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SABİAD

SAĞLIK BİLİMLERİNDE İLERİ ARAŞTIRMALAR DERGİSİ

JOURNAL OF ADVANCED RESEARCH IN HEALTH SCIENCES

1ST INTERNATIONAL BASIC ONCOLOGY CONGRESS

- **THE THEME WITH "NEW HORIZONS IN CANCER RESEARCH: BIG DATA, SYSTEM BIOLOGY, NEW MOLECULAR DISCOVERIES"**

02-04 JUNE 2022

- **THE COURSE TITLED 'OMICS TECHNOLOGIES AND BIOLOGICAL INTERPRETATION IN CANCER RESEARCH'**

04 JUNE 2022

İSTANBUL UNIVERSITY PRESS

Dizinler / Indexing and Abstracting

ULAKBİM TR Dizin

CAB Abstracts

CABI Global Health

CABI Nutrition and Food Sciences

EBSCO CINAHL Ultimate

EBSCO Central & Eastern European Academic Source

ASOS Index

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JOURNAL OF ADVANCED RESEARCH IN HEALTH SCIENCES
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1st INTERNATIONAL BASIC ONCOLOGY CONGRESS

NEW HORIZONS IN CANCER RESEARCH: BIG DATA, SYSTEM BIOLOGY, NEW MOLECULAR DISCOVERIES

• 02-04 June 2022 •

"OMICS TECHNOLOGIES AND BIOLOGICAL INTERPRETATION IN CANCER RESEARCH" COURSE

• 04 June 2022 •

ONLINE

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Editorial

Dear Colleagues,

The 1st International Basic Oncology Congress organized by Basic Oncology Society, with the theme of "New Horizons in Cancer Research: Big Data, System Biology, New Molecular Discoveries". has been performed virtual on 2nd-4th June 2022.

In this congress, scientific information exchanges about study design, applications and interpretations of omics technologies by bringing together expert scientists working in the fields of multi-omics technologies in the international platform was aimed. In addition, the course titled with "Omics Technologies and Biological Interpretation in Cancer Research" on 4th June 2022, was achieved to provide training on omics technologies and applications.

All scientific studies' abstracts presented by invited, oral and poster presenters in the 1st International Basic Oncology Congress has been published in the special issue of The Journal of Advanced Research in Health Sciences (SABIAD) (e-ISSN: 2651-4060).

We would like to thank all participating scientists for their scientific contributions to our congress and the SABIAD journal team for their contribution to the publication of scientific information, and hope to see you among us in the scientific meetings we plan to hold in the future.

Prof. Dr. Semra DEMOKAN

Editor of supplement
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CONGRESS PROGRAM

02 June 2022	
12:00-12:30	**OPENING SESSION** **ZULFIKAR O. Bulent, Prof.Dr., Istanbul University, Director of Oncology Institue** **DEMOKAN Semra, Prof.Dr., Istanbul University, President of the Basic Oncology Society**
12:30-13:30	**EPIGENOMICS RESEARCH IN CANCER** ***Moderator: BAYRAK Omer Faruk, Prof.Dr., AYCAN - YERER Mukerrem Betul, Prof.Dr.*** **KUÇUK Omer, Prof.Dr.,** Epigenetic Mechanisms of Soy Isoflavones in Prostate Cancer Treatment **DEMOKAN Semra, Prof.Dr.** Discovery of Novel Epigenetic Biomarkers in Oral Malignant and Premalignant Lesions by Epigenomics and Transcriptomics Approaches
13:30-13:45	**Coffee Break**
13:45-14:45	**BIOINFORMATICS - APPLICATION AND CHALLENGES - I** ***Moderator: SEZERMAN Ugur, Prof.Dr., BAYSAN Mehmet, Assist.Prof.Dr.*** **SEZERMAN Ugur, Prof.Dr.** Multiomic Approaches in Personalized Cancer Medicine **BAYSAN Mehmet, Assist.Prof.Dr.**Data Science, Cancer and Sequencing Analysises
14:45-14:50	**Break**
14:50-16:20	**CANCER AND MICROBIOTA** ***Moderator: DEMOKAN Semra, Prof.Dr., OZMEN Fusun, Assoc.Prof.Dr.*** **CANER Ayse, Assoc.Prof.Dr.** Tumor-Associated Microbiome **CAKIR Muharrem Okan, Assist.Prof.Dr.,** Updates on High-Risk HPV Types and Cancer **KARABEKMEZ Muhammed Erkan, Assist.Prof.Dr.** Computational Metabolic Modeling of Gut Microbiota in Cancer Research
16:20-16:25	**Break**
16:25-16:55	**CANCER AND COVID-19 OMICS** ***Moderator: KOCDOR Hilal, Prof.Dr., DEMOKAN Semra, Prof.Dr.*** **NOORBAKHSH Farshid, Assoc.Prof.Dr.** SARS-Cov2 Proteins Might İnterfere with Molecular Pathways Involved in Carcinogenesis; A Bioinformatics Study
16:55-17:00	**Break**
17:00-18:00	**PROTEOMICS** ***Moderator: DEMOKAN Semra, Prof.Dr., YAYLIM Ilhan, Prof.Dr.*** **OZLU Nurhan, Prof.Dr.** Applications of Proteomic Approaches in Renal Cancer **DOGANAY Dinler Gizem, Prof.Dr.** Interactome Analysis to Determine Protein-Protein Interaction Hubs in Cancer Cells
18:00-18:30	**TERRA ANALYSIS AND MEASUREMENT TRADE CO. INC. SATELLITE SYMPOSIUM** ***Moderator: DEMOKAN Semra, Prof.Dr., KOCDOR Hilal, Prof.Dr.*** **FREDERIKSEN Frost Signe, Junior Application Scientist MALDI imaging,** MALDI imaging is more than pretty images: SpatialOMx and Introducing new powerful tools
18:30-19:14	**ORAL PRESENTATION** ***Moderator: PODA Mehves, Prof.Dr.***

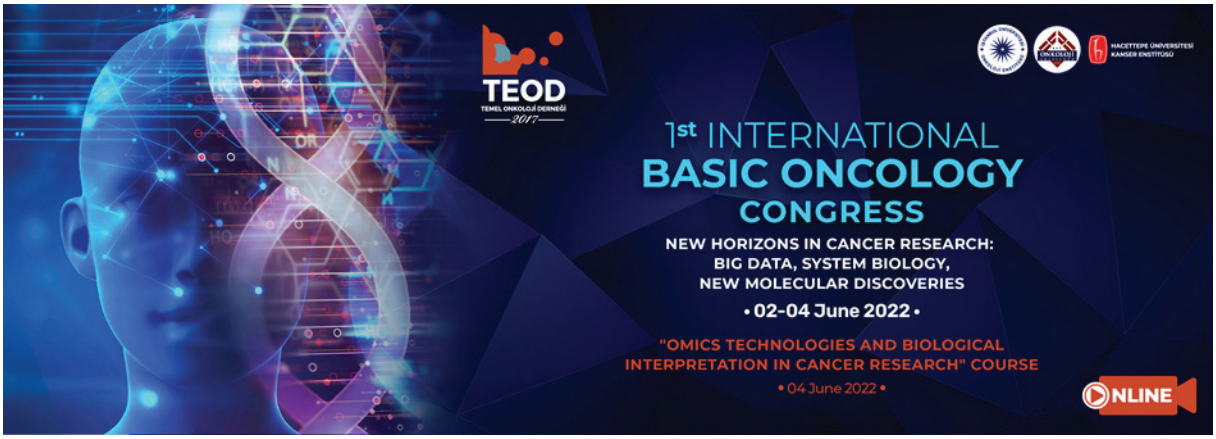
03 June 2022	
08:30-09:30	**CANCER IMMUNOLOGY-OMICS RESEARCH** ***Moderator: DENIZ Gunnur, Prof.Dr., GURBUZ Orkun, Assist.Prof.Dr.*** **ESENDAGLI Gunes, Prof.Dr.** Dissection of T Cell Activation Phases for Check Point Blockade Immunotherapy **TELATAR Milhan, Dr.** Impact of Comprehensive Genomic Profiling NGS Panels in Precision Oncology: The City of Hope CMDL Experience
09:30-09:35	**Break**
09:35-10:05	**BIOINFORMATICS - APPLICATION AND CHALLENGES - II** ***Moderator: DEMOKAN Semra, Prof.Dr., KARABEKMEZ Muhammed Erkan, Assist.Prof.Dr.*** **DURDAGI Serdar, Prof.Dr.** Virtual Screening of Ultra Large Ligand Libraries for The Identification of Novel Anti-Cancer Therapeutics Against Malignant Glioma
10:05-10:10	**Break**

10:10-11:10	**EFFECTS OF NANOTECHNOLOGY ON VACCINES, DRUGS AND EPIGENETICS IN CANCER - I** ***Moderator: SAVRAN OGUZ Fatma, Prof.Dr., GEZER Ugur, Prof.Dr.***
	DOGANAY Dinler Gizem, Prof.Dr. Developing Biotechnological Drugs to Target Cancer Pathways **DEMIRCI Hasan, Assist.Prof.Dr.** Serial Femtosecond Structural Studies of Supra- and Macromolecular Drug Targets at Ambient Temperature
11:10 -11:15	**Break**
11:15-12:00	**ORAL PRESENTATION** ***Moderator: PODA Mehves, Prof.Dr.***
12:00-12:05	**Break**
12:05-13:05	**QIAGEN SATELLITE SYMPOSIUM** ***Moderator: DEMOKAN Semra, Prof.Dr., OZMEN Fusun, Assoc.Prof.Dr.*** **BUNGARTZ Kathryn, Assist.Prof.Dr.** Somatic Variant Interpretation: From FASQ to Report
13:05-13:10	**Break**
13:10-14:10	**CANCER - METABOLOMICS RESEARCH** ***Moderator: ZEYBEK Umit, Prof.Dr., DEMOKAN Semra, Prof.Dr.***
	TUZUNER Bora, Assist.Prof.Dr. Steroidogenesis Pathway and Breast Cancer: Empowering Personalized Treatment with a Metabolomics Approach **MERT Ufuk, Assist.Prof.Dr.** Circular RNAs in Cancer Mechanism, Diagnosis and Treatment
14:10-14:15	**Break**
14:15-15:15	**EFFECTS OF NANOTECHNOLOGY ON VACCINES, DRUGS AND EPIGENETICS IN CANCER – II** ***Moderator: ZEYBEK Umit, Prof.Dr., CEBI Aysegul, Prof.Dr.***
	DUMAN Cansaran Demet, Prof.Dr. Determination of the Therapeutic Effect of Vulpinic Acid and Vulpinic Acid-Responsive miR-197-3p in Breast Cancer Treatment by *In Vitro* and *In Vivo* Studies **KOCABAS Fatih, Assoc.Prof.Dr.,** When MEIS is up in Prostate Cancer, then MEISi?
15:15-15:20	**Break**
15:20-15:50	**OMICS AND HEALTHCARE IN CANCER** ***Moderator: ALTUN Zekiye, Prof.Dr., TUNCER Bugra Assist.Prof.Dr.***
	OZDEMIR Ozkan, Dr. Generations of Genome/Transcriptome Sequencing and Its Implementation of Healthcare in Terms of Cancer Diagnostics, Predisposition and Treatment
15:50-15:55	**Break**
15:55-16:25	**TRANSCRIPTOMICS AND CANCER** ***Moderator: YAZICI Hulya, Prof.Dr., HEPOKUR Ceylan, Assist.Prof.Dr.***
	GOKMEN POLAR Yesim Assoc.Prof.Dr., Applications of Transcriptomics Technologies in Breast Cancer
16:25-16:30	**Break**
16:30-18:00	**OMICS RESEARCH IN TARGETED CANCER THERAPIES - I** ***Moderator: OZMEN Fusun, Assoc.Prof.Dr., AKTAS Safiye, Prof.Dr.***
	AYHAN ACILAN Ceyda, Assist.Prof.Dr. Reversıon of Taxane Resıstance in Prostate Cancers Vıa Epıgenetıc Modıfıers **OZPOLAT Bulent, Prof.Dr.** Development of Novel Targeted Therapeutics for Breast Cancer **VERMA Amit, Dr.** Precision Oncology: Basic to Bedside
18:00-18:52	**ORAL PRESENTATION** ***Moderator: PODA Mehves, Prof.Dr.***

