ABSTRACTS OF 7th International and 9th National IASBS Symposium on Biological Sciences

May 6 & 7, 2025

Institute for Advanced Studies in Basic Sciences, Zanjan, Iran

Scientific committee:
Dr. Maryam Rouhani, Dr. Shiva Akbari-Birgani and Dr. Mohammad Masoudi

General chair:
Dr. Mohammad Masoudi

Invited speakers:
Dr. Shumpei Ishikawa (The University of Tokyo)
Dr. Giulia Biffi (University of Cambridge)
Dr. Bidyut Roy (Indian Statistical Institute, Kolkata)
Dr. Emilio Hirsch (University of Turin)
Dr. Maryam Rouhani (Institute for Advanced Studies in Basic Sciences)
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Institute for Advanced Studies in Basic Sciences
Gava Zang, Zanjan, Iran

7th International and 9th National IASBS Symposium in Biological Sciences

Cancer: Molecular Cell Approach

Major Topics

- Cancer Biology
- Cancer Metabolism
- Tumor Microenvironment
- Cancer Genomics and Informatics
- Cellular Mechanotransduction Systems

Invited Speakers

Conference website
https://iasbs.ac.ir/~biosymp/1404/

Tuesday May 6, 2025		
9:30-10	Opening	
10-10:45	Talk session 1 (Dr. Shiva Akbari-Birgani) (in Persian) Development of Brest Cancer Organoid Models for Basic Research and Drug Resistance Studies	
10:45-11:30	Poster session	
11:30-12:15	Talk session 3 (Dr. Mohammad Masoudi) (in English) In search for new treatments for	
12:15-13	Talk session 4 (Dr. Giulia Biffi) (in English) (Online) Distinct Genetics differentially shape Malignant cell-Stromal cell Crosstalk in Pancreatic Cancer	
13-14:30	Lunch time	
14:30-15:15	Talk session 5 (Dr. Shumpei Ishikawa) (in English) (Online) Diversity of Gastric Cancer Genome Profiles and Characteristics of Asian East Gastric Cancer	
15:15-16:30	Poster session	
16:30-17:15	Talk session 7 (Dr. Bidyut Roy) (in English) (Online) Genetics of Birt-Hogg-Dube syndrome: Indian Patients	
Wednesday May 7, 2025		
9:30-10:15	Talk session 8 (Dr. Maryam Rouhani) (in Persian) Sensitizing breast cancer cell lines to radiotherapy and chemotherapy by targeting the GSK-3 beta protein	
10:15-11	Talk session 9 (Dr. Hossein Ammarlou) (in Persian) Question and Answers about clinical features of	
11-11:30	Poster session	
11:30-12:15	Talk session 10 (Dr. Emilio Hirsch) (in English) (Online) Unexpected roles of phosphoinositides in cytokinesis and cancer progression	
12:15-14	Lunch time	
14-14:30	Best Poster presentation	
14:30-15	Closing	

On-site Registration for Attendees is Available

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ABSTRACT **Open Access**

7th International and 9th National IASBS Symposium on Biological Sciences
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Studying the effect of differentiation inducing factor-3 on the repair of doxorubicin-induced DNA damages in MDA-MB-231 breast cancer cell line

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Breast cancer is the most common diagnosed malignancy and, is the main cause of cancer-related mortality among women. The biological characteristics of the tumors frequently determine the treatment strategy of breast cancer. Four main subtypes are luminal-A, luminal-B, human epidermal growth factor receptor 2 (HER2)- enriched, and triple-negative Breast Cancer (TNBC). Despite significant advances in the development of effective targeted treatments for TNBC patients, chemotherapy remains the primary therapeutic option but this method of cancer treatment has its own side effects and cancer cells usually become resistant to chemotherapeutic agents. Doxorubicin, one of the anthracycline chemotherapy drugs, inhibits topoisomerase II activity and also causes DNA damages and thereby induces apoptotic cell death. Differentiation-inducing factors (DIFs) discovered in Dictyostelium discoideum have antiproliferative and anti-tumor effects on mammalian cells. In current study, the effects of DIF-3 on the sensitivity of MDA-MB-231 cells to Doxorubicin was investigated by clonogenic assay. Additionally, the damage and repair of doxorubicin-induced damages was compared in the present and absence of DIF-3 by using alkaline comet assay. The RT-qPCR technique was also used to measure the expression level of Mre11, which is a sensory protein in the MRN complex that helps repair of DNA double- strand breaks. The results showed that DIF-3 made MDA-MB-231 cells more sensitive to doxorubicin and inhibited the repair of doxorubicin-induced DNA damages, probably by decreasing the expression of Mre11 protein.

