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A research pipeline for the discovery of bioactive small molecules with anti-aging activity from the Marine Mesophotic Zone

In the frame of TASCAR more than 180 existing collection of invertebrates (MACLIB library) and 179 targeted marine invertebrates species (TARMAC library) were collected from the under-investigated mesophotic zone (between 30 and 100 meters depth) of the Indian ocean, the Red sea and the Mediterranean. Furthermore, more than 300 (MICLIB library) and 312 (TARMIC library) associated microorganisms of MACLIB and TARMAC libraries respectively, were collected. The samples were extracted and libraries of extracts were sent for biological evaluation. According to the results for MACLIB library, 5.30% of the extracts showed elastase and tyrosinase inhibitory activity, 7.94% inhibition to Fyn kinase, 6.35% to proteasome and 4.76% to CDK7 kinase. For TARMAC library 16.3% of the extracts showed tyrosinase inhibitory activity, 12.4% elastase inhibitory activity, 5.03% to FYN kinase, 15.64% to CDK7 kinase and 20.67% to proteasome. All active extracts were investigated for their chemical profiling employing UHPLC-HRMS techniques and the metabolites present in each extract were identified using molecular networks, in silico fragmentation and classical dereplication techniques based on databases. Selected extracts were fractionated and a library of fractions has been forwarded for bio-evaluation. From the active fractions compounds of interest have been isolated and identified by NMR and LC-MS. Furthermore, the biological activity of the associated microorganisms was examined. For MICLIB library, the microorganisms showed 0.5% inhibition activity to tyrosinase and elastase, 0.9% to Fyn kinase, 6.67% to CDK7 kinase and 1.67% to proteasome. For TARMIC extracts, ~80.1% were found to inhibit tyrosinase activity, 22.8% showed elastase inhibitory activity, 14.19% to FYN kinase, 7.67% to proteasome and 7.43% to CDK7 kinase. Finally a comparison between the LC-MS profiles of the invertebrate extracts and the profiles of the microbial symbionts was performed showing overlapping of 4 to 14% indicating the contribution of microorganisms to the whole invertebrate metabolome.

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