Microalgae carotenoids induce apoptosis and chemosensitization of human melanoma cells to vemurafenib and dacarbazine

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Melanoma is an aggressive tumor with invasive and metastatic potential, frequently exhibiting multidrug resistance. A large number of studies established that plant and algae carotenoids have great potential as natural anti-melanoma compounds as they exert cytotoxic, cytostatic, antimetastatic, anti-inflammatory and antiangiogenic activities. Fucoxanthin, an epoxycarotenoid purified from brown algae inhibits melanoma cells and tumor growth *in-vitro* and *in-vivo*. It also limits melanoma metastasis in murine models, suggesting that it also has clinical efficacy in humans. In the continuity of this work, we addressed the question of whether microalgae carotenoids could have the interest to sensitize cancer cells to conventional anticancer drugs used in clinical chemotherapy. In a first step, a panel of marine microalgae was selected to identify cytostatic pigments inhibiting melanoma cells proliferation. These pigments were then used in combination with anti-melanoma drugs to determine if they could potentiate their cytotoxic activity or restore the sensitivity of melanoma cells to these drugs. All pharmacological assays were performed on A2058 cells expressing the oncogenic B-RAF V600E mutation and resistant to dacarbazine treatment. We show that several microalgae pigments extracts induce significant growth inhibition at 100µg.mL^{-1}. The cryptophyte *Rhodomonas salina* was further selected for purification of carotenoids with anti-melanoma and chemosensitizing activities. Flash chromatography of R. *salina* ethanol extract led to the purification of two carotenoids (alloxanthin and crocoxanthin) never tested for anticancer activity. Alloxanthin and crocoxanthin showed moderate antiproliferative activity against A2058 cells, exhibiting IC_{50} of 29 and 50µM respectively. These carotenoids promoted growth inhibition, decreased cell migration and induced apoptosis and sub-G1 cells accumulation after 72h of treatment. In addition, alloxanthin potentiated the cytotoxic activity of vemurafenib (a B-RAF inhibitor) and restored the sensitivity of A2058 cells to dacarbazine treatment. These outcomes encourage the use of classic anticancer drugs combined with microalgae carotenoids to improve their efficiency in melanoma treatment.

Biography: Laurent Picot is Professor Assistant in Biochemistry at the department of Biotechnology, La Rochelle University, France. He holds a Ph.D. in Microbiology and a Professional Habilitation in Biochemistry. He teaches marine pharmacology, biotechnology, microbiology, and immunology. His research activity deals with the isolation and study of anticancer natural products from various sources including phytoplankton and terrestrial plants. He has expertise with extraction, purification, high-resolution molecular characterization and pharmacological assessment of natural pigments and synthetic anticancer drugs. He has been involved in various national and international research projects dealing with microalgae pigments, marine pharmacology, and natural products from Brazilian plants. He is currently Associate Editor of Marine Drugs.

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