Keywords: Breast cancer; Differentiation-inducing factor-3; Doxorubicin; DNA double-strand breaks; DNA Repair system

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ABSTRACT **Open Access**

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Cytotoxic effect of the *Zygnema* green algae extract on MDA-MB-231 breast cancer cell line

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The most effective cancer treatment, namely chemotherapy, still has various side effects such as nausea, hair loss, pain, fatigue, and diarrhea. In the long term, these symptoms can harm the patient's quality of life and put them at risk of death. Therefore, algae are one of the richest plant sources of bioactive compounds. Algae contain various secondary metabolites that have biological activity and have the potential to be used as drugs and antioxidants, as well as anticancer, antibacterial, anti-inflammatory, and antiviral agents. This study was conducted to determine the anticancer activity of the methanolic extract of Zygnema green algae in the MDA-MB-231 breast cancer cell line and determine the level of antioxidant activity. Methanolic extract of Zygnema algae was prepared by solvent soaking method and cytotoxicity against breast cancer cells was investigated using the MTT method. Antioxidant activity was evaluated based on DPPH free radical scavenging. According to the MTT results, the cytotoxicity and cell lethality increased with increasing concentration, so that the highest cytotoxicity of methanolic extract of algae was obtained at a concentration of 1000 µg/ml with a lethality percentage of 24% and IC50 equal to 193 µg/ml on breast cancer cells. Also, the antioxidant activity of the methanolic extract of algae showed a direct relationship with increasing extract concentration. Further studies are needed to investigate the effectiveness of the bioactive compounds of this algae in breast cancer cells to definitively state that this algae is a suitable candidate for anticancer drugs.

Keywords: Antioxidant; Breast Cancer; Bioactive Compounds; Cytotoxicity; Green Algae

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ABSTRACT **Open Access**

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Investigating the Relationship Between *Caspase-8* and *RIPK1* Genes in Colorectal Cancer Patients

Tina Abdollahi[a], Hanieh-Sadat Mostafavi-Fini[b], Farzaneh Kashef, Mohammad Fazel Mollaverdi , Zahra Zakhmi-Alishah, Zahra Ghasemi, Shahla Mohammad Ganji*

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Necroptosis is a non-apoptotic form of cell death that occurs non-programmed, involving several key genes and proteins. Necroptosis occurs in some diseases, including cancer and inflammatory diseases, and may contribute to the progression or tissue damage. Necroptosis in cancers may contribute to the progression, inhibition, or resistance of cancer apoptosis. *RIPK1* is a kinase involved in the initiation of necroptosis in cancer cells. *RIPK1* activates the necroptosis pathway by binding to death receptors. *Caspase-8*, with a significant role in apoptosis, can, under certain conditions, help inhibit necroptosis. Inhibition of *Caspase-8* can lead to activation of the necroptosis pathway. This study aimed to investigate the relationship between the *Caspase-8* and *RIPK1* genes in patients with colorectal cancer and their association with necroptosis and patient survival. In this study, tumor and adjacent tumor samples were taken from 40 patients with colorectal cancer referred to the Cancer Institute of Imam Khomeini Hospital. They were unrelated, had no family history of cancer, didn't receive any treatments, and their CRC was not due to metastasis of other cancers. Samples were transferred to the laboratory under cold chain conditions. Informed consent and relevant questionnaires were completed, and the code of ethics was obtained. Real-time PCR was performed for *RIPK1*, *Caspase-8*, and *β-actin* genes. The results were analyzed using REST and SPSS software, and statistical tests, such as the t-test and one-way ANOVA, were employed. The results showed that 72% of the patients were over 50. The sample consisted of 52% females and 48% males, and 84% had experienced a weight loss of more than 5 kg. In tumor samples, the expression level of the *RIPK1* gene increased by 3.5 times compared to adjacent tumor tissues, while the expression level of the Caspase8 gene decreased by 50% ($P < 0.05$). The results also showed a significant relationship between the expression level of these genes and the stage of the disease ($P < 0.05$), as well as the N factor ($P < 0.05$). The inhibition of *Caspase-8* and increased expression of the *RIPK1* gene in this study can indicate that necroptosis has occurred in the patients studied. This inhibition can aid in cancer progression and serve as a marker for prognos

Keywords: *RIPK1; Caspase-8;* Necroptosis; Colorectal Cancer

*a and b authors have equal roles in this research.

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ABSTRACT **Open Access**

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Dual Blockade of EGFR/NFkB and TNF/NFkB Pathways in Triple-Negative Breast Cancer: A Potential Therapeutic Strategy

