Mining for new drugs in the ocean

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Credit: Marcel Jaspers, University of Aberdeen

Each time we use an antibiotic, the weaker strains of infection are killed off while the stronger, more virulent strains are left behind to multiply. In the past, this has not caused much concern, as there has always been a new drug available to fight the infection. Now however, we are running out of options.

In fact, as Professor Marcel Jaspars from the University of Aberdeen in the UK explains, there has not been a new antibiotic registered since 2003. Interest in developing new antibiotics has waned, as they are only used for short periods of time and their efficacy is limited to about ten years. This does not make them a profitable investment for drug companies, and as a result, our supply is running dry. "If nothing's done to combat this problem we're going to be back to a 'pre-antibiotic-era' in

around ten or twenty years, where bugs and infections which are currently quite simple to treat could be fatal," says Jaspars.

Drug discovery is therefore a serious health issue. However, scientists believe that the ocean could provide answers to the problem of developing new novel drugs. The majority of currently used antibiotics have been isolated from terrestrial sources, and recent attempts at terrestrial bio-prospecting have mainly resulted in the rediscovery of known antibiotics or their close analogues. Recent data strongly suggest that the marine environment represents an untapped source for new biologically active molecules, in particular antibiotics. Scientists have long searched the world's oceans for new drug candidates, though this quest has mainly focused on tropical waters.

The PharmaSea project aims to combat the growing problem of antibiotic resistance by looking for new drugs in the ocean. The novelty of this project is that it will be exploring some of the deepest and coldest oceans on the planet. This should be interesting, as there have hardly been any samples collected from the regions of the Arctic and Antarctic before.

This large scale, four year project will bring European researchers from the UK, Belgium, Norway, Spain, Ireland, Germany, Italy, Switzerland and Denmark together to collect and screen samples of mud and sediment from huge, previously untapped, oceanic trenches. It is backed by more than ?9.5 million of EU funding, and brings together 24 partners from 14 countries from industry, academia and non-profit organisations.

One of the aims of PharmaSea is to look for new antibiotics in newly discovered marine bacteria. It will also focus on drug discovery for neurological, inflammatory, and other infectious diseases.

Researchers have known for some time that the rich diversity of marine life in the oceans represents what could amount to a previously unexplored pharmaceutical goldmine. The oceans are the source of a large group of structurally unique natural products that are mainly accumulated in invertebrates such as sponges, tunicates, bryozoans, and molluscs. Several of these compounds (especially the tunicate metabolite ET-743) show pronounced pharmacological activities and are interesting candidates for new drugs primarily in the area of cancer treatment. Other compounds are currently being developed as an analgesic (ziconotide from the mollusc Conus magus) or to treat inflammation. Numerous natural products from marine invertebrates show striking structural similarities to known metabolites of microbial origin, suggesting that microorganisms - bacteria, microalgae - are at least involved in their biosynthesis.

The PharmaSea will not only be exploring new territory at the bottom of the oceans, but also new areas in 'chemical space'. "With our broad platform of cutting-edge bioassays to detect drug-like activity, we'll be testing many unique chemical compounds from these marine samples that have literally never seen the light of day. We're quite hopeful that we'll find a number of exciting new drug leads," says Dr. Camila Esguerra, Industrial Research Fellow and Lecturer with the Laboratory for Molecular Biodiscovery at the University of Leuven in Belgium. Marine organisms that live more than 2 000 metres below sea level are considered to be an interesting source of novel bioactive compounds as they survive under extreme conditions. "Trenches are separated from each other and represent islands of diversity. They are not connected to each other and life has evolved differently in each one," explains Jaspars.

The international team will employ strategies commonly used in the salvage industry to carry out sampling. Using fishing vessels, researchers will drop a sampler on a reel of cables to the trench bed in order to collect sediment. Scientists will then attempt to grow unique bacteria and

fungi from the sediment that can be extracted to isolate novel drug-like molecules for pharmacological testing. Partners from China, Chile, Costa Rica, New Zealand and South Africa will also support the PharmaSea project. The first field tests will be carried out next autumn in the Atacama Trench in the Eastern Pacific Ocean, off the coast of Chile and Peru. The team will also search the Arctic waters off Norway and the Antarctic with Italian and South African partners. Deep trenches will also be accessed off New Zealand and China.

"We're quite hopeful that we'll find a number of exciting new drug leads," says Jaspar. The team hopes that the drugs they discover will be ready for patient use in ten years, if all goes well. This will help tackle the issue of bacterial infections, from which some 25 000 EU citizens die from every year.

More information: For more information, please visit:

PharmaSea
www.pharma-sea.eu

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