"Anti-Aging": Exploiting the Greek microbial diversity for the discovery and development of novel antiaging molecules.

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Greek ecosystems are a fertile yet under-explored ground for the study of Actinobacteria, known producers of bioactive compounds. By exploring this under-investigated biodiversity and chemodiversity of Greek actinobacterial strains (mostly of *Streptomyces* sp.), the "Anti-Aging" project aims to uncover potentially novel natural compounds with anti-aging activity, that can be formulated as cosmeceutical products. In total, 1000 isolates belonging to the Athens University Bacterial & Archaea Culture Collection were studied. A customized *in-house* library of 2000 extracts was generated (EtOAc and MeOH/H_2O), all of which were investigated for potential anti-aging properties. This biological evaluation was performed though elastase (anti-aging activity) and tyrosinase (whitening activity) inhibition *in vitro* assays. A small yet significant number of extracts demonstrated >50% elastase inhibitory activity, whereas a considerably larger number exhibited >50% tyrosinase inhibitory action. Interestingly, in some cases the bioactivity exceeded 80% in *in vitro* assays. The biological properties of ~100 non-cytotoxic extracts were also tested on human diploid fibroblasts (BJ) for their anti-aging activity, and on melanocytes (B16F10) for their whitening activity. Fractions (~120) of the most active, non-toxic extracts tested for elastase and tyrosinase inhibition activities in cell-free and cell-based *in vitro* assays. The most promising highly active fractions were subjected to compound isolation and bioactivity assessment. Isolated compounds tested for their ability to activate cyto-protective mechanisms in cell-based assays, while their anti-aging effects also tested in *in vivo Drosophila melanogaster* models, for their ability to induce antioxidant mechanisms through activation of the Nrf2/cncC transcriptional factor. Our promising results show a hidden yet powerful potential of harnessing Greek microbial wealth in the context of anti-aging.

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