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Breast cancer has become the leading cause of cancer-related deaths among women worldwide. Although triple-negative breast cancer (TNBC) rarely occurs, it is one of the hardest types to treat due to its aggressiveness and heterogeneity. TNBC tumors do not overexpress estrogen, progesterone, or HER2 receptors; thus, receptor-targeted therapies are ineffective. The only available treatment is chemotherapy. However, resistance to chemotherapy often occurs, leading to tumor recurrence, attributed to several factors. Among the most critical mechanisms are growth factors and inflammatory elements derived from cancer cells and the tumor microenvironment. Epidermal growth factor (EGF) and tumor necrosis factor (TNF) are two major factors responsible for activating signaling pathways associated with cell proliferation and inhibition of apoptosis, conferring resistance to chemotherapy. In this study, we demonstrated that dual blockade of EGFR and TNF pathways increased TNBC cell sensitivity to the chemotherapeutic drug doxorubicin and significantly inhibited cancer cell growth and proliferation. To understand the underlying mechanism, we analyzed the related protein-protein interaction (PPI) network and identified NFκB as the key downstream hub regulating cell cycle proteins. Targeting NFκB through EGFR inhibition with panitumumab and TNF inhibition with infliximab led to cell cycle arrest and apoptosis, even when treated with doses of doxorubicin far below its IC50. Our findings suggest that simultaneous targeting of EGFR and TNF pathways offers a promising therapeutic strategy for patients with aggressive and poor-prognosis TNBC.

Keywords: Breast cancer; Panitumumab; Infliximab; NFκB; Doxorubicin

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Evaluation of Paclitaxel-HSA Nanoparticles potential for Co-Loading Ascorbyl Palmitate and Vitamin E Succinate

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The development of multifunctional nanocarriers capable of co-delivering synergistic therapeutic agents presents a promising strategy to enhance the efficacy of breast cancer treatment. In this study, we designed a novel co-loaded drug delivery system based on human serum albumin (HSA) nanoparticles to encapsulate Paclitaxel (PTX) along with two lipophilic antioxidants: Ascorbyl Palmitate (AP) and Vitamin E Succinate (VES). AP, a derivative of vitamin C, and VES, a potent mitochondria-targeting compound, were selected for their complementary mechanisms in promoting apoptosis and oxidative stress modulation in cancer cells. The nanoparticles were prepared using the nab (nanoparticle albumin-bound) method and characterized for their physicochemical properties. Dynamic light scattering (DLS) analysis revealed a uniform size distribution with an average diameter of approximately 220 nm. The zeta potential was measured at −54 mV, indicating a stable colloidal dispersion. The encapsulation efficiencies for Paclitaxel (PTX), Ascorbyl Palmitate (AP), and Vitamin E Succinate (VES) were 89%, 87%, and 91%, respectively, demonstrating efficient drug loading into the HSA matrix. In vitro release studies showed a sustained and controlled release profile for PTX, with approximately 85% of the drug released over 96 hours. These findings suggest that the co-loaded HSA nanoparticle system may provide prolonged therapeutic action and improved delivery efficiency for breast cancer treatment. Although optimization of the formulation, in vitro cytotoxicity and in vivo studies are ongoing, the current physicochemical and release data support the potential of this co-loaded HSA nanoparticle system as a promising platform for breast cancer therapy through synergistic action and controlled drug delivery.

Keywords: Ascorbyl Palmitate; Breast Cancer; nab method; Paclitaxel; Vitamin E Succinate

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Suppression of the *SH3D21* gene using antisense oligonucleotides (ASOs)

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Pancreatic cancer is known for its high mortality rate, making it one of the most challenging cancers to treat. The median survival duration for patients diagnosed with this disease typically ranges from 6 months to 1 year, underscoring the urgency for effective treatment options. Chemotherapy is the first-line treatment for pancreatic cancer, with gemcitabine being the most commonly prescribed drug. While gemcitabine is widely utilized in clinical practice, its effectiveness in significantly improving survival rates and overall survival of patients with pancreatic cancer is limited. In this study, we focused on the Panc-1 cell line, which is notable for exhibiting more resistance to gemcitabine than other widely studied pancreatic cancer cell lines. It has been demonstrated that when Panc-1 cells experience knockout of the *SH3D21* gene, they demonstrate more sensitivity to gemcitabine. This finding highlights the potential of the *SH3D21* gene as a target for therapeutic intervention in the quest to improve gemcitabine efficacy against pancreatic cancer. So far, CRISPR/Cas9 and siRNA have been used for *SH3D21* knockout and knockdown, respectively. In this study, we planned to use antisense oligonucleotides (ASOs) to knockdown *SH3D21* gene expression. Here, ASOs against *SH3D21* mRNA were designed alongside control ASOs. The primers were designed for *SH3D21* mRNA, and RT-qPCR was performed using mRNA extracted from Panc-1 cells. Our results indicated that all three designed ASOs reduced *SH3D21* mRNA levels, compared to the control ASOs, while ASO number 1 was the most effective.