04 June 2022

08:30-10:00	**OMICS RESEARCH IN TARGETED CANCER THERAPIES – II** ***Moderators: DEMOKAN Semra, Prof.Dr., DOGANAY Dinler Gizem, Prof.Dr.***
	TUZMEN Sukru, Prof.Dr. Identification of Novel Biosignatures as Drug Targets in Cancer Treatment **KUCUK Can, Assoc.Prof.Dr.**Therapeutic Implications of Targeted Sequencing and Mirna-Seq of B Cell Lymphomas **KOCAL-CALIBASI Gizem, Assoc.Prof.Dr.** Dietary-Based Molecular Targets and Therapeutic Opportunities in Cancer
10:00-10:30	**NANOTECHNOLOGY IN CANCER - OMICS RESEARCH** ***Moderator: DEMOKAN Semra, Prof.Dr., PODA Mehves, Assist.Prof.Dr.***
	DEMIRCI Hasan Assist.Prof.Dr. Bright Future Enabled by "Turkish DeLight": High-Resolution and High-Throughput Structural Studies of Anti-Cancer Drugs at Physiological Temperature

10:30-11:00	**BIOSTATISTICS - OMICS RESEARCH** ***Moderator: ALTUN Zekiye, Prof.Dr., KOCDOR Hilal, Prof.Dr.***
	GUNVER Mehmet Guven, Assist.Prof.Dr. Real World Evidence and Big Data
11:00-11:30	**NATURAL PRODUCTS in CANCER - OMICS RESEARH** ***Moderator: DEMOKAN Semra, Prof.Dr., AYCAN - YERER Mukerrem Betul, Prof.Dr.***
	FARUQUE Omar Mohammad, Assoc.Prof.Dr., Isolated Compound from an Ethnomedicinal Plant Congea Tomentosa Mediates Anticancer Effect by Inhibiting STAT3 And AKT Activation to Induce Apoptosis in Human U251 Glioma Cells
11:30-12:00	**ETHICS IN OMICS TECHNOLOGIES** ***Moderator: YAZICI Hulya, Prof.Dr., BASBINAR Yasemin, Prof.Dr.***
	URESIN Ali Yagız, Prof.Dr. Ethics in Translational Research
12:00-12:30	**CLOSING CEREMONY**

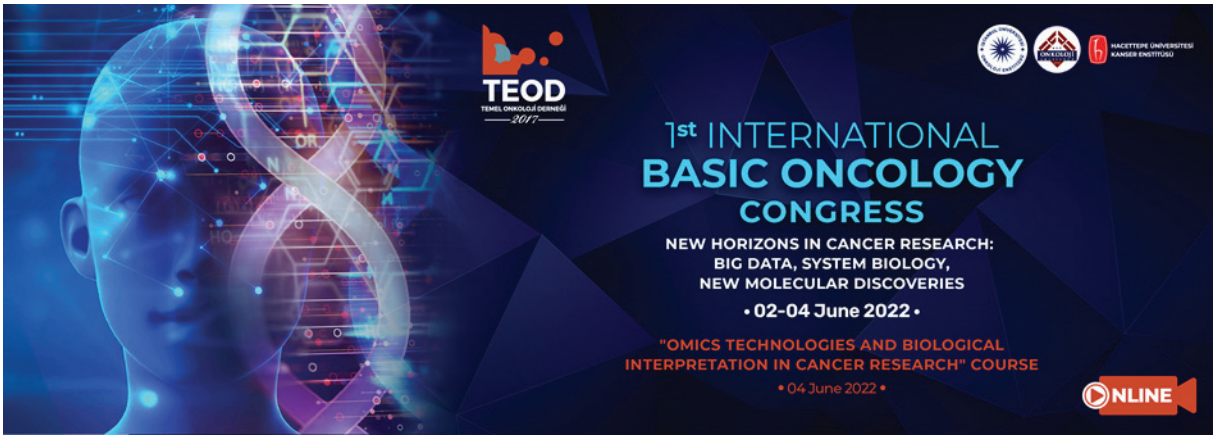


ORAL PRESENTATION (OP) ABSTRACTS

(OP1 – OP17)

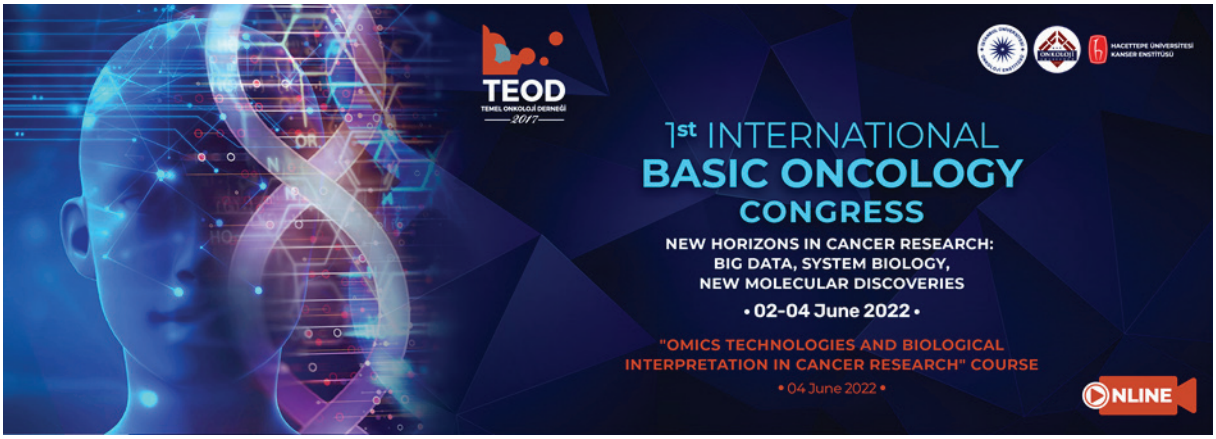
02.06.2022 18:00 – 18:45		
18:30 – 18:37	**TURKCAN KURU Gozde**	OP1- **Transcriptomic differences in monozygotic twins with ovarian cancer**
18:38 – 18:45	**DELEK PEKTOPAL Fatma Seher**	OP2- **miR-3653-3p expression in peripheral blood of patients with ovarian carcinoma**
18:46 – 18:52	**GIDER Yasemin**	OP3- **Investigation of the expression level of miR 142-3p in ovarian carcinoma**
18:53 – 18:59	**ASADI Milad**	OP4- **Downregulation of SLC-16 can increase apoptosis level in gastrointestinal cancer**
19:00 – 19:07	**AKTAS Tekincan Cagrı**	OP5- **Precision medicine in neuroblastoma: experience with next generation sequencing**

03.02.2022 11:45-12:30		
11:15 – 11:22	**ARZUK Ege**	OP6- **Repurposing drugs for cancer therapy**
11:23 – 11:30	**SALIHOGLU - MISER Ece**	OP7- **The effect of silencing the *Tip60* gene on the response to radiotherapy in breast cancer cells**
11:31 – 11:38	**ONER Suleyman Kaan**	OP8- **Animal models in osteosarcoma**
11:39 – 11: 45	**MERT Ufuk**	OP9- **Investigation of circular RNAs as biomarkers in head and neck cancer cells and the effects of radiotherapy on circular RNAs**
11:46 – 11:52	**MUTLU - AKIN Beyza**	OP10- **The *WISP-1* gene expression in breast cancer cell lines**
11:53 – 12:00	**GEZICI Sevgi**	OP11- **Exosomes – A new frontier in cancer therapy**
03.02.2022 18:00 – 18:52		
18:00 – 18:07	**ONER Suleyman Kaan**	OP12- **Low back pain because of insidious metastasis**
18:08 – 18:15	**OZGUR Emre**	OP13- **Targeted sequencing of human satellite 2 repeat sequences in blood plasma of cancer patients**
18:16 – 18:22	**SEN Sena**	OP14- **Novel epigenetic biomarker determination for OSCC by array-based epigenomic and transcriptomic techniques**
18:23 – 18:29	**ESENTURK Gizem**	OP15- **Methylation and expression validation results of *GPRC5C* gene obtained from epigenomics and transcriptomics data in oral cavity tumors**
18:38 – 18:44	**DEMIR Ayse Banu**	OP16- **A phylogenetic approach to evaluate the relation between miRNA expressions and Hepatitis C virus in hepatocellular carcinoma**
18:45 - 18:52	**COSKUN Ayca**	OP17- **Long non-coding RNAs and autophagy in osteosarcoma**



POSTER OF PRESENTATION (PP) ABSTRACTS

SATTAROVA Afet	PP1 - **CircRNAs of Saliva as Potential Biomarkers for Colorectal Cancer Diagnosis**
TASKIRAN Hilal	PP2 - **Generation and Characterization of Tumor Spheroids from Gastric Cancer Cell Lines, Snu-484 and Nci-N87**
RAHIMI Saina	PP3 - **Evaluation of Exosome-Derived CircRNA Expression Patterns in Lung Cancer Radiotherapy**
HEMMATVAND Keyvan	PP4 - **Lipopolysaccharide Inhibits Autophagy in Human Dermal Fibroblasts *invitro***
ASADI Milad	PP5 - **MicroRNA as a Promising Potential Biomarker for Colorectal Cancer**
ASADI Milad	PP6 - **Potential of microRNAs as a Biomarker for Laryngeal Cancer**
SANLAV Gamze	PP7 - **S-100 Protein Expression Levels as a Potential Prognostic Marker in Neuroblastoma**
BARAN Burcin	PP8 - **Analysis of Tribbles Homolog 3 (TRIB3) Expression Levels in Neuroblastoma: Preliminary Study**
DEMOKAN Semra	PP9 - **Investigation of Methylation and Expression Status of *PAX1* Gene Via Epigenomic Profiling in Oral Malignant Lesions**
DEMIRTAS OCAL Muge	PP10 - **miRNA-Regulated Pathways of Cd8+ T Cells in TNBC Mouse Model**
GURKEBABCI Ipek	PP11 - **Investigation of the Effect *Pistacia Vera* from Different Regions on Oxidative Stress and Proliferation in Breast Cancer Cell Line**
OZSENGEZER KUM Selen	PP12 - **Investigation of the Potential Effects of YAP-1 and Nestin on Risk Classes and Prognosis in Neuroblastoma**
KAYA Yagmur	PP13 - **Antimetastatic Potential of Curcumin in Anaplastic Thyroid Cancer and Combined Activity with Docetaxel**
SALMAN Tarık	PP14 - **Investigation of the Antimetastatic Potential of *T. Spicata* in Human Breast Adenocarcinoma Cells Combined with Standard Chemotherapy**
AKTAS Safiye	PP15 - **Effect of Thymoquinone in Combination with Nivolumab on Experimental Renal Cell Cancer Models**
OKMEN Sena	PP16 - **Clinical Significance of NRF2 and KEAP1 Expressions in non-Small Cell Lung Carcinoma**



