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INFLUENCE OF THE BACTERIAL PIGMENT PRODIGIOSIN ON THE CYTOSKELETON OF CANCER AND NORMAL CELL LINES *

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Abstract

Cancer cells are known for their uncontrolled growth and ability to invade surrounding tissues. One promising area of research in cancer treatment is the use of the pigment prodigiosin, produced by the bacteria *Serratia marcescens*, due to its selective effect. In our work, we showed that prodigiosin at a concentration of 1–5 μg/ml disrupts the cytoskeleton of cancer cells without affecting normal cells.

In recent years, there has been an increase in research in the field of practical application of prodigiosin (PG), mainly devoted to its production, as well as its antimicrobial and anticancer potential. PG has some advantages in the biomedical field, for example, the selective activity against cancer cells was identified recently, but exact mechanism of this phenomenon remains unclear. The therapeutic use of PG requires systematic preclinical and clinical studies. It is known about a number of clinical trials of the anticancer drug obatoclax, which is a derivative of PG. Several phase II clinical studies have been completed examining the use of obatoclax in the treatment of leukemia, lymphoma, myelofibrosis and mastocytosis. Currently, there are no clinical trials being conducted, but there has been a growing interest among researchers in studying the various therapeutic properties of PG. One of the possible mechanisms of the selective action of PG on cancer cells is damage to the cytoskeletal elements in these cells, which have a higher proliferation rate compared to surrounding normal cells.

In our work, we used a simple method for modeling the microenvironment of a cancer tumor by forming a mixed culture based on a human hepatoma cell line (HepG2) and fibroblasts (HSF). Co-cultivation of the cells continued until a complete monolayer was achieved and clear, visually distinguishable islets of cancer cells surrounded by fibroblasts were formed. Additionally, HepG2 cells were labeled with the membrane dye Dil. Prodigiosin was added in DMSO solution to a final concentration of 1, 2,5 and 5 μg/ml. After 24–48 h of incubation, cell viability was studied using the LIVE/DEAD double staining method and the cytoskeleton was visualized using FITC-conjugated phalloidin. Using fluorescence microscopy, it was revealed that even at a concentration of 1 μg/ml, the cytoskeleton structure in HepG2 cells was disrupted, while in fibroblasts it retained its native structure. At the same time, this concentration had virtually no effect on the viability of both normal and malignant cells. At a concentration of 2,5 and 5 μg/ml, 70–90 % of HepG2 cells died and the cytoskeleton of the remaining cells in the monolayer was fragmented. Fibroblasts retained their morphology and cytoskeleton structure, but at a concentration of 5 μg/ml, the number of viable fibroblasts decreased to 50 %. Prodigiosin lead to disorganization of the nucleus structurecas well as vacuolization and reducing the cytoplasm volume in HepG2 cells. At the same time HSF nuclei remain normal morphology, while slight vacuolization observed. Thus, vitro anticancer effects of PG were manifested in the suppression of HepG2 cells proliferation, followed by alteration of cell morphology and F-actin structure disorganization.

The ability of prodigiosin to impact the cytoskeleton in cancer cells without affecting normal cells holds great promise for cancer treatment. By specifically targeting the cytoskeleton, prodigiosin could serve as a novel therapeutic approach for inhibiting cancer cell growth and metastasis. Furthermore, the selectivity of prodigiosin for cancer cells could reduce the side effects commonly associated with traditional cancer treatments. In conclusion, prodigiosin's unique mechanism of action in targeting the cytoskeleton of cancer cells while sparing normal cells represents a significant advancement in cancer research. By understanding how prodigiosin affects the cytoskeleton and its differential impact on cancer cells and normal cells, researchers can explore new avenues for developing more effective and targeted cancer treatments.

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