Keywords: Pancreatic cancer; *SH3D21*; Panc-1; Antisense oligonucleotides; RT-qPCR

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lnvestigating the effect of proanthocyanidins on the expression of apoptotic genes in the H-1299 lung cell line

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Lung cancer remains one of the most common and fatal cancers worldwide, and continued issues with delayed diagnosis and drug resistance continue in standard treatment regimens. The goal of this investigation was to delineate the effects of grape seed-derived antioxidant proanthocyanidins on apoptotic gene expression within the human lung carcinoma cell line H-1299, which originated from tumor cells. This research examined the effect of varying proanthocyanidin levels on programmed cell death and correlations with pro- and anti-apoptotic gene expression changes following proanthocyanidin treatment, qrt-pcr, Trizol-mediated RNA extraction, apoptotic gene expression, and cell culture using the MTT assay. Total evidence shows that proanthocyanidins have a potential to modulate expression with respect to apoptosis, and help maintain the balance of expression between pro-apoptotic and anti-apoptotic genes, in summary, proanthocyanidins have some promise as a supplement treatment for lung cancer, and validates the requirement for the development of natural therapy alternatives. Lastly, we see this study as a potential future direction for creating natural therapies and exploring multiple modes of lung cancer treatment that potentially could improve patients' outcomes.

Keywords: H-1299 cell line; Apoptosis; Proanthocyanidins; Gene expression; Cancer

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ABSTRACT **Open Access**

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The effect of cinnamaldehyde and paclitaxel on apoptosis genes in H-1299 lung cancer cells

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Lung cancer is one of the most common and lethal human cancers. Smoking, exposure to cigarette smoke, and other toxic substances such as environmental pollutants and asbestos have increased the prevalence of this disease in recent years. One of our main concerns is providing timely and effective treatment for individuals suffering from this disease, and we must identify treatments that cause the least harm to the patient. Previous studies have examined cinnamaldehyde, which is responsible for the smell of cinnamon and has anti-inflammatory and antioxidant properties, as a herbal medicine in lung cancer cell lines and have confirmed the effectiveness of this substance on lung cancer. Therefore, in this study, we evaluated the effect of cinnamaldehyde and paclitaxel, a chemotherapeutic drug, on apoptosis in lung cancer cells of the H-1299 cell line. The cells were treated with cinnamaldehyde and paclitaxel, and the results from MTT and Real-time PCR assays demonstrated that the combination of these two substances increased apoptosis in the H-1299 cell line. The findings suggest that cinnamaldehyde may act as a complementary treatment in lung cancer therapy when combined with paclitaxel. Furthermore, combining natural and chemical drugs presents a novel approach for developing medications with fewer side effects for patients.

Keywords: Cinnamaldehyde; Paclitaxel; H-1299 cells; Apoptosis; Lung cancer

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The Effect of Beta-Boswellic Acid on the Expression of Genes Related to Apoptotic Proteins in JIMT_1 Breast Cancer Cells

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Breast cancer is one of the most noticeable health complications throughout the world and turns out to be most rampant among women. Mutation triggers, or apoptosis, are necessary to inhibit a tumor's growth. Techniques such as surgery, chemotherapy, and hormone therapy have made the treatment of breast cancer complex because of the variety of features of the tumor and its resistance to drugs. Natural compounds have been gaining popularity in treating a broad spectrum of ailments for quite some time. Beta-boswellic acid, known as frankincense extract, has also been widely researched for its anticancer activity. This study intends to examine the effectiveness of beta-boswellic acid as a possible therapeutic agent in JIMT-1 breast cancer cells by determining its efficacy in gene expression of apoptosis markers. JIMT-1 cells were cultured and treated with different concentrations of beta-boswellic acid. Cell viability was measured by MTT assay. Total RNA was extracted from the cells using TRIzol. The expression of apoptotic genes was studied in qRT-PCR. JIMT-1 cell viability was significantly reduced by beta-boswellic acid treatment. qRT-PCR results showed that beta-boswellic acid treatment upregulated Bax and Bad while downregulating Bcl-2. Based on these results, it can be concluded that beta-boswellic acid induces apoptosis in JIMT-1 breast cancer cells by modulating the expression of apoptosis-related genes. These results strongly suggest that beta-boswellic acid should be further studied as a new, promising candidate for breast cancer treatment.

Keywords: Breast Cancer; beta-boswellic Acid; Apoptosis; Gene Expression; JIMT_1 Cell Line

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The effect of Extract of *Cannabis sativa* seed on Pancreatic cancer cells

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Pancreatic ductal adenocarcinoma (PDAC) is one of the most fatal cancers, with a five-year survival rate below 5% and high resistance to current therapies, making it a significant clinical challenge. *Cannabis sativa* has garnered attention for its potential anticancer properties, though most studies have focused on its leaves. This study investigates the effects of an ethanolic extract from *C. sativa* seeds on pancreatic cancer cells (PANC-1). Cytotoxicity was evaluated using MTT assay on both PANC-1 and human fibroblast (HFF) cells and colony formation assay was conducted. A wound healing assay examined extract's effect on cell migration. Additionally, flow cytometry with propidium iodide (PI) staining was used to analyze cell cycle and apoptosis. This study demonstrated for the first time that the ethanolic extract of *C. sativa* seeds has anti-proliferative effects on pancreatic cancer cells (PANC-1) while sparing normal human fibroblast (HFF) cells. The extract induced G1 phase arrest, promoted apoptosis, inhibited colony formation, and reduced cell migration capacity of PANC-1 cells. These findings suggest that *C. sativa* seed extract may be a potential promising candidate for pancreatic cancer treatment.