COURSE SPEAKER (CS) ABSTRACTS

(CS1 – CS5)

04 June 2022 ''Omics Technologies and Biological Interpretation in Cancer Research'' Course	
12:30-12:45	**OPENING SESSION** **SEZERMAN Ugur, Prof.Dr., Acibadem Mehmet Ali Aydinlar University, Biostatistics and Medical Informatics** **DEMOKAN Semra, Prof.Dr. Istanbul University, President of the Basic Oncology Society**
	Moderators: SEZERMAN Ugur, Prof.Dr., DEMOKAN Semra, Prof.Dr.
12:45-13:30	CS1 - **CICEK Ercument, Assist.Prof.Dr.** High Throughput Sequencing and Bioinformatic Analyses for Characterization of Genetic Diseases
13:30-13:40	**Break**
13:40-14:25	CS2 - **SEZERMAN Ugur, Prof.Dr.** Drug Targeting
14:25-14:35	**Break**
14:35-15:20	CS3 - **CAKIR Tunahan, Assoc.Prof.Dr.** Metabolic Networks and Omics Data
15:20-15:30	**Break**
15:30-16:15	CS4 - **TUNCBAG Nurcan, Assoc.Prof.Dr.** Network Medicine: Leveraging Integrated Connections of Multi-Omic Data
16:15-16:25	**Break**
16:25-17:10	CS5 - **GUNGOR-BAKIR Burcu, Assist.Prof.Dr.** Network and Pathway Based Analysis of Multi-Omic Data to Enlighten Molecular Mechanisms of Complex Diseases
17:10-17:20	**Break**
17:50-18:00	**CLOSING CEREMONY**

From the Editor

Journal of Advanced Research in Health Sciences started its publication life in 2018. It is one of the periodicals of Istanbul University and published in accordance with international standards three times a year, in February, June and October.

It is my pleasure to share that our journal is included in the indexes of TR Index as of 2021, and as of 2022, EBSCO CINAHL Ultimate, EBSCO Central & Eastern European Academic Source, CAB Abstracts, CABI Global Health, CABI Nutrition and Food Sciences, and Directory of Open Access Journals (DOAJ).

Two Supplements were published until today in our journal which provides a wide range of services in the field of health: One on Covid-19 in June 2020 under the editorship of Assoc Prof Selda Hançerli, and the other on Covid-19 and Ethics in October 2021 under the editorship of Prof İlhan İlkılıç.

This year, we are here with an additional issue consisting of the abstracts of the 1st International Basic Oncology Congress held in our country under the presidency of Prof Semra Demokan. New Horizons in Cancer Research: Big Data, Systems Biology, New Molecular Discoveries were presented and discussed at the congress, with endless thanks to the contributing scientists.

Prof. Zeynep Karakas

Editor

Journal of Advanced Research in Health Sciences

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INVITED SPEAKER ABSTRACTS
Journal of Advanced Research in Health Sciences /
Sağlık Bilimlerinde İleri Araştırmalar Dergisi 2022
DOI: 10.26650/JARHS2021-1133643 [IS-001]

EPIGENETIC MECHANISMS OF SOY ISOFLAVONES IN PROSTATE CANCER TREATMENT

Ömer KÜÇÜK[1]

[1]Winship Cancer Institute of Emory University, Atlanta, Georgia, USA

ABSTRACT

Soy intake has been associated with a lower risk of prostate cancer. Soybeans contain isoflavones, genistein, daidzein and glycitein, which have shown anti-cancer effects in cell culture and animal studies. Recently clinical trials of soy isoflavones in humans have also shown promising results. Soy isoflavones have anti-oxidant and anti-inflammatory properties which may be important for their anticancer effects. In addition, recent studies have shown significant epigenetic effects of soy isoflavones. DNA methylation and histone acetylation has been reported to be modified by genistein. Therefore, genistein may have effects similar to the commonly used cancer drugs, demethylating agent 5-azacytidine and histone deacetylase inhibitor drug Vorinostat. Thus, combining genistein with cancer chemotherapeutic agents may have potential benefits. Furthermore, radiation therapy and conventional cancer therapeutic agents activate NF-kappa-B resulting in resistance to chemotherapy and radiation. Genistein is a potent inhibitor of NF-kappa-B, and thereby may sensitize cancer cells to chemotherapy and radiation therapy. While sensitizing cancer cells chemotherapy and radiation, at the same time genistein may protect the normal tissues from adverse effects of radiation chemotherapy which are due to their oxidative and inflammatory effects. Clinical trials investigating the chemotherapy and radiation therapy potentiating as well as toxicity reducing effects of soy isoflavones are warranted. In addition, adverse effects of androgen deprivation therapy, such as metabolic syndrome, hypertension, diabetes and cardiovascular disease could also be potentially prevented by soy isoflavones.

Keywords: Isoflavones, Prostate Cancer, Epigenetic Mechanism

INVITED SPEAKER ABSTRACTS
Journal of Advanced Research in Health Sciences /
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DISCOVERY OF NOVEL EPIGENETIC BIOMARKERS IN ORAL MALIGNANT LESIONS BY EPIGENOMICS AND TRANSCRIPTOMICS APPROACHES*

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ABSTRACT

Objectives: DNA methylation, which is the most frequently observed epigenetic change, is very important because it is seen in the early stages of cancer. Abnormal methylation of promoter regions and silencing of tumor suppressor genes play a key role in the development of oral squamous cell carcinoma (OSCC). In our study*, it was aimed to identify and validate new biomarker candidates via epigenomics/transcriptomics approaches, to understand the molecular mechanisms of OSCC and to discover new biomarkers for early diagnosis.
Materials and Methods: After DNA/RNA isolation of tumor/matched-normal tissue samples from 6 OSCC patients, BC-DNA/cDNA synthesis was performed, respectively. The methylation and expression profiles were analyzed by the R(v3.5.1) environment methods using IlluminaHumanMethylation450chips and IlluminaiScan, respectively. A candidate gene showing methylation-dependent expression loss after bioinformatic analysis was validated by QRT-PCR AND QMSP methods in tissues and body fluids of 20 OSCC and 20 oral premalignant lesions (OPML) patients, respectively.
Results: To identify epigenetic biomarker candidate, we selected gene which show either hypermethylation and lower expression patterns. This candidate gene (unpublished data), which is belong subfamily of the protein-tyrosine kinase, was found to be methylated in 65% of tumors, 20% of matched-normal tissues of OSCC. The methylation rates of the candidate gene in tumor, matched-normal tissues and saliva of OPML patients were found to be 55%, 40% and 10%, respectively. The decreased expression levels of candidate gene were observed in 55% OSCC and 35% OPML tumors, respectively.
Conclusions: Our candidate gene could be a biomarker for early detection of OSCC.
Keywords: Epigenomics, Transcriptomics, OSCC, Biomarker, Non-Invasive

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DATA SCIENCE, CANCER AND SEQUENCING ANALYSES

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ABSTRACT

Recent developments in technology led to exponential growth in processing speed, storage capacities and communication rates. These available resources allowed the creation of thousands of applications that run on smart devices and the world wide web. Today we generate lots of data using these applications and the availability of vast digital data created a new field: data science. Data science aims to utilize digital data to develop solutions to improve human life. Next-generation sequencing technologies enabled the generation of high-throughput genomic data from DNA and RNA. Considering the great potential for genomic data to understand biological functions and the substantial drop in sequencing costs; the amount of available data increased exponentially over time. Sequencing technologies are based on the shredding of the DNA and capture of short reads. These reads are then combined to identify the genomic map of the biological sample. Some of our studies are based on extraction of multiple samples from a tumor and application of sequencing on these samples to understand the tumor development, progression and drug response. Unfortunately, all the frequently used analysis algorithms are based on optimistic assumptions. High level of disparity is observed in literature and in our studies when we compare different algorithms. Currently, we do extensive testing on realistic scenarios to understand the sources of variation in the results. Finally, we develop a user-friendly analysis platform for comparative sequencing analyses to enhance the cooperation among scientists with different backgrounds on sequencing projects.
Keywords: Data Science, Genomic Data, Sequencing Technologies

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TUMOR-ASSOCIATED MICROBIOME

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ABSTRACT

The human body is an intricate complex containing an estimated three trillion Mo members alongside its own cells and genes. Host-microbiome interactions in many parts of the body comprehensively govern multiple physiological processes and various multifactorial disease conditions. In the last decade, with advances in next-generation sequencing, the study of the human microbiome in oncology has become a rapidly developing and interesting field. It has been suggested that microbiome communities influence the development, progression, metastasis formation, and treatment response of multiple cancer types. Understanding the molecular mechanisms of such cancer-modulating interactions and the effects on cancer therapy is considered of great scientific and clinical importance. Although causal evidence of microbial effects on cancer biology is beginning to emerge and the microbiome can enable the development of new cancer-related diagnoses and treatments, little is still known. Microbes and microbiota contribute to carcinogenesis through multiple mechanisms. Specially, microbiome-cancer modulation is driven by a host-microbe interactions such as contact-dependent, contact-independent, and immunological mechanisms, by altering the balance of host cell proliferation and death, and influencing the immune system functions, the metabolism of host-produced factors, and the formation of microbial products. Beyond the gut, the tumor-associated microbial communities, located in the tumor, tumor microenvironment, and other part of the body, can interact with the tumor cells, immune cells, and tumor microenvironment, subsequently leading to cancer progression and treatment outcome. However, there is still a great need for standardization of the methodology and the quality control in microbiome studies, alongside further translational studies.
Keywords: Cancer, Microbiome, Dysbiosis, Carcinogenesis, Immune Mechanism

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DISSECTION OF T CELL ACTIVATION PHASES FOR CHECK POINT BLOCKADE IMMUNOTHERAPY

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ABSTRACT

Checkpoint blockade immunotherapy relies on the restoration of effector responses in precursor-exhausted T cells. Nevertheless, many inhibitory receptors are upregulated soon after the activation and reach high levels at effector phases. In addition to the functional status of type 1 helper T (Th1) cells, the timing and duration of PD-1 and CTLA-4 blockade are considered as critical factors for retaining T cell responsiveness. Here, we used a previously established ex-vivo model to display the decline in Th1 responses and to determine the state-of-function which may critically modulate the success of checkpoint blockade. In the absence of PD-1 and/or CTLA-4 blockade, proliferation and IFN-γ, TNF-α, IL-2 secretion capacities of Th1 cells were gradually abolished as the stimulation was continued. When applied at an early activation stage, the extension of blockade period interfered with the upregulation of multiple inhibitory receptors (PD-1, LAG3, TIM-3, and CTLA-4) and restricted Th1 hyporesponsiveness. The inhibitory receptors that were already expressed prior to the blockade were also downregulated potentially through an endocytic pathway. A time point representing the late stages of effector Th1 responses, which preceded the exhaustion, was determined as a therapeutic window for a short-term check point blockade. In conclusion, PD-1 and CTLA-4 checkpoint inhibitor therapy not only adjust the reactivation of hyporesponsive T cells but can also restrict the induction of de novo T cell exhaustion.

