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in the Prenylation Pathway, consisting on methylation of the newly generated C-terminus on the cysteine. This modification regulates critical functional aspects of substrate proteins among which there are several members of the Ras and Rho GTPases families. ICMT has emerged as an interesting target for novel anti-cancer therapies. We have previously shown that *ICMT* is repressed by the p53 tumor suppressor and that its overexpression enhances tumor development and metastasis. Moreover, breast and lung cancer patients with elevated *ICMT* expression showed a significant reduction in survival. In order to identify novel ICMT inhibitors we generated a collection of Farnesylthiosalisilic acid (FTS) derivatives. This molecule, commercially known as Salirasib, was reported to inhibit ICMT and has recently reached clinical trials for the treatment of Non-Small Cel Lung Carcinoma (NSCLC). Starting with an initial collection of 27 compounds, we showed that the presence of long chain substituents was related to enhanced antiproliferative activity. We concentrated on three molecules showing higher activity and predicted to bind ICMT more strongly than Salirasib. We further characterized the effect of these candidate molecules and found structural features associated with a specific antiproliferative effect against tumor cells. We analyzed cell cycle alterations by flow cytometry and apoptosis induction by annexin V staining. In order to gain insight into the mechanisms activated by these compounds we studied their effect on MAPK and AMPK pathways through western blot with phosphospecific antibodies. In addition, we found a remarkable increase in antiproliferative activity under serum deprivation conditions. To understand the mechanisms underlying this enhanced sensitivity, we analyzed if AKT-mTOR inhibition may be responsible for the effect. We also studied if selected compounds affect the function of ICMT substrates, such as Rho GTPases. We analyzed their effect on Rac1 subcellular localization by immunofluorescence and confocal microscopy. Collectively, our results allowed us to identify a structural backbone with enhanced and specific antiproliferative activity in cancer cells.

ST-15

PHYTOHORMONE AND MOLECULAR ANALYSIS OF POTATO PLANTS INOCULATED WITH Methylobacterium sp. 2A AND INFECTED WITH Phytophthora infestans

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Methylobacterium sp. 2A is a plant growth-promoting rhizobacteria (PGPR) that was isolated from potato roots. This isolate can antagonize plant pathogens and reduce disease symptoms in potato plants infected with *Phythophthora infestans*. In this work, we aim to understand if the inoculation with *Methylobacterium* sp. 2A enhances plant defense in potato plants through an induced systemic resistance (ISR) or by direct antagonism with the pathogen. To this end, potato plants grown on solid MS for 10 days were inoculated with 25 µl of a suspension of *Methylobacterium* sp. 2A cells (0.05 OD_{600} units in 0.85% NaCl, I) or with 0.85% NaCl (control, C). These plants were allowed to grow in vitro and at day 21 were transferred to pots. Three weeks later, 2 leaves/plant were either treated with 2 drops of a *P. infestans* suspension (10 µl/drop, 50 zoospores/µl; Pi plants) or with 2 drops of sterile distilled water (10 µl/drop; control plants). At 2- and 5-days post-infection (dpi) infected and distal leaves (IL, DL) from the 4 conditions (C, I, Pi, I+Pi) were collected to conduct expression analysis. *EF-1α* was used as a reference gene. In the Pi IL, the expression of *chitinase* was induced at 2 dpi, and *StPAL1, StPR1-b, StPR2*, and *StCDPK2* were enhanced at 5 dpi. The induction of *chitinase, StPAL1, StPR1-b*, and *StCDPK2* was significantly lower when the IL were previously inoculated with *Methylobacterium* sp. 2A (I+Pi). In addition, phytohormone analysis was performed by UPLC-MS/MS in different sets of *in vitro* grown potato plants (5 biological replicates, 2 technical replicates). Whole-plant samples of 12 days old plants were collected 48 h post-inoculation with *Methylobacterium* sp. 2A (I) or with distilled water (control, C). At day 21 another set of C and I plants were infected with *P. infestans* (Pi and I+Pi) as described above. At 3 dpi, whole-plant samples were collected from the four treatments (C, I, Pi, I+Pi; n = 10 plants per treatment). In *Methylobacterium* sp. 2A-inoculated samples, MeJA increased at 48 hours, and this increase remained constant even at 14 days post-inoculation while an increase in indole-3-acetic acid (IAA) and jasmonic acid (JA) content was observed at 14 days post inoculation. On the other hand, a significant increase in salicylic acid concentration was observed after infection with *P. infestans*. Finally, potato plants grown on solid MS for 21 days in which the plant-*Methylobacterium* sp. 2A interaction was already established (I) and control (C) plants were harvested. Total RNA was obtained from root or shoot samples from I and C plants (two replicates each) and sent to Novogene for RNA-seq analysis. We compared the expression of roots vs. shoots and of I vs. C. We identified 98 differentially expressed genes (DEGs) in roots and 17 DEGs in shoots; 81 of the genes expressed in roots were induced upon inoculation with *Methylobacterium* sp. 2A and 18 of them correspond to heat-shock proteins. Our results show that the inoculation with *Methylobacterium* sp. 2A modulates gene expression and phytohormone levels in potato plants.