Keywords: Pancreatic cancer; PANC-1 cell line; Cannabis Sativa seed; Apoptosis; Cell cycle arrest

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Investigating the effect of Steviol glycoside on inducing cell death and inhibiting the growth of H -1299 lung cancer cells

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Lung cancer affects the most patients across the world, and it is the highest cause of cancer death. Various anticancer techniques such as surgery and chemotherapy are used to treat cancer; however, the need for more effective treatments arises because of the therapeutic agent's inability to overcome drug resistance, non-specificity, and toxicity to normal cells. Historically, medicinal plants have been among the best sources of lead compounds in drug development. Steviol glycosides, the main sweet ingredients of the stevia plant, have been found to possess a range of medicinal qualities in recent times. The study aim is investigating the effect of steviol glycoside on growth inhibition of H-1299 cells. The objective is to elucidate the therapeutic properties of steviol glycoside on cell viability. H-1299 cells were treated with different doses of steviol glycoside, and cell viability was analyzed by MTT assay, and total RNA was extracted by the TRIZOL method, in which cells are lysed, the phase is separated, and RNA is finally precipitated, supplemented with quantitative real-time PCR. Steviol glycoside treatment inhibited H-1299 cell proliferation and viability significantly in a dose-dependent manner, as detected by the MTT assay. Changes in mRNA expression levels of apoptosis-related genes were determined by qRT-PCR analysis, which indicated increased expression of the Bax gene coupled with decreased expression of the Bcl-2 gene. results indicate that, steviol glycoside induced apoptosis in H-1299 cells, thus presenting itself as a potential therapeutic agent for lung cancer treatment.

Keywords: Steviol glycoside; H-1299 cells; Apoptosis; Growth inhibition; Cell death

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Synergistic Effects of Glycyrrhizic Acid and 5-Fluorouracil on Apoptotic Genes Expression in HCT116 Colorectal Cancer Cells

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Colorectal cancer (CRC) is one of the most common malignancies of the digestive system, requiring effective therapeutic strategies. 5-Fluorouracil (5-FU) is a standard chemotherapeutic agent for CRC, but its efficacy is limited by drug resistance and systemic toxicity. Glycyrrhizic acid (GLA) a bioactive compound derived from Glycyrrhiza glabra, exhibits anti-cancer and pro-apoptotic properties. This study investigated the combined effects of glycyrrhizic acid and 5-FU on apoptotic gene expression in HCT116 cells. Cells were treated with glycyrrhizic acid, 5-FU, and their combination. After 24,48 hours, cell viability was assessed via the MTT assay. Bax and Bcl2 expression levels were quantified using Real time-PCR. The combination treatment significantly increased apoptosis and reduced cell viability. Moreover, Bax upregulation and Bcl2 downregulation were observed, indicating mitochondrial pathway activation. These findings suggest that GLA enhances 5-FU efficacy, offering a potential strategy to overcome chemoresistance in CRC.

Keywords: Colorectal cancer; 5-Fluorouracil; Glycyrrhizic acid; HCT116; apoptosis; Bax; Bcl2

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Diagnostic and prognostic relevance of *RAF1* gene in acute myeloid leukemia

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Acute Myeloid Leukemia (AML), one of the most prevalent blood cancers, is a disease marked by its intricate complexity and diversity. As AML continues to challenge clinicians with its varied manifestations, there is a growing demand for precise and dependable diagnostic tools. By integrating advanced techniques like Real-Time PCR and cutting-edge molecular methods, researchers can unlock deeper insights into the disease's biology, paving the way for more accurate diagnoses and personalized treatment strategies. This study, explored the expression patterns, interconnections, and diagnostic potential of a specific molecular network—RAF1, miR-146b-3p, and Circ-RPL15—in AML patients compared to healthy individuals. The investigation included 40 AML patient samples and 32 control samples from healthy participants. Using Real-Time PCR, RNA expression levels was measured in both groups, analyzing differences, correlations, and the network's potential as a diagnostic and prognostic tool. Interestingly, correlation analyses revealed no significant relationships between the components of this molecular trio. However, RAF1 emerged as a standout biomarker, showing a marked difference in expression between AML patients and the control group. This finding suggests that RAF1 could serve not only as a robust diagnostic indicator but also as a promising target for refining prognostic assessments. RAF1's prognostic value in AML was assessed using the Kaplan-Meier Plotter, analyzing survival data from 1,608 patients. Significant findings (log-rank P=0.0002, HR=0.79, CI: 0.7–0.9) confirm RAF1 as a key biomarker for predicting survival outcomes in AML.

