Drug discovery: going with the tide

Mechanisms of both offence and defence are in a process of constant evolution in the world of microbes. Thus, Flemming's observation of this warfare in an abandoned petri dish led to the discovery of penicillin, which marked the onset of the era of antibiotics. Most of the currently used antibiotics are derived from limited molecular frameworks whose effective lives have been stretched by synthetic modifications of the molecules[1]. Prolonged and indiscriminate use of such antibiotics with limited structural diversity has resulted in bacteria developing antibiotic resistance genes (resistomes), culminating in the appearance and spread of multiple drug resistant (MDR) pathogens[2–4]. To control MDR pathogens, it is essential to look for new molecular structures with antibiotic properties. Here, natural products research is imperative because combinatorial chemistry has fallen short of our hyped expectations of it[5,6]. In this context, screening microbes from unexplored and little-studied ecological niches for novel metabolites appears to be a promising exercise[1].

Among such organisms marine fungi associated with sponges, corals, seaweeds, mangroves, marine detritus, tunicates, fish, seagrass, marine sediments, etc. appear to be prolific producers of molecules of unprecedented structures with potential pharmaceutical importance[7–10]. Many nations have realized the potential of marine fungi as a source of remarkable chemical diversity and several pharmaceutical companies are screening these organisms for novel metabolites, including enzymes[8]. For example, a marine *Aspergillus* species associated with a marine alga collected from Korea has yielded novel antibiotics effective against methicillin-resistant *Staphylococcus aureus*[11]. Marine fungi from various countries including Australia, the Caribbean island of Dominica, China, Egypt, Hong Kong, Korea, Japan, the Republic of Palau and Thailand are being routinely screened for antibiotics, anticancer and antidiabetic compounds[12]. Bioassay-guided studies from our laboratory have indicated that endophytic fungi associated with mangroves and marine algae from the coast of Tamil Nadu produce antibacterial, antifungal and antioxidant chemicals[13]. The crude culture extracts of one marine fungus associated with a sponge inhibited the growth of cancer cells in culture by breaking down microtubules (Figure 1).

Hence, there is an urgent need for studying marine fungal ecology coupled with biodiscovery, involving our national laboratories and industries. Marine fungi of India, being an untapped genetic resource, if subjected to modern methodologies such as automated separation and structure analyses, metabolic engineering and manipulation of genes to alter synthetic pathways are expected to pay rich dividends[14,15].

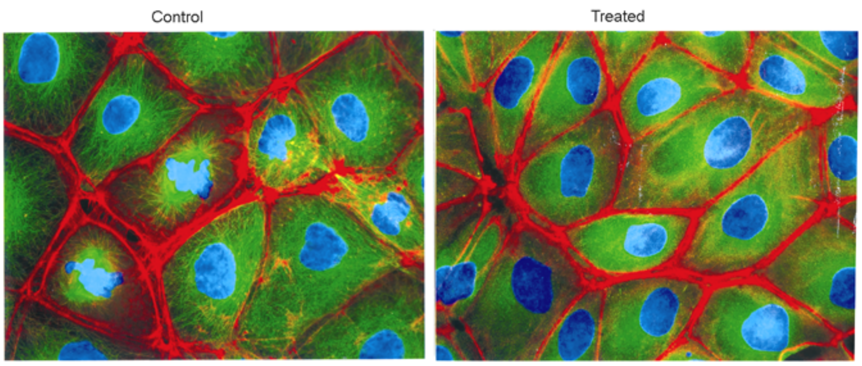

Figure 1. Effect of culture extract of a fungus VIG 501 (isolated from a marine sponge off Mandapam, Tamil Nadu) on potoroo kidney cell line PtK2. Note absence of nuclear division and loss of microtubules (strained green) in treated cells.

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