Keywords: Immunotherapy, Checkpoint Inhibitor, Therapy

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IMPACT OF COMPREHENSIVE GENOMIC PROFILING NGS PANELS IN PRECISION ONCOLOGY: THE CITY OF HOPE CMDL EXPERIENCE

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ABSTRACT

The City of Hope (COH) Comprehensive Cancer Center provides a multidisciplinary, collaborative environment where basic, clinical, and translational research intersect and is recognized as one of the leaders in cancer treatment. The COH Clinical Molecular Diagnostic Laboratory (CMDL) has been a pioneer in molecular diagnostics with over twenty years of clinical experience in both somatic and germline molecular testing.
The CMDL has been offering multiple next generation sequencing (NGS)-based comprehensive genomic profiling panels, HopeSeq Panels, for many years to guide clinicians in diagnosis, prognosis, and therapeutic strategies in cancer treatment by providing expanded coverage for the clinical trials and the gene targets which are recommended and cited by the professional organizations including the World Health Organization (WHO), the European Leukemia Net (ELN), the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO). Being a designated laboratory for the NCI-ComboMATCH study by the National Cancer Institute (NCI), these comprehensive genomic profiling panels have strengthened COH's leading position in cancer research and treatment and have further expanded its position as a leading provider of Precision Oncology.
The comprehensive genomic profiles of each patient are reviewed in daily multidisciplinary genomic tumor board meetings by an expert team which includes molecular pathologists, clinical molecular geneticists, hematopathologists and clinicians prior to reporting to ensure the variants are appropriately classified based on AMP/ACMG guidelines in the context of the patient's cancer.
Keywords: Genetic Profile, Deep Sequencing, Personalized Medicine, Genomic Tumor Board

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STEROIDOGENESIS PATHWAY AND BREAST CANCER: EMPOWERING PERSONALIZED TREATMENT WITH A METABOLOMICS APPROACH

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ABSTRACT

The relationship between steroid hormones and breast cancer has been known for decades. Steroid hormones play an active role in cellular proliferation in this cancer type and show their mitogenic effects by binding to estrogen, progesterone, and androgen receptors. Reducing the concentrations of active hormones in the systemic circulation may be insufficient to prevent the progression of the cancer, as it will enable the selection of tumor/peripheral cells that synthesize active steroids from circulating steroid precursors. The intracrine capacity of breast tissues now also has become an emergent area of interest in metabolomic research.

With the development of the current omics technologies, we are able to define and quantify small metabolic differences with precision not only from body fluids but tissues which can be associated with clinicopathological factors in early-stage invasive breast cancer cases. As our understanding grows about the regional steroid metabolism in breast cancer tissues, metabolomic biomarkers will be used more and more to shape the best way of personalized treatment approach of this deadly disease.

Keywords: Steroid Hormone, Breast Cancer, Steroidogenesis Pathway

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DETERMINATION OF THE THERAPEUTIC EFFECT OF VULPINIC ACID AND VULPINIC ACID-RESPONSIVE miR-197-3P IN BREAST CANCER TREATMENT BY *IN VITRO* AND *IN VIVO* STUDIES

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ABSTRACT

Breast cancer is the most common type of cancer in women and an effective treatment method has not been developed yet. Researchers are working on alternative treatment options that do not have toxic side effects based on the patient's resistance to chemotherapeutics over time. Our study revealed molecular characterization and in vivo experimental studies of vulpinic acid and vulpinic acid-responsive miRNAs on breast cancer. miRNAs formed by the application of vulpinic acid on breast cancer and normal cells were determined by microarray analysis. The genes and pathway analyses targeted by miRNAs were determined using bioinformatics tools. As a result of the bioinformatic analysis, it was determined that miR-197-3p was associated with breast cancer. The anti-proliferative activity of miR-197-3p responsive to vulpinic acid was determined in MCF-7 breast cancer and MCF-12A cells. Peptide identification was performed to evaluate the effect of vulpinic acid-responsive miR-197-3p at the proteome level, and the relationship between target proteins was determined using bioinformatics tools. A xenograft breast cancer model was used to understand the in vivo effects of vulpinic acid and miR-197-3p on breast cancer. The obtained results revealed the effect of vulpinic acid-responsive miR-197-3p on the development of breast cancer and strengthened the possibility of an alternative treatment method in the future. With the data obtained, the effect of vulpinic acid-responsive miR-197-3p in breast cancer treatment was determined for the first time and presented to the literature and the pharmaceutical industry as an effective, reliable, and cost-effective treatment approach.

Keywords: Vulpinic acid, Drug Candidate Molecule, miR-197-3p

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WHEN MEIS IS UP IN PROSTATE CANCER, THEN MEISi?

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ABSTRACT

Prostate cancer (PCa) is the second most diagnosed cancer in males. Understanding the molecular mechanism and investigation of novel ways to block PCa growth or metastasis are vital and a medical necessity. In this study, we examined differential expression of MEIS1/2/3 and its associated factors in PCa cell lines. MEIS1/2/3 content, reactive oxygen species, cell cycle status, metastatic activities were analyzed in PCa cells pre and post MEIS inhibitor (MEISi) treatments, which is developed in our laboratory as a first-in-class small molecule inhibitor. A correlation was detected between MEIS content and MEISi IC50 values of PCa cells. MEISi decreased the viability of PC-3, DU145, 22Rv-1 and LNCaP cells, and significantly increased apoptosis in parallel with the increased cellular ROS content. The efficacy of MEISi was shown to positively correlate with the levels of MEIS1/2/3 proteins and the long-term exposure to MEISi elevated MEIS1/2/3 protein content in PCa cells. Administration of MEISi was also tested in PC-3 and 22Rv1 xenograft models of SCID mice to block in vivo tumor growth and metastasis. Our findings suggest that MEISi could be used to target PCa with high MEIS expression to lower PCa viability and growth, however, further studies are needed to achieve in vivo efficacy.
Keywords: Prostate cancer, MEIS, Small Molecules

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NEXT-GENERATION SEQUENCING IN CANCER: GENETIC DIAGNOSIS, RISK PREDICTION AND CLASSIFICATION

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ABSTRACT

In recent years, developments in the field of next-generation sequencing have led to a decrease in prices, making NGS an essential tool in routine diagnosis. Targeted approaches such as gene panels and exome sequencing have provided many advantages in discovering somatic variants with the help of powerful computational algorithms. However, such targeted approaches fall short regarding the discovery of structural variants and regions of non-coding DNA such as introns, non-Coding RNAs, or regulatory elements. Today, the use of whole-genome sequencing is increasing; open-source databases are developing. However, the difficulty of functional studies related to non-coding regions slows down the development of knowledge on this subject and creates a bottleneck in cancer diagnosis and treatment processes. The combination of new generation technologies such as CRISPR-Cas9, Single-cell sequencing, and long-read sequencing provides excellent advantages in discovering and interpreting variants in non-coding regions but creates new generation problems. The ever-increasing need for computational power and the need for trained and highly qualified personnel make the institutionalization of NGS infrastructures rather difficult, which affects the diagnostic processes of patients at the end of the day. Within the scope of this talk, current developments and new generation approaches to these issues will be focused.

Keywords: Next-Generation Sequencing, Exome Sequencing, Cancer Diagnosis

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APPLICATIONS OF TRANSCRIPTOMICS METHODS IN BREAST CANCER

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ABSTRACT

Gene expression studies using cDNA microarrays have revolutionized the breast cancer subclassification. The application of RNA sequencing technologies has revealed additional complexity of breast cancer. The integrated genomic/transcriptomic analysis of breast tumors (METABRIC) and the Cancer Genome Atlas (TCGA) with clinical follow-up data shaped the molecular landscape of breast cancer the last decade. High-throughput RNA sequencing technologies have shown that large proportions of mammalian transcriptome include regulatory non-protein-coding RNAs (ncRNAs) besides protein-coding RNAs. Role of ncRNAs have been well documented in breast cancer. Using RNA sequencing and probe-based transcriptome analyses, several studies, including ours, have emphasized the role alternative splicing events in breast cancer progression. We have demonstrated that Epithelial Splicing Regulatory Protein 1 (ESRP1), a splicing factor, is associated with poor prognosis and endocrine resistance in human ER-positive (ER+) breast tumors. These studies have further implicated that aberrant regulation of alternative splicing plays an important role in all hallmarks of cancer and provide novel strategies for the therapeutics in breast cancer. In addition to bulk sequencing, deconvolution methods such as CIBERSORT was useful to understand the role of individual cells in cancer progression. Using TCGA and METABRIC cohorts, we identified immune-subtypes with better outcomes in triple negative breast cancer (TNBCs). Recently, single cell RNA-seq (sc-RNAseq) and spatial RNA-seq technologies have enabled analysis of single tumor cell phenotypes and intratumor heterogeneity. The application of these technologies to formalin-fixed paraffin-embedded (FFPE) tumor samples with clinical outcomes will present a valuable resource for understanding the inter and intra-tumor heterogeneity in breast cancer.

Keywords: Breast Cancer, RNA Sequencing, ncRNAs, Alternative Splicing, CIBERSORT, Spatial Transcriptomics

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PRECISION ONCOLOGY- BASIC TO BEDSIDE

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ABSTRACT

Basic science technologies and platforms have unraveled the molecular basis of carcinogenesis, both genetic and epigenetic events. Few of the events which are repeatedly observed and are actionable, gave birth to the science "Precision Oncology". The evolution of molecular testing has made a major stride in the recent times, and has empowered personalized cancer medicine over the conventional blanket treatment. Among the important diagnostic technologies, Next Generation Sequencing (NGS) based in-vitro diagnostics have contributed substantially to comprehensive genomic profiling (CGP) in clinical practice that is meant for the detection of substitutions, insertions and deletions (indels), copy number alterations, and gene rearrangements, as well as genomic signatures including Microsatellite Instability (MSI), Loss of Heterozygosity (LOH), Homologous Recombination Defect (HRD Score), Tumor Mutation Burden (TMB). CGP has come into clinical practice with various guidelines endorsing its clinical utility in various indications, both tumor specific and tumor agnostic. Lung cancer is an excellent example where the role of NGS based comprehensive genomic profiling (CGP) has been recommended upfront either on tissue or blood (Liquid Biopsy). In ovarian cancer, calculation like LOH or HRD score, based on the tissue NGS, has widen the eligibility of PARP inhibitor drugs. Further, NTRK fusions, MSI and TMB biomarkers are universal supporting tumor agnostic approach. CGP is a tremendous diagnostic application but brings challenges especially interpretation which are affected by intra/inter tumor heterogeneity, identification of multiple driver mutations, multiple targets and treatment options, cross talk of various mutations and genomic signatures, and various signaling pathways, variable variant allele frequency (VAF), cut-offs for various scores like TMB, LOH, HRD. All these challenges are currently overcome by Molecular Tumor Boards, where basic science understanding in conjunct with clinical experience, has made a huge difference. Thus, offering true precision oncology with unique treatment options for individual patient.