Keywords: Acute myeloid leukemia; Diagnostic indicator; Prognostic value; RAF1; Kaplan-Meier plotter

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ABSTRACT **Open Access**

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Phycobiliproteins as natural bioactive compounds in targeted breast cancer therapy

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Phycobiliproteins, a class of naturally occurring bioactive compounds derived from red algae and cyanobacteria, have gained attention for their potential therapeutic applications in cancer treatment. These pigments exhibit strong light-absorbing properties and have demonstrated anti-inflammatory and anti-proliferative effects on various cancer cell lines. Given their solubility and stability under diverse pH conditions, phycobiliproteins hold promise as novel therapeutic agents. This study aims to investigate the cytotoxic effects of extracted phycocyanin and phycoerythrin pigments on MDA-MB-231 breast cancer cells. Phycobiliproteins were extracted and their concentrations were determined spectrophotometrically.Purification was performed using novel chromatographic techniques to enhance the isolation and purity of the extracted compounds, followed by SDS-PAGE analysis to assess purity and molecular weight.The cytotoxic effects of purified pigments were evaluated on MDA-MB-231 breast cancer cells and MCF-10A normal epithelial breast cells using cell viability assays. The findings of this study demonstrated the significant cytotoxic effects of these compounds on breast cancer cells. Further investigations are required to elucidate their precise molecular mechanisms and potential clinical applications.

Keywords: Breast cancer; Phycobiliproteins; Phycocyanin; Phycoerythrinm; Viability assays.

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Three-dimensional co-culture condition for U266 myeloma cells; towards mimicking the bone marrow microenvironment

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Multiple myeloma (MM) is one of the most common hematologic malignancies worldwide and remains incurable due to genetic instability and tumor-promoting bone marrow (BM) microenvironment. Three-dimensional (3D) interactions between myeloma cells and extracellular matrix, along with other cellular components in the BM, play a crucial role in disease progression and drug resistance. Conventional myeloma models often rely on patient samples or artificial substances, which are not naturally found in the BM microenvironment, limiting their applicability and relevance. To address this, we developed a simple, patient-free and cost-effective 3D co-culture model for U266 myeloma cells to better understand disease biology and facilitate drug-screening studies. Peripheral blood plasma from three healthy donors was used to generate fibrin gel structures. U266 cells, human umbilical vein endothelial cells (HUVECs) and BM mesenchymal stem cells (BM-MSCs) were co-cultured under different gel-free and fibrin gel matrix-based conditions. Proliferation and survival rates of U266 cells in each condition were evaluated and compared. Fibrin gels supported increased viability and proliferation of U266 cells in 3D mono-culture conditions. However, in co-culture conditions, U266 cells aggregated and formed 3D structures in gel-free cultures, with significantly higher viability and expansion rates compared to the fibrin gel-based conditions. Therefore, 3D co-culture of U266 cells with HUVECs and BM-MSCs in gel-free condition resulted in increased proliferation and survival of the myeloma cells, highlighting the potential of this simple 3D model for future drug screening studies.

Keywords: Multiple myeloma; Co-culture; Three-dimensional cell culture; Fibrin gel; Proliferation

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Synergistic Effect of Quercetin and Berberine on LNCaP Cancer Cells

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Prostate cancer is a common malignancy and one of the five leading cancers in men [1]. Plants contain bioactive phytochemicals that can help suppress cancer development [2]. Quercetin is a beneficial flavonoid found in fruits and vegetables. In addition to its beneficial effects, it serves a crucial role as an anticancer agent [3]. The anticancer effects of Quercetin include promoting cell death, apoptosis, and autophagy by modulating the PI3K/Akt/mTOR, Wnt/β-catenin, and MAPK/ERK1/2 pathways [4]. Berberine, an isoquinoline quaternary alkaloid derived from plants, has many therapeutic applications against various diseases. Recent studies have shown that berberine can inhibit cell proliferation and exhibit cytotoxic effects on cancer cells [5]. This research used quercetin and berberine simultaneously to determine their synergistic effects on prostate cancer cells. Quercetin and Berberine were combined at half of their respective concentrations. The vitality of the cancer cells was determined using the MTT assay (3-(4,5-dimethylthiazolyl)-2,5-diphenyl-tetrazolium bromide), and the expression of apoptosis-related genes was evaluated by the qRT-PCR method. MTT assay analyses showed that the viability of cancer cells after treatment depends on concentration and time. However, combination therapy showed more substantial and practical effects than quercetin and berberine alone. Evaluation of apoptosis-related genes showed that the Bax gene was expressed more frequently in the treated cells, while the Bcl2 gene was expressed less frequently. In general, the results of this study showed that co-treatment with quercetin and berberine showed the most potent anticancer activity and could be used as an adjuvant treatment for prostate cancer therapy.