ST-16

DECIPHERING THE MECHANISM OF QUERCETIN-INDUCED CELL DEATH IN ENDOTHELIAL CELLS TRANSFORMED BY VIRAL G PROTEIN-COUPLED RECEPTOR EXPRESSION

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Quercetin (QUE) is a natural flavonoid classified as a phytoestrogen due to its resemblance with human estrogens. Although its anticancer properties are well-known in various cancer models, its effect on viral-induced cancers has been less studied. Kaposi's sarcoma (KS) is a virally induced cancer caused by Kaposi's sarcoma-associated herpesvirus, which contains a constitutively activated viral G protein-coupled receptor (vGPCR) expressed during the viral lytic phase, leading to oncogenesis and angiogenesis through the activation of several signaling pathways. Our previous studies indicated that QUE inhibits vGPCR-mediated cell proliferation in vitro and tumor growth in vivo. In this work, we investigated the mechanism by which QUE exerts its antitumoral effects. QUE treatment (30 µM) for 24 h induced marked morphological changes in vGPCR cells consistent with apoptosis, including cell shrinkage and the formation of apoptotic bodies, as observed by scanning electron microscopy. In parallel experiments, a highly significant increase in cleaved caspase-3 protein levels was detected by Western blot analysis, further confirming apoptotic induction. To investigate oxidative stress, vGPCR cells were treated with QUE (5-45 µM) for 24 h or hydrogen peroxide (0.5 mM, 45 min) as a positive control, and intracellular oxidant levels were measured using the fluorogenic probe 2′,7′-dichlorofluorescin diacetate. QUE treatment led to a concentration-dependent increase in oxidant levels. Additionally, lipid peroxidation levels, evaluated by TBARS assay, were significantly increased by QUE (30 µM). Moreover, comet assay analysis of vGPCR cells treated with QUE (30 µM) for 48 h indicated a significant increase in DNA damage, evidenced by longer comet tails. Further exploration of signaling pathways by Western blot revealed that QUE (10-50 µM) for 48h increased p38 and ERK1/2 phosphorylation, whereas AKT phosphorylation remained unchanged. In conclusion, our findings suggest that QUE-induced oxidative stress and DNA damage may lead to apoptosis, with concurrent activation of stress-responsive signaling pathways (p38 and ERK1/2) potentially serving as adaptive responses to mitigate QUE's cytotoxic effects.

BIOTECHNOLOGY

BT-2

EFFECT OF MELATONIN ON THE PHYSIOLOGICAL PROPERTIES OF *Rhodococcus* sp. F27

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Various microorganisms are valuable tools for addressing environmental contamination. Our research focuses on the development of bioproducts containing environmental bacteria for the removal of petroleum compounds. In the formulation of these bioproducts, selected bacteria can be combined with various substances to stimulate their growth and/or enhance physiological properties of interest. The objectives of this study were: (1) to assess the effect of melatonin (an indoleamine) on the growth and auto-aggregation capacity of *Rhodococcus* sp. F27 (F27), and (2) to determine the influence of different concentrations of melatonin on the removal of aromatic petroleum compounds. *Rhodococcus* sp. F27 cultures were grown in LB broth with varying concentrations of melatonin (0, 21.5, and 64.6 µM) at 30°C with shaking (180 rpm) for 48 h. Growth was assessed by counting colony-forming units on agar plates and measuring optical density at 600 nm. After 48 h of incubation, bacterial auto-aggregation was measured in saline using spectrophotometry. For the second objective, F27 was activated in LB with different concentrations of melatonin (0, 21.5, and 64.6 µM), and each subculture was used as an inoculum in JPP medium supplemented with polycyclic aromatic hydrocarbons (PAH: acenaphthene, fluoranthene, and pyrene, 0.2 mM each) and dibenzothiophene (DBT, 0.2 mM), along with different concentrations of melatonin (0, 21.5, and 64.6 µM). Cultures were incubated for 7 days at 30°C with shaking (180 rpm). The concentration of PAH and DBT was quantified by HPLC. Results were statistically analyzed using a general linear model ANOVA. Melatonin did not significantly affect the growth of *Rhodococcus* sp. F27. A slight increase in CFU/mL was observed after 48 h of incubation in LB with 21.5 and 64.6 µM melatonin compared to the control. In contrast, melatonin concentration of 21.5 µM significantly enhanced the formation of bacterial auto-aggregates. Moreover, the highest removal of acenaphthene and DBT was observed in JPP with 21.5 or 64.6 µM melatonin, respectively, using an inoculum prepared in the absence of melatonin. The removal of fluoranthene and pyrene by F27 was negligible under all conditions tested. In conclusion, the presence of melatonin primarily enhanced the auto-aggregation of *Rhodococcus* sp. F27 and had a beneficial effect on the biological removal of acenaphthene and DBT. Both *Rhodococcus* sp. F27 and melatonin show promise for inclusion in eco-friendly bioproducts for the bioremediation of petroleum-contaminated environments.