Keywords: Precision Oncology, Personalized Cancer Medicine, Next Generation Sequencing, Comprehensive Genomic Profiling

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THERAPEUTIC IMPLICATIONS OF TARGETED SEQUENCING AND miRNA-SEQ OF B CELL LYMPHOMAS

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ABSTRACT

Objective: Next-generation sequencing (NGS)-based approaches facilitated the identification of genomic and transcriptomic alterations associated with the development of B-cell lymphomas. Identification of these aberrancies during diagnosis may be helpful in choosing the most appropriate targeted therapy. Follicular lymphoma and Burkitt lymphoma are B-cell non-Hodgkin lymphomas with the potential to benefit from molecular targeted therapy.
Materials and Methods: Targeted sequencing or miRNA-Seq were performed on FFPE tumor tissues of FL and pediatric BL (pBL) cases, respectively, using the HiSeq system. Cancer- associated somatic mutations were identified in FL tumor tissue DNA samples through a computational bioinformatics pipeline. miRNAs overexpressed in pBL cases compared with the tonsil centroblasts of non-cancer control cases were identified through differential expression analyses. Sanger sequencing or qRT-PCR were used to cross-validate targeted NGS and miRNA-Seq results, respectively. The literature search was performed to evaluate the therapeutic potential of these somatic mutations and upregulated miRNAs.
Results: Targeted sequencing of FL tumor tissues revealed activating mutations in genes of biological processes or oncogenic signaling pathways. Several miRNAs were identified to be significantly overexpressed in pBL cases. The literature search revealed that targeted therapeutic approaches may be available for the FL or pBL patients with the identified mutations or upregulated miRNAs in tumor tissues.
Conclusion: Targeted NGS may be applied during diagnosis to choose appropriate therapy for FL patients. Upregulated miRNAs provide unique opportunities for personalized targeted therapy of pBL patients.
Keywords: Follicular Lymphoma, Burkitt Lymphoma, Next-generation Sequencing, Molecular Targeted Therapy, Precision Medicine

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DIETARY-BASED MOLECULAR TARGETS AND THERAPEUTIC OPPORTUNITIES IN CANCER

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ABSTRACT

Diet influence human health in different ways. But it is well known that diet can adversely affect various human pathologies, like obesity, diabetes, hypertension, and cancer. The relationship between diet, obesity and cancer has been studied for different types of cancer such as breast, colorectal and gastric cancers. High fat diet induced obesity is an established risk factor for cancer in many tissues. In the mammalian intestine, tumorigenesis is facilitated by a pro-obesity high-fat diet (HFD) by enhancing PPAR (peroxisome proliferator-activated receptor) nuclear receptor activation. PPARs induced fatty acid oxidation increased stem cell number and tumorigenesis. The rate controlling enzyme of fatty acid oxidation, CPT1A, dampens the pro-tumorigenic phenotype by blunting HFD effect in ISCs. High-fat ketogenic diet also elevates ISC function and regeneration capacity through βOHB-mediated Notch signaling, but a glucose-supplemented diet has the opposite effects. High glucose diet also presents an indirect link between sugar and cancer. The relationship dietary supplements used in addition to the diet and cancer is frequently studied. In literature, there is strong evidence on the anticancer effects of anthocyanins, curcumin, vitamin D, and their mechanisms.

Keywords: Cancer, Diet, Molecular Targets, Therapy Medicine

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REAL WORLD EVIDENCE AND BIG DATA

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ABSTRACT

Knowledge has been the key to better organization and new developments. With more information, what kind of arrangement and organization is needed to present the best? Indeed, data collection on its subject is an essential part of any organization. Beyond the purpose of accurately reflecting the current status of certain criteria, these data can also be used for anticipatory-predictive prediction of future trends, and this process is carried out considering that this can have many benefits.

Today, this knowledge accumulation and evaluation effort has created the need to deal with tons of data from all areas of our lives such as security, social activities, science, work, and health. But after a point, this 'data storm' flow, provided by current technologies, became unmanageable with the technologies at hand, the number of experts who could evaluate and interpret, and the time that could be allocated. In this way, the term 'big data' was coined to describe large and no longer adequately manageable data. Now there is a need for new strategies that will allow us to organize the data and produce useful information, to use this big data to meet various future needs. This has become so important that a new field of science called 'data Science' has emerged. data science; It deals with data management for the flow, storage, classification-management of data and its analysis in order to obtain deeper estimations, and it is of great importance in the functionality or services of the system that will provide this.

Keywords: Biostatistics, Big data, Research Design, Real World Evidence

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TRANSLATIONAL RESEARCH ETHICS

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ABSTRACT

The purpose of translational research is to test novel therapeutic strategies and drugs throughout basic and clinical research. The basic concept of translational research is 'Bench to Bedside', defining the collaboration between clinicians and basic scientists. That means translational research involves synergistic partnerships between industry, foundations, and public health services. The collaboration between partners provides a network structure that uses multiple methods and technologies to harmonize parameters such as complexity, expertise, safety, and efficiency with national regulations, institutional policies, and best practices that govern cell, animal, and human research. One might think that the ethics of translational research is simple because there are extensive rules regarding basic and clinical research ethics. Nevertheless, translational research brings new tools to the scene such as employing biomarkers based on omics technology and genomics. On the other hand, data science using real-world data, big data, data mining, and artificial intelligence is another huge leverage for translational research bringing new ethical and legal issues, especially concerning data protection. Therefore, new ethical issues arise that have not been addressed before. As the name reflects, translational research ethics should be considered as the means of a literal translation as well. Ethics should serve to translate the language used by different disciplines and moreover by all stakeholders including social areas from the public to the governmental bodies etc. to translate these different languages and attitudes to each other and make the science more transparent and reliable.

Keywords: Translational, Research, Clinical, Ethic

ORAL PRESENTATION ABSTRACTS

ORAL PRESENTATION ABSTRACTS
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TRANSCRIPTOMIC DIFFERENCES IN MONOZYGOTIC TWINS WITH OVARIAN CANCER

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ABSTRACT

Objectives: The most significant barrier to treating epithelial ovarian cancer(EOC), is the late diagnosis and the emergence of chemotherapy resistance in the early stages.The ineffectiveness of standard treatment protocols in advanced-stage cases highlights the value of individualized EOC treatment.Even monozygotic(MZ) twins, with almost the same genotype in nature, can develop different phenotypic characteristics throughout life.
Materials-Methods: In this context, the peripheral blood and ovarian tissues of monozygotic twins who are discordant in terms of ovarian cancer and the other healthy sibling who is a BRCA1 mutation carrier were compared in the study to analyze all RNA molecules transcribed at the genome level using next-generation sequencing technology.Through analyzing the molecules transcribed in the whole genome,the genetic variations underlying the development of ovarian cancer in a high-risk family bearing the BRCA1 mutation but only one of whom was found to have ovarian cancer were examined.
Results: As a result of the transcriptomic analysis of the total RNA of 6 samples obtained from the ovarian tissues and peripheral blood samples of MZ twins with ovarian cancer and healthy sibling, the protein-encoding protein that shows expression changes in tissue and blood compared to healthy people genes,lncRNAs,precursor-miRNAs and fusion-transcripts have been identified.Filtering procedures and expression change coefficients(log2Fc) were calculated based on the expression data of identified ovarian cancer tumor markers CA125 and CA15-3.
Conclusions: According to our study the expression levels of 66 protein-coding genes,23 novel lncRNAs,9 miRNAs and,2 fusion transcripts were found to vary in three groups and,these molecules are thought to be candidate molecules associated with epithelial ovarian cancer.
Keywords: monozygotic twins, Epithelial Ovarian Cancer, RNA Sequence Analysis, Gene Expression Profiling

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miR-3653-3P EXPRESSION IN PERIPHERAL BLOOD OF PATIENTS WITH OVARIAN CARCINOMA

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ABSTRACT

Ovarian cancer is a late-stage cancer with early and frequent recurrence, and there is still no effective treatment.There are no sensitive and specific biomarkers to be used effectively in the early diagnosis and treatment of the disease.Those currently used in the clinic are extremely insufficient for the early diagnosis and treatment follow-up of the disease, in terms of accurately determining the minimal residual disease.Many studies have shown that deregulation or dysfunction of miRNAs in the small non-coding RNA class contributes to cancer development However, it is known that the expressions of a number of miRNAs differ in ovarian cancer. Examining the expression patterns of known miRNAs in cancer research by comparing them between patients and healthy people is extremely important in terms of finding disease-specific biological markers, and determining the roles of these molecules in the pathogenesis of ovarian cancer is also significant.In the thesis study presented, the expression profile of miR-3653-3p was investigated in a control group consisting of 150 high-risk ovarian cancer patients and 100 healthy individuals, and both groups were compared with each other.It was found that the expression level of miR-3653-3p in the peripheral blood of ovarian cancer patients was 9.49 times higher than the control groups and the results were shown to be statistically significant($p = 0.00$).In addition to these results, whether miR-3653-3p can be used as a non-invasive biomarker in peripheral blood for ovarian cancer was evaluated by ROC analysis and it was shown that the molecule in question was a statistically significant biomarker.
Keywords: Ovarian Carcinoma, miRNA Expression, miR-3653-3p, Biomarker

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INVESTIGATION OF THE EXPRESSION LEVEL OF miR 142-3P IN OVARIAN CARCINOMA

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ABSTRACT

Objective: The most common cancers in women are breast, thyroid, colorectal, uterine corpus, lung and ovarian cancer. Ovarian cancer causes more than 150,000 deaths annually worldwide. The fact that this cancer manifests itself in the late stage and is a disease characterized by poor prognosis causes the vast majority of cases to result in death.The target of diagnosis and treatment of ovarian cancer is to reduce the number of deaths and to increase the quality of life.miRNAs play a role in the pathology of many diseases, including cancer.
Materials and Methods: In the preliminary study on miRNA in our group, 99 candidate miRNAs were found to be used in the diagnosis and followup of ovarian cancer. In the presented thesis study, the expression level of miR-142-3p among these miRNAs was examined comparatively with a larger ovarian cancer patient group and control group. In the study, which includes 147 patients and 100 healthy control groups, the expression level of miR-142-3p was determined using the RealTime PCR method. Differences between the expression levels of miR-142-3p detected in peripheral blood lymphocytes of ovarian cancer patients and healthy controls were statistically evaluated.
Result: It was found that miR-142-3p expression level increased more than 3 times in ovarian cancer patients compared to healthy controls, and this difference was found to be statistically significant (p = 0.00).
Conclusion: As a result suggest that miR-142-3p may be a sensitive, non-invasive biomarker in the early diagnosis of ovarian cancer, but further research is needed to investigate and evaluate the related molecule in ovarian benign diseases.
Keywords: Ovarian cancer, miR-142-3p Expression, Biomarker

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DOWNREGULATION OF SLC-16 CAN INCREASE APOPTOSIS LEVEL IN GASTROINTESTINAL CANCER

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ABSTRACT

Background: Gastrointestinal cancers constitute 35% of all cancer-related deaths and chemotherapy resistance is a major challenge for the treatment of these cancers. The SLC gene family encodes various group of membrane transmitters that play critical roles in establishing cellular homeostasis by transporting ions and different molecular groups. To date, studies have revealed the active roles of some of SLC members in chemotherapy resistance in various malignancies. However, there is no study to investigate the roles of SLC-16 gene in tumor biology. Therefore, we aimed to consider the effects of downregulation of SLC-16 in cell lines related to gastrointestinal cancers.
Methods: SCL-16 expression was downregulated in SW-480, KATO-3and PANC-1 cell lines using sh-RNA transfection. RT-PCR and western blot were performed to prove downregulation of SCL-16 knockdown levels in these cell lines. Then, Oxaliplatin was treated to all cells and the effects of this drug were evaluated by cell cycle, apoptosis, and cell migration assays in downregulated SRC cells.
Results: SLC-16 was found to be down-regulated after sh-RNA transfection at the mRNA and protein levels. In the downregulated group of SCL-16, it was detected that Oxaliplatin increased apoptosis and cell numbers in the G-1 of the cell cycle but had no effect on the cells' ability to metastasize.
Conclusion: SLC-16, one of the SLC families, plays critical roles in the stabilization of cancer cells, and targeting applications of this gene may be a potential way to enhance the effects of chemotherapy in gastrointestinal cancer.
Keywords: Gastrointestinal cancer, SLC-16, Chemotherapy