Keywords: Quercetin; Berberine; Prostate cancer; LNCaP cell line; Phytochemical

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Inducible Caspase-9 Restores Tamoxifen Sensitivity in Resistant MCF-7 Cells

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Tamoxifen is a widely used treatment for estrogen receptor-positive (ER+) breast cancer; however, the development of resistance significantly reduces its effectiveness and leads to treatment failure. One of the key mechanisms of tamoxifen resistance is the ability of cancer cells to evade apoptosis, or programmed cell death, which allows them to survive despite treatment. Finding ways to restore sensitivity to tamoxifen in resistant cancer cells is crucial for improving patient outcomes. In this study, we investigated whether activating caspase-9, a key player in the intrinsic apoptotic pathway, could enhance tamoxifen-induced cell death in tamoxifen-resistant MCF-7 (TamR-MCF-7) cells. We first confirmed resistance to apoptotic cell death in these cells using annexin V/PI staining and trypan blue exclusion assays, both of which showed no significant apoptosis upon caspase-9 activation. To overcome the resistance to tamoxifen and apoptotic cell death, we combined tamoxifen treatment and caspase-9 activation, and assessed its effects using calcein-AM/PI staining. Interestingly, we observed a significant increase in cell death in tamoxifen-treated iC9-transfected cells compared to the untreated ones. This suggests that activating caspase-9 can help bypass apoptotic defects and restore tamoxifen sensitivity. Therefore, engaging caspase-9 activation could be a promising approach to overcoming endocrine resistance in breast cancer.

Keywords: Tamoxifen resistance; Breast cancer; Caspase-9; Apoptosis; Endocrine therapy

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Investigating the cytotoxic effect of *Zygnema circumcarinatum* green algae extract on the expression of OCT_4 and SOX_2 genes in MDA-MB-231breast cancer cell line

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Breast cancer remains the most common cancer among women, posing significant challenges to treatment. One promising therapeutic approach involves using bioactive natural compounds with anticancer properties. This study investigated the cytotoxic effects of the methanolic extract of the green alga *Zygnema circumcarinatum* on the expression of OCT_4 and SOX_2 genes in the MDA-MB-231 breast cancer cell line. These genes are crucial regulators of cancer stem cell self-renewal and differentiation, and their downregulation may contribute to tumor suppression. Bioactive compounds in the extract were identified using gas chromatography-mass spectrometry (GC-MS). Phytochemical analysis revealed considerable levels of chlorophyll a (55.728 ± 1.008 µg/g), chlorophyll b (82.723 ± 1.286 µg/g), carotenoids (4.252 ± 0.6 µg/g), anthocyanins (0.861 ± 0.6 mg/ml), total phenols (0.369 ± 0.009 mg GAE/g DW), and total flavonoids (0.311 ± 0.001 mg QE/g DW). Antioxidant activity, assessed by DPPH radical scavenging assay, showed a concentration-dependent increase. Cytotoxicity was evaluated via the MTT assay, demonstrating a significant, dose-dependent inhibition of cell proliferation. Real-Time PCR analysis revealed a marked downregulation of OCT_4 and SOX_2 after treatment with the extract, findings further confirmed at the protein level by flow cytometry. Overall, these results suggest that *Z. circumcarinatum* methanolic extract possesses potent anticancer potential by targeting stemness-related pathways. However, further mechanistic studies and in vivo investigations are needed to confirm its therapeutic applicability.

Keywords: Breast Cancer; Cytotoxic; OCT_4, SOX_2; Zygnema circumcarinatum algea

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Optimizing *Bacillus cereus* Asparaginase Activity under Variable Conditions for Advancing Cancer Therapies

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L-asparaginase was the first enzyme clinically employed as an anticancer agent and was approved for the treatment of childhood acute lymphoblastic leukemia within a therapeutic protocol. This enzyme inhibits protein synthesis in cancer cells by depleting asparagine, an essential amino acid required for cell growth, thereby suppressing tumor cell proliferation. Gram-negative and gram-positive bacteria, isolated from diverse terrestrial and marine environments, are recognized as the primary sources of L-asparaginase production. Additionally, the enzyme demonstrates efficacy in treating ovarian cancer by reducing extracellular glutamine levels, which decreases the survival of ovarian cancer cells. L-asparaginase hydrolyzes L-asparagine in two stages: first, its nucleophilic residue attacks the amid carbon, forming a β-acyl-enzyme intermediate, which is then hydrolyzed at the ester carbon to produce L-aspartic acid and ammoni. This study focuses on optimizing the temperature and pH conditions for L-asparaginase activity to enhance its effectiveness in inhibiting tumor cell growth and improving anticancer treatment outcomes. The findings could contribute to the improved clinical application of L-asparaginase and enhanced therapeutic outcomes in cancer management. The optimal temperature for L-asparaginase activity was assessed by varying temperatures from 25 to 50°C in a 50 mM Tris HCl buffer (pH 8.0). The optimal pH was determined at 37°C using various 50 mM buffers, including citrate-sodium citrate (pH 4.0–6.0), phosphate (pH 6.0–9.0), glycine-sodium hydroxide (pH 9.0–10.0), and sodium carbonate-sodium hydroxide (pH 10.0–12.0). Enzymatic activity was precisely evaluated using spectroscopic and colorimetric methods, with changes in light absorbance over time measured to determine reaction rates under varying temperature and pH conditions. Based on the results, optimizing temperature and pH conditions significantly enhances L-asparaginase's capacity to inhibit cancer cell growth.

