Exploiting the Greek microbial diversity for the discovery and development of novel antiaging molecules.

Konstantinos Gaitanis[1], Nikolaos Tsafantakis[1], Eirini Gkogkou[2], Despoina D. Gianniou[2], Stavroula Kaili[3], Paris Laskaris[3], Georgia Ntroumpogianni[3] Evangelia Tsiokanos[1], Dimitris Hatzinikolaou[3], Ioannis P. Trougakos[2], Amalia Karagouni-Kyrtsou[3], Nikolas Fokialakis[1]

1 Section of Pharmacognosy & Chemistry of Natural Products, Department of Pharmacy, National and Kapodistrian University of Athens, Panepistimiopolis Zografou 15771, Athens, Greece; 2 Section of Cell Biology and Biophysics, Department of Biology, Panepistimiopolis Zografou 15784, Athens, Greece; 3 Section of Botany, Department of Biology, Panepistimiopolis Zografou 15784, Athens, Greece.

Actinobacteria from Greek ecosystems are renowned for producing bioactive compounds. To this purpose, the "AntiAging" project sought to uncover new, promising natural compounds with anti-aging properties, which could be incorporated into cosmeceutical/nutraceutical formulations. Herein, 1000 isolates originating from the Greek natural environment and belonging to the ATHUBA collection (Athens University Bacterial & Archaea Culture Collection), were investigated. A unique library of ~2000 extracts (EtOAc and MeOH/H2O) was generated, and the tyrosinase and elastase inhibition activity was evaluated via enzymatic assays. Out of the top 100 extracts with the highest inhibitory activity, 28 were found to be non-cytotoxic when tested on cell-based assays. Those extracts were then analyzed by HPLC-DAD-ELSD and UPLC-HRMS. The top 3 microbial strains, belonging to *Amycolatopsis* sp. and *Streptomyces* sp. families, were subsequently grown using four different cultivation media. The most promising cultures were subjected to a scale-up process (2L) and fractionation, and their bioactivity was further assessed. A customized bio-guided workflow was then applied, combining a high-throughput dereplication and molecular networking method (UPLC-HRMS), along with the bioactivity of each fraction. To meet the requirements of the isolation procedure, the microbial strain M43B was subjected to an 8L cultivation, extracted with EtOAc and fractionated using Sephadex® LH-20. The purified molecules were characterized by an extensive analysis of NMR and HRMS spectra data and will be further evaluated for their antioxidant activity, the proteasome activation and their impact on longevity of *in vivo* models (*Drosophilla* sp.). Our ultimate goal is the targeted identification and isolation of bioactive compounds, which can be integrated into cosmeceutical formulations. The plethora of identified molecules highlight the significant potential for exploiting Greek microbial diversity in the realm of anti-aging research.

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