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PRECISION MEDICINE IN NEUROBLASTOMA: EXPERIENCE WITH NEXT GENERATION SEQUENCING

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ABSTRACT

Objectives: The objective of this study is to examine neuroblastoma patients that were examined by next generation sequencing (NGS) for targeted therapy related specific gene mutations including Anaplastic Lymphoma Kinase (ALK)
Materials and Methods: Molecular examinations of neuroblastoma according to Turkish Pediatric Oncology Group protocols (Nmyc amplification, 11q23 deletion, 1p36 deletion, DNA ploidy by Cell cycle kit in flow cytometer) is studied in our department in all cases collected from Turkey. Among these cases, the patients that recurred even after multi model therapies, are requested NGS to evaluate for targeted therapy decision. We study single nucleated variations after DNA isolation using Pillar Onco/Reveal Multicancer v4 with CNV Panel with 60 genes (ALK, BRAF, ERB2, PIK3CA, EGFR, KRAS, MET, ….) on İllumina Miniseq platform.
Results: We especially reported ALK mutations which has indication for crizotinib or alectinib. Out of our investigated patients only 22% (9/41) had ALK mutations. Two patients (22%) had R1275Q mutation, six patients (66,7%) had F1174L mutation and one patient (11%) had L1226F, S1189F, V1135A and G1225S mutations.
Conclusion: Our patient cohort seems to be showing ALK mutations and F1174L (sensitive to alectinib) mutation more often than R1275Q mutation (sensitive to crizotinib) in neuroblastoma cases. The reason that ALK mutation ratio is higher than literature. The reason of this might be because of selection of patients by the clinicians. These patients received targeted therapies and had longer survival.
Keywords: Neuroblastoma, Next Generation Sequencing, Anaplastic Lymphoma Kinase

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REPURPOSING DRUGS FOR CANCER THERAPY

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ABSTRACT

Cancer remains a second leading cause of death worldwide. The economic burden of cancer is increasing day by day due to the morbidity, recurrence, and poor prognosis of this disease. Over the last decades, there is an increasing need to discover and development effective and safe therapeutic agents for cancer. Traditionally, the development and approval of new drugs are long term and also costly. Therefore, this has encouraged scientists to repurposing of known drugs for the treatment of cancer. This strategy has been considered as a good way to offer safe, effective and cost-effective new anticancer drugs. Approximately, 300 non-cancer drugs have been shown to exhibit anticancer effect on different cancer cells, thus they are promising anticancer potential and, candidates for development. However, the appropriate and comprehensive research is required in order to define exact mechanism, dosage and toxicity potential of repurposed drugs. A broad range of therapeutic strategies should be used in order to assess the success of repurposed drugs in replacement of conventional cancer therapies or enhancement of chemotherapy.
Keywords: Cancer, Drug Repurposing, Therapy, Off-Target, Oncology

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THE EFFECT OF SILENCING THE Tip60 GENE ON THE RESPONSE TO RADIOTHERAPY IN BREAST CANCER CELLS

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ABSTRACT

One of the most important problems encountered in patients with triple-negative breast cancer (BC) treatment is the inadequate response of tumor tissue to treatment. The high expression of the Tip60, which is involved in the repair of DNA double-strand breaks, will increase the repair of DNA damage to be created in tumor cells, especially during the radiotherapy treatment process, thus reducing the treatment response and having a negative effect. In this study, the *Tip60* gene was silenced using siRNA in MCF-7 and MDA-MB-231 cell lines, and their response to radiotherapy was monitored. To determine whether gene silencing was successful or not, Tip60 mRNA and protein expression values were measured. Cytotoxicity and DNA damage in UV-treated cells were analyzed by MTT and COMET methods, respectively. According to the results of the study, more DNA damage was observed in the MCF-7 in which the *Tip60* gene was silenced and UV-treated compared to the non-*Tip60* gene-silenced and UV-treated cells. On the other hand, more DNA damage was observed in the MDA-MB-321 in which the *Tip60* gene was non-silenced and applied UV, compared to the cells in which the Tip60 gene was silenced. However, excessive DNA damage was already observed in the untreated MDA-MB-231. According to the results, silencing of the TiP60 gene in the MCF-7 may be beneficial in reducing resistance to radiotherapy, but no effect is expected in the MDA-MB-231. This can be explained by the fact that they are heterogeneous tumors. These data could use for future treatment development studies.
Keywords: Breast cancer cells, Tip60, siRNA, Radiotherapy, Comet

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INVESTIGATION OF CIRCULAR RNAs AS BIOMARKERS IN HEAD AND NECK CANCER CELLS AND THE EFFECTS OF RADIOTHERAPY ON CIRCULAR RNAs

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ABSTRACT

Objective: The head and neck squamous cell carcinoma (HNSCC) is the sixth most common type of cancer worldwide and the 5-year survival rate of patients is by 40-50 %. Radiotherapy is one of the important treatments for HNSCC. circRNAs, which are much more stabil than other RNAs because of their circular structure, have the potential to be a biomarker for all types of cancer. Therefore, the alterations of circRNAs expression in HNSCC cells and after irradiation was investigated.
Methods: Pharyngeal cancer (Detroit-562) and healthy fibroblast (WI-38) cell lines were used. After appropriate irradiation dose for Detroit-562 cells was determined by colony formation assay, Detroit-562 cells were irradiated with 4 grays. The expression levels of 122 circRNA molecules in all groups were examined by RT-qPCR. The results were evaluated using CircNet and TCGA platforms.
Results: In this study, 60 circRNAs were not expressed in any cell line, whereas 62 were found to be expressed in at least one of the groups, including irradiated Detroit-562, Detroit-562, and WI-38 cell lines. Among them, seven circRNAs were detected in all groups and expressed higher in Detroit-562 than two groups. Interestingly, these circRNAs were significantly decreased in irradiated group, exhibiting similar expression levels with healthy group. Bioinformatics analyses showed that the host genes of these circRNAs was also higher expressed in HNSCC tissue.
Conclusions: Differential expression of circRNAs in cancers and changes with treatment revealed that they could be potential diagnostic and monitoring biomarkers in cancer. However, further studies need in this regard.
Keywords: circRNA, Biomarker, Irradiation, Head and Neck Cancer, Gene Expression

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EXOSOMES – A NEW FRONTIER IN CANCER THERAPY

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ABSTRACT

Exosomes, also called exosome vesicles (EcVs), contain DNA, RNA (including mRNA, miRNA, and ncRNA), proteins, lipid layer molecules, metabolic enzymes, signal transduction molecules, and other components and are produced in the endosomes of almost all cells, tissues, and body fluids. As exosomal cargoes, they play key roles in signaling pathways, immune regulation, cellular development, carcinogenesis, and homeostasis, providing a potential portal for cell-free drug delivery systems. Exosomal components that vary from cell-to-cell and organ-to-organ, are used to evaluate a biological response. Thus, the variation in the exosomal components makes them promising candidates for biomarkers for cancer detection and diagnosis. Moreover, the recent advances in medicine have revealed that exosomes are capable of crossing the blood-brain barrier and transporting drugs. A growing number of studies have been conducted to understand the therapeutic potential of exosomes in cancer. Because exosomes alter the local and systemic environment for cancer cell development, inhibiting their release is an important treatment strategy. In addition to the targeted use of exosomes, there are also treatment approaches in cancer therapy in which exosomes are used directly for therapeutic purposes. However, previous studies show that exosome-based therapy is very promising. Nevertheless, further research is needed to determine unique biomarkers for clinical application. Therefore, the emerging therapeutic and regulatory potentials of exosomes in the field of cancer research are highlighted through a comprehensive literature review.
Keywords: Exosomes, extracellular vesicles, drug delivery, cancer, biomarkers

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NOVEL EPIGENETIC BIOMARKER DETERMINATION FOR OSCC BY ARRAY-BASED EPIGENOMIC AND TRANSCRIPTOMIC TECHNIQUES

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ABSTRACT

Objectives: Oral squamous cell carcinoma (OSCC) has a high morbidity and mortality rates, but there are no reliable biomarkers to define patients in early phases of disease. In our study (TUBITAK-SBAG-114S497), we aimed to investigate the potential epigenetic biomarker candidate genes observed methylation-dependent expression loss via methylation and expression array methods in OSCC patients.
Material and Methods: Methylation and expression profiling in tumor and conjugate-normal tissue samples of 6 OSCC patients were analyzed by "IlluminaHumanMethylation450 chips" and "Illumina iScan", respectively. Methylation/expression array data were analyzed and interpreted by R(v3.5.1) environment using ChAMP and limma/lumi packages, and then the significant decreased expression changes due to hypermethylation of the candidate gene was detected. The selected candidate gene was validated in tumor and matched-normal tissues and body fluids (serum and saliva) of 20 OSCC patients by QRT-PCR/QMSP methods.
Results: According to the array results, it was determined that the expression levels of the candidate gene were decreased due to methylation (DiffScore:13.18826; FoldChange:-1.08345). This candidate gene (unpublished data), which plays an important role in ubiquitin-ligase activity, was found to be methylated in 45% tumor, 40% matched-normal tissue, 10% serum and 30% saliva samples. 50% of the patients observed methylation in the tumor tissue showed the differentially decreased expression levels.
Conclusion: It is thought that this candidate gene, whose expression level decreased due to methylation, will be a candidate epigenetic biomarker for the early diagnosis of the subtypes of OSCC. Further validation of this candidate gene will be needed in the larger OSCC cohorts.
Keywords: Oral Squamous Cell Carcinoma, Methylation, Expression, Biomarker

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METHYLATION AND EXPRESSION VALIDATION RESULTS OF *GPRC5C* GENE OBTAINED FROM EPIGENOMICS AND TRANSCRIPTOMICS DATA IN ORAL CAVITY TUMORS

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ABSTRACT

Objective: Demokan et.al idetified *G/Protein/Coupled/Receptor/Class-C/Group-5/Member-C (GPRC5C)* as a candidate gene in OSCC via expression and methylation array results (logFC:0.59663; DeltaBeta: -0.130984561) from their previous unpublished data. In our study, the methylation and expression status of *GPRC5C* gene was investigated in a larger group of OSCC patients and healthy cohort for further validation. Its potential candidate biomarker was evaluated for early diagnosis of OSCC by non-invasive methods.
Materials and Methods: DNA and RNA were isolated from tissues/body fluid samples of 30 patients OSCC and 15 healthy individuals. The methylation and expression levels were analyzed by using QMSP and QRT-PCR methods, respectively. The data were compared with clinical parameters and evaluated by statistical analysis.
Results: Decreased expression levels were observed in 43% and increased expression levels were observed in 33% in the tumor tissues compared to corresponding-normal tissues of OSCC patients. Methylation-based expression loss was observed in 4 patients having the ratio between 3.4 and 12.2%. We also observed a decrease in expression in OSCC patients with observed methylation. There was statistical significance between differentiation degree and expression in OSCC.
Conclusion: It was concluded that *GPRC5C* may play a role as a potential methylation biomarker candidate of specific subgroups of the oral cavity. Other mechanisms need to be explored to understand the differences in expression levels.
Keywords: gene expression, DNA methylation, OSCC, *GPRC5C*

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A PHYLOGENETIC APPROACH TO EVALUATE THE RELATION BETWEEN miRNA EXPRESSIONS AND HEPATITIS C VIRUS IN HEPATOCELLULAR CARCINOMA

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ABSTRACT

Objective: Hepatitis C virus(HCV) infection increases the risk for Hepatocellular carcinoma (HCC) development, which is the sixth most common cancer type worldwide. HCV-related HCC has high mortality rates and HCV genotype is shown to affect survival in HCC. Two molecules that are known to be associated with poor cancer prognosis in HCC are endoplasmic reticulum transmembrane stromal interaction molecule 1(STIM1) and plasma membrane calcium channel(Orai1).
Materials and Methods: In this study, we have enhanced STIM1 and/or Orai1 expressions in subpopulation of cancer-stem-cell-like cells in Huh7 HCC cell line in order to mimic poor cancer prognosis and performed next generation sequencing on small RNA samples isolated from these cells in order to identify the changes in miRNA expression patterns. Multiple alignment and phylogenetic analysis were used on stem loop sequences of miRNAs with significant expression changes and tried to identify a possible evolutionary relation of these miRNAs with HCV genotypes.
Results: Our results showed that there were 5 different regions in HCV genome where these miRNAs are mostly aligned. miR4521, miR3651, miR7974 and miR6715a showed closed relations with HCV-genotypes-1 and -7 within these regions. These miRNAs also known to be related with cancer progression in several cancer types including HCC.
Conclusion: We propose that a phylogenetic approach can be helpful to evaluate the evolutionary strategies of cancer promoting viruses as well as possible viral origins of miRNAs that play role in cancer progression.
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Keywords: Hepatocellular carcinoma, Hepatitis C Virus, miRNA

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LONG NON-CODING RNAs AND AUTOPHAGY IN OSTEOSARCOMA

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ABSTRACT

Osteosarcoma (OSA) is an aggressive bone tumor that occurs primarily in children and adolescents worldwide, with a high metastatic and recurrence ability. OSA is characterized by the transformation of mesenchymal cells and the formation of osteoid tissue. Although recent advancements have improved the current therapeutic management of OSA, the clinical outcomes of the disease still remain unsatisfactory. Therefore, it is important to determine the novel diagnostic markers and/or therapeutic targets for OSA. Autophagy is a highly conserved self-degradative process that plays a crucial role in various physiological mechanisms such as survival, homeostasis, development and differentiation. Dysfunction of autophagy is the relationship with the onset and development of several types of cancer, including OSA. Long non-coding ribonucleic acids (lncRNAs), a group of non-coding RNAs, regulate various pathophysiological mechanisms such as inflammation, autophagy and apoptosis. Recent studies investigating the role of lncRNAs in the pathogenesis of OSA have shown that these molecules might have diagnostic and therapeutic importance for the prevention of OSA. Here, we focus on lncRNAs that modulate autophagy in OSA and discuss the potential clinical values of lncRNAs for OSA. The current study contributes to a better understanding of OSA pathogenesis and to the development of novel therapeutic approaches for the prevention of OSA.
Keywords: Autophagy, Cancer, Osteosarcoma, LncRNA

POSTER PRESENTATION ABSTRACTS

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CircRNAs OF SALIVA AS POTENTIAL BIOMARKERS FOR COLORECTAL CANCER DIAGNOSIS

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ABSTRACT

Objective: Early and accurate diagnosis are key factors in the successful treatment of colorectal cancer (CRC). Therefore, the discovery of new, reliable, and non-invasive biomarkers in CRC patients is becoming an attractive topic in cancer research. Circular RNAs (circRNA) are RNAs that have high stability and can be tissue specific. In addition, expression levels can be detected in various non-invasive samples such as saliva and serum, due to these properties, they can be a biomarker for various cancer, can be substituted by invasive methods in CRC
Methods: In this study, 25 circular RNAs in the literature related to CRC were evaluated for the first time in saliva samples. For this purpose, the expression level of 25 circular RNAs in saliva samples of 25 CRC patients was investigated by comparing them with 25 healthy control samples.
Results: We found that the expression level of 9 circular RNAs varied significantly between the two groups. In addition, ROC curve analysis showed that hsa_circ_0078767 could potentially be a biomarker candidate in CRC diagnosis.
Conclusion: The study showed the potential for circRNAs, particularly hsa_circ_0078767, to be a noninvasive biomarker in CRC, but further studies with more subjects are needed to confirm these results.
Keywords: Colorectal Cancer (CRC), Circular RNA (circRNA), Real time PCR, Saliva

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EVALUATION OF EXOSOME-DERIVED CircRNA EXPRESSION PATTERNS IN LUNG CANCER RADIOTHERAPY

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ABSTRACT

Background: Radiotherapy is an effective method used in the treatment of lung cancer. However, it is very difficult to assess the clinical manifestations of radiotherapy at an early stage and the relevant criteria are very limited. Exosome-derived circRNAs (exo-circRNAs) have potential as biomarkers for early a cancer diagnosis and treatment assessment as exosomes are present in a variety of body fluids and circRNAs in exosomes exhibit high stability. Therefore, we aimed to investigate for potential biomarker candidates by evaluating changes in exo-circRNA expression with radiotherapy in lung cancer.
Method: In this study, lung cancer epithelial (A549) and healthy lung fibroblast (WI38) cell lines were used. After colony assay, both cell lines were irradiated with 4 Gy and exosomes were isolated by ultracentrifugation method. Exosomes were characterized by flow cytometry and nanoparticle tracking analysis, and RNA isolation was performed by trizol protocol. Then, the expression levels of 40 exo-circRNAs in all groups were examined by RT-qPCR.
Results: Of the exosomal circRNA investigated, 5 exo-circRNAs were found to be expressed in at least one of the groups, including A549, WI38, irradiated A549 and irradiated WI-38 cell lines. In particular, hsa_circ_0014235 and hsa_circ_0001900, which were found to be expressed in all groups, were more upregulated in cancer cell lines than healthy cell line. Significant changes were detected in the expression levels of these exo-circRNAs after irradiation.
Conclusions: Differential expression of exo-circRNAs between cancer and healthy group and alterations by irradiation suggests that they may be potential diagnostic and monitoring biomarkers in cancer.
Keywords: Exosome, CircRNAs, Lung Cancer, Radiotherapy, Biomarkers

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LIPOPOLYSACCHARIDE INHIBITS AUTOPHAGY IN HUMAN DERMAL FIBROBLASTS *IN VITRO*

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ABSTRACT

Objective: Fibroblasts are mesenchymal cells of dermal origin that provide structural integrity for connective tissue by producing the extracellular matrix proteins. They are the dominant component of the tumor microenvironment and are then referred to as cancer-associated fibroblasts (CAFs). CAFs play an important role in cancer cell growth. Autophagy is an intracellular self-degradative process that balances cell energy sources and regulates tissue homeostasis. Autophagy is now considered a critical process in skin health and skin cancer. The objective of this study is to investigate the effect of lipopolysaccharide (LPS) on the autophagy mechanism in human dermal fibroblasts (HDFs) in vitro.

Methods: HDFs were incubated with 0.1, 0.5, 1 and 5 µg/mL of LPS for 24 h. The viability of cells was determined using WST-1 assay. The protein expressions of beclin-1, p62, LC3-I and LC3-II were analyzed by Western blotting.

Results: The viability of HDFs incubated with 0.1, 0.5, 1 and 5 µg/mL of LPS did not show any significant differences compared to untreated cells. Beclin-1 protein expression was upregulated with all LPS concentrations. The protein expression of p62 was also induced with all LPS concentrations. Furthermore, the ratio of LC3-II/LC3-I protein expression was increased with all LPS concentrations.

Conclusion: Our results demonstrate that LPS inhibits autophagy in HDFs through the upregulation of p62 and LC3 protein expression. These findings suggest the relationship between inflammation and autophagy in skin cells and might contribute to understanding the key role of autophagy in the development of skin cancer.

Keywords: Autophagy, Human Dermal Fibroblast, Inflammation, Lipopolysaccharide

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microRNA AS A PROMISING POTENTIAL BIOMARKER FOR COLORECTAL CANCER

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ABSTRACT

Objectives: Colorectal cancer (CRC)is a highly preventable and treatable disease when detected early. microRNAs (miRNAs) have the potential to serve as ideal noninvasive biomarkers. The aim of this study was to determine the diagnostic and prognostic biomarker potential of some miRNAs in serum samples of patients with CRC.
Methods: 75 patients with CRC and 75 healthy individuals were enrolled in the study. Serum samples of the patients were obtained before and three months after surgery and once from healthy controls. The relative expression levels of miR-23, miR-223, miR-12469, and miR-150 in the serum of samples were determined using quantitative real-time PCR. The results were evaluated the receiver operating characteristic (ROC) curve analysis.
Results: The expression level of mir-150 was significantly up-regulated in CRC compared to healthy group. The expression levels of miR-23 and miR-223 in serum were non-significantly up-regulated in CRC patients. But there were no changes in the expression level of miR-1246 in both groups. In addition, expression levels of miR-23 and miR-223 were significantly down-regulated three months after surgery, whereas miR-150 showed a significant level of up-regulation. However, there is no significant relationship between the serum levels of these genes and the clinical characteristics of CRC patients. By ROC curve analysis, only miR-23 and miR-150 were found to be able to distinguish CRC patients from controls with relatively high accuracy.
Conclusions: Taken together, the expression levels of miR-23 and miR-150 in serum may be potential biomarker candidates for the diagnosis and prognosis of CRC.
Keywords: Colorectal cancer (CRC), micro-RNAs (mi-RNAs), miR-23, miR-223, miR-12469 and miR-150

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POTENTIAL OF microRNAs AS A BIOMARKER FOR LARYNGEAL CANCER

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ABSTRACT

Objective: Laryngeal malignancy known as the most frequently diagnosed cancer between head and neck tumor, covering 2.4% of all tumors and is the 11th most occurrence and deadliest tumor in the world. Research has shown that microRNAs (miRNAs) play a considerable role in the development of laryngeal malignancy. Moreover, studies also focus on the relationship between clinical relevance and miRNA deregulation in cancer illness. According to recent evidence, miR-205, miR-126, miR-302, and miR-132 have possible roles in the carcinogenesis process of the LSCC. Therefore, in this research, we aimed to investigate whether there are any considerable changes in the microRNAs expression level and also if they have any remarkable potential as a prognostic or diagnostic biomarker for laryngeal squamous cell carcinoma (LSCC).
Methods: Thirty LSCC patients were included in this research, and tumor tissues and healthy normal tissues were collected during laryngectomy. Total RNA extraction from the normal and cancer tissues was accomplished and after the quality control, cDNA was synthesized, and finally, target miRNAs expression was determined by qPCR. The expression level of genes and their relationship with the patient's clinicopathological characteristics were analyzed using appropriate statistical tests.
Results: According to the study results, miR-302 (fold change: 1.o5, P-value = 0.0001) and miR-132 (fold change: 1.28, P-value = 0.0001), is considerably overexpressed in cancer tissues compare to normal peripheral tissues. We also found that miR-126 (fold change: 0.251, P-value = 0.0001) and miR-205 (fold change: 0.241, P-value<0.0001) is down-regulated in LSCC tumor tissue. Among these microRNAs, only mir-205 expression had no association with clinical-pathological features in tumor tissue.
Conclusion: The results of this research revealed the potential of the miR-302, miR-132, miR-126, and miR-205 as prognostic or diagnostic biomarkers in LSCC.
Keywords: Laryngeal cancer, Micro-RNAs, Biomarker

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S-100 PROTEIN EXPRESSION LEVELS AS A POTENTIAL PROGNOSTIC MARKER IN NEUROBLASTOMA

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ABSTRACT

Objective: S-100 is an acidic-calcium-binding protein and was first described in cells of neuroendocrine origin. It plays an important role in various cellular processes such as cell differentiation and proliferation. S-100 is described to be a negative prognostic marker for the advanced stages of melanoma and was evaluated to be prognostic biomarker for different cancers. Neuroblastoma(NB) is remarkable for its broad spectrum of clinical behavior, varying from spontaneous regression to progressive disease and accounts for ~15% of childhood cancer-related mortality. This diversity in behavior correlates closely with defined clinical and biologic features and combinations of prognostic variables are used for risk-group assignment. The aim of this study is to investigate the S-100 expression levels among neuroblastoma patients and to determine if S-100 expression levels could be prognostic biomarker for neuroblastoma.

Materials and Methods: Histological tumor sections of 40 cases of varying stages and risk groups of neuroblastoma were studied. The patients were staged according to criteria defined by Turkish Pediatric Oncology Group and International Neuroblastoma Staging System(INSS). Risk groups were determined according to the International Neuroblastoma Risk Group(INRG) classification system. S-100 protein expression levels were evaluated by immunohistochemical staining on paraffin sections of neuroblastoma patient tissue samples. All sections were independently and blindly studied for protein expression under microscopic examination. P values<0.05 was accepted statistically significant.

Results: Schwann cells in the ganglioneuromas and ganglioneuroblastomas always strongly stained. Neuroblastoma cases with early stage and low-to-intermediate risk showed upregulated expression.

Conclusion: While study is still ongoing, preliminary results showed that S-100 could be a candidate prognostic marker for neuroblastoma patients.

Keywords: Neuroblastoma, Prognosis, S-100, Biomarker

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ANALYSIS OF TRIBBLES HOMOLOG 3 (TRIB3) EXPRESSION LEVELS IN NEUROBLASTOMA: PRELIMINARY STUDY

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ABSTRACT

Objective: Tribbles protein (TRIB) family was first identified in Drosophila, plays role in coordinating cell division and morphogenesis. TRIB3 is one of the members of this family, its protein expression levels and patient prognosis has been examined in various studies. While TRIB3 expression was correlated with poor prognosis in hepatocellular cancer patients, its expression levels were associated with increased disease-free survival and a better response to therapy in luminal breast cancer patients.

Neuroblastoma (NB) is the most common solid tumor in children and accounts for ~15% of childhood cancer-related mortality. In the present study, we aimed the investigate the TRIB3 expression levels among NB patients and to determine if TRIB3 expression levels could be prognostic biomarker for NB.

Materials and Methods: 40 children with different stages of NB were studied. The patients were staged according to criteria defined by Turkish Pediatric Oncology Group and International Neuroblastoma Staging System. Protein expression levels of TRIB3 was determined with immunohistochemical staining on paraffin sections of NB patient tissue samples. All sections were independently and blindly studied for protein expression under microscopic examination. P values <0.05 was accepted statistically significant.

Results: TRIB3 expression was found to be upregulated in low grade samples and ganglioneuroblastoma samples and downregulated in neuroblastoma cells in the tissue sections of high-grade NB samples.

Conclusion: While study is still ongoing, preliminary results showed that TRIB3 could be a candidate prognostic marker for NB patients.

Keywords: Neuroblastoma, Cell signaling, Biomarker, Prognostic marker

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INVESTIGATION OF METHYLATION AND EXPRESSION STATUS OF *PAX1* GENE VIA EPIGENOMIC PROFILING IN ORAL MALIGNANT LESIONS

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ABSTRACT

Introduction: Our previously study (TUBITAK-SBAG-114S497) showed hypermethylation of the *PAX1* gene in Turkish oral squamous cell carcinoma (OSCC) patients via methylation-array results. In this study, we aimed to validate its potential as an epigenetic biomarker for OSCC by analyzing the methylation status and the changes in methylation-related gene expression of the *PAX1* gene in Turkish OSCC patient and healthy groups.
Material and Methods: Expression and methylation levels of *PAX1* gene were analyzed by Quantitative Real Time-PCR and Quantitative Methylation Specific PCR methods respectively, in tissues and body-fluid samples of 30 OSCC patients and 30 healthy individuals.
Results: The methylation rates of the *PAX1* gene in matched-normal tissue, tumors, serum and saliva samples of OSCC patients were 50%, 73%, 40%, and 66%, respectively. The methylation rates of the *PAX1* gene in normal mucosa, serum and saliva samples of healthy individuals were found to be 6%, 0 and 10%, respectively. In the malignant group, 59% patients in whom methylation was observed in the promoter region of the *PAX1* gene in the tumor tissue was found to have decreased expression levels in the tumor tissues compared to the matched-normal tissues.
Conclusion: DNA hypermethylation of *PAX1* gene may play a role in oral carcinogenesis and may be used as an epigenetic biomarker.
Keywords: OSCC, Hypermethylation, Epigenetic Biomarker, *PAX1*

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miRNA-REGULATED PATHWAYS OF CD8+ T CELLS IN TNBC MOUSE MODEL

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ABSTRACT

Objective: Triple negative breast cancer, which constitutes 20% of all breast cancer is the most aggressive breast cancer subtype. Although breast cancer is known as immune cold, recent studies have revealed that there is an immune response on the basis of subtypes. miRNAs are involved in regulating many biological processes of CD8+ T lymphocytes, which are adaptive immune system cells that effectively destroy tumor cells. Our aim is to examine the regulative roles of miRNAs in CD8+ T lymphocytes during the formation of triple negative breast tumors in mice.
Materials and Methods:4T1 cells and Balb/c mice were used for the allograft breast cancer model. After 2 weeks, tumor-bearing and control mice were sacrificed, and spleens were harvested for CD8+ T cell isolation. Following RNA isolation, miRNA microarray analysis was performed. Differentially expressed miRNAs between the groups were detected. DIANA-mirPath web tool was used to investigate the target genes of miRNAs and in which pathways these genes are enriched.
Results: Microarray analysis indicated that 41 miRNAs are differentially expressed in CD8+ T cells from tumor-bearing mice compared to the control group. The KEGG analysis results showed that the targets of differentially expressed miRNAs were significantly enriched in immune response-related pathways like ECM-receptor interaction, PI3K-Akt signaling, and tryptophan metabolism pathways.
Conclusion: The pathways in which miRNA-target genes are enriched are associated with T cell metabolism and cell survival. It may be concluded that there are changes in the systemic adaptive immune response during TNBC formation and that miRNAs regulate these changes.
Keywords: Triple Negative Breast Cancer, CD8-Positive T-Lymphocytes, Adaptive Immune Response, microRNA

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INVESTIGATION OF THE EFFECT *PISTACIA VERA* FROM DIFFERENT REGIONS ON OXIDATIVE STRESS AND PROLIFERATION IN BREAST CANCER CELL LINE

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ABSTRACT

Objective: To investigate the effectiveness of extracts obtained from the inner shell of *P. vera* plants collected from different regions
Materials and Methods: Flavanol and methanol extracts were prepared from the inner shell of *P. vera*. The cytotoxic effects of the prepared extracts on invasive breast cancer cell lines were determined by our modified MTT cytotoxicity test. Total antioxidant and total oxidant tests were applied, and oxidative stress indices were examined. Migration test was used to investigate the effects of the agents used on the motility of the cells, and colony formation assay was performed to investigate the effect on the colony forming feature.
Results: *P. vera* methanol extracts were found to be more cytotoxic than flavanol extracts. Siirt *P. vera* Methanol extract was found to be the most cytotoxic extract. *P. vera* Urfa dissolved in methanol extract due to has high oxidative stress was the most effective in reducing migration in MDA-MB-231 cell line among the groups.
Conclusions: Urfa *P. vera* Methanol extract is most effective in invasive breast cancer cells due to high oxidative stress level that occurs.
Keywords: P. vera, MTT, Cytotoxicity, Migration, Colony Formation

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INVESTIGATION OF THE POTENTIAL EFFECTS OF YAP-1 AND NESTIN ON RISK CLASSES AND PROGNOSIS IN NEUROBLASTOMA

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ABSTRACT

Introduction: Neuroblastoma (NB) is the most common solid tumors in childhood. MYCN is the main prognostic factor for risk classification and staging in NB patients. YAP (Yes Associated Protein) plays a critical role in many types of cancer. In NB, YAP expression levels may be correlate with advanced tumor staging. Nestin is an important neuronal differentiation and cancer stem cell marker in NB. The aim of this study is to examine the potential roles of YAP-1 and Nestin expressions in terms of prognosis and risk classifications for neuroblastoma.
Materials and Methods: Histological tumor sections of 55 cases were examined. YAP-1 and Nestin protein expression levels were evaluated by immunohistochemical staining on paraffin sections of different neuroblastoma risk groups. YAP-1 and Nestin expression levels were evaluated with clinical findings of NB patients. P value was <0.05 accepted as a statistically significant.
Results: 55 patient tissues were included in this study, of which 24 were male and 21 were female. The ages of the patients are between 1 month to 11 years. YAP-1 protein was expressed in 36.4% in MYCN(+)and 14.6% in MYCN(-) patients. Nestin protein was expressed 36.4% in MYCN(+), and 20.6% in MYCN(-) patients. YAP-1 was expressed 18% in all tissues. Nestin expressions were determined 20.4% in all tissues. YAP-1 was expressed in 26.9% in high-risk and 11.5% in low-risk groups. Nestin was expressed 24.4% in high-risk and 33.3% in low-risk groups.
Conclusion: YAP-1 and Nestin might be a clinically risk markers for neuroblastoma patients.
Keywords: Neuroblastoma, YAP-1, Nestin

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ANTIMETASTATIC POTENTIAL OF CUCUMIN IN ANAPLASTIC THYROID CANCER AND COMBINED ACTIVITY WITH DOCETAXEL

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ABSTRACT

Anaplastic thyroid cancer (ATC) is one of the deadliest human malignancies, with no effective treatment, survival limited to a few months. The disease is characterized by a high rate of metastasis and is resistant to almost all available cytotoxic. There is an urgent need for chemicals with an effective, low toxicity profile.

Objective: In study, the antimetastatic property of tetrahydrocurcumin (THC), the active metabolite of Curcuma Longa, was compared with docetaxel and the presence of synergism in the combination of the two substances was investigated in vitro.

Material and Method: IC25 and IC50 concentrations of THC and (DX) in CAL62 and 8505C cells were determined by modified MTT method we developed in our laboratory. These 2 concentrations were compared with the control in the treatment groups. Cell motility as an indicator of metastatic