Keywords: *Bacillus cereus*; Childhood acute lymphoblastic leukemia; L-asparaginase; L-asparagine; Tumor cells

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Apoptosis Resistance in Triple-Negative Breast Cancer Cells with Mutant p53: Evaluating Gene Therapy Potential of miR-34b

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Triple-negative breast cancer (TNBC) represents one of the most aggressive and therapeutically The subtypes of breast cancer that present significant challenges are distinguished by the lack of estrogen receptors (ER) and progesterone receptors (PR). and HER2 amplification, TNBC is often associated with poor prognosis, high recurrence rates, and resistance to conventional therapies. A prominent molecular feature of TNBC is the high frequency of TP53 mutations, which are present in approximately 80% of cases. These mutations disrupt the normal apoptotic Roles of p53 and play a role in tumor development progression, chemoresistance, and failure of targeted therapies. miR-34b, a member of The miR-34 family is directly regulated by wild-type p53 and is crucial for controlling apoptosis., cell cycle arrest, and oncogenic signaling. Recent studies have proposed the use of synthetic miR-34 mimics as a potential gene therapy approach to restore tumor suppressor pathways in cancer cells. However, the therapeutic efficacy of miR-34b in tumors with mutant or absent p53 remains poorly understood.In this study, we explored the pro-apoptotic potential of exogenously delivered miR-34b in MDA-MB-231 cells, a TNBC cell line harboring mutant p53. Cells were transfected with synthetic miR-34b mimics, and apoptotic responses were evaluated using Annexin V/PI staining, MTT assay, and analysis of apoptotic marker expression. Our findings revealed that miR-34b alone was insufficient to significantly induce apoptosis in p53-mutant cells, suggesting a critical dependence on functional p53 for the apoptotic activity of miR-34b. These observations align with previous reports indicating that the tumor-suppressive effects of miR-34b are largely mediated through the p53 signaling pathway. Furthermore, the lack of apoptotic response highlights the potential need for combinatorial strategies or restoration of p53 function to enhance the therapeutic efficacy of miR-34b in p53-deficient TNBC modelsThese results highlight a major limitation in the application of miR-34b-based gene therapy in TNBC patients with mutant p53 and emphasize the importance of considering p53 status in designing personalized therapeutic strategies. Further studies are warranted to explore combinational treatments that may restore or bypass p53-dependent apoptotic signaling.

Keywords: Apoptosis; p53 Mutation; miR-34b; Gene Therapy; Triple-Negative Breast Cancer

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Investigation of the *p21* and *p27* expression in Iranian patients with Non-Small Cell Lung Cancer (NSCLC)

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P21 and *p27* are cell cycle inhibitors that play complex roles in non-small cell lung cancer (NSCLC). These proteins function as tumor suppressor genes, critical for preventing uncontrolled cell division. Frequently, *p21* and *p27* are downregulated in various human cancers, which correlates with a worse prognosis. Notably, *p21* can act as a tumor suppressor and, in specific contexts, as an oncogene. The oncogenic activity of *p21* is linked to its ability to activate CDK4/6-cyclin D complexes, which are involved in early G1 phase progression of the cell cycle, and its anti-apoptotic properties. This study investigated the relationship between *p21* and *p27* as cell cycle inhibitors in patients with non-small cell lung cancer (NSCLC) and their association with patient prognosis. This study collected tumor tissues and adjacent tumor tissues (ATT) from 33 NSCLC patients referred to Masih Daneshvari Hospital in Tehran between 2022 and 2024. These patients had no family history of cancer, were unrelated, had not received previous treatments, and their cancer was not a result of metastasis from other cancers. The samples were transported to the laboratory under cold chain conditions and informed consent and relevant questionnaires were completed. Real-time PCR was conducted to analyze *p21*, *p27*, and *β-actin* genes. The results were evaluated using REST and SPSS software, with statistical tests including the t-test and one-way ANOVA applied. The findings indicated that 51% of the patients were smokers, comprising 55% males and 45% females. Notably, 79% of participants experienced a weight loss exceeding 5 kg. In tumor samples, *p21* was positive in 72% of NSCLC tumor tissues, compared to 12% in ATT ($P < 0.05$). Additionally, *p27* levels were reduced in 83% of NSCLC cases relative to ATT ($P < 0.05$). There was also a significant correlation between these genes' expression levels and the disease stage ($P < 0.05$). In conclusion, while *p21* and *p27* are recognized as cell cycle inhibitors, their roles in NSCLC are complex. The observed reduction in *p27* expression is often linked to a worse prognosis, whereas the role of *p21* remains more controversial. This research underlines the importance of further examination of these proteins for insights into the biology of tumors and potential prognostic markers in NSCLC.

Keywords: *p21*; *p27*; NSCLC; Expression

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