



Department of Biotechnology
Ministry of Science and Technology
Government of India

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DAILAB

Classroom for Advanced & Frontier Education
CAFE

Series - 49

Date & Time: August 03, 2020 (3:00 PM JST)
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Title: Resveratrol causes protection against cellular stress and induces differentiation in cancer cells - Implications for its use in stress and cancer management

Increasing bio-insults of environmental stressors, exhaustive industrialization and chemical use in daily lives has contributed to rapidly increasing number of stress-related diseases (cancer, neurodegenerative disorders, or premature aging). We have seen several milestone developments in anticancer pharmaceuticals in the previous few decades, yet they are limited with severe shortcomings, such as (i) extreme unaffordability, (ii) poor availability, (iii) severe adverse effects and (iv) development of drug resistance. Owing to these reasons, the world urgently requires a parallel setup to develop newer strategies to prevent such diseases, with natural, economic and welfare (NEW) medicines as both mainline and supporting regimens. Especially in case of brain cancers, when the conventional anticancer techniques (surgery, radio- and chemotherapy) to resect the cancer tissue are contraindicated, reprogramming these 'cancer' cells to their 'physiological' forms may prove to be an attractive solution. With this aim, we recruited glioma and neuroblastoma cells, and subjected them to various stresses to mimic the regular stressful situations. Using cell-based, biochemical and advanced imaging assays, we show that the non-toxic doses of resveratrol, a naturally occurring stilbenoid, protected these cells against cellular stresses that are largely involved in age-related brain pathologies (oxidative, DNA damage, metal toxicity, heat, hypoxia and protein aggregation). It also caused differentiation of these cells to functional astrocytes and neurons as characterized by their functional phenotype and changes in the expression of specific proteins. These findings endorse (i) development of differentiation inducing techniques to be implemented in cancer clinics, and (ii) multiple bioactivities and benefits of resveratrol to be tested in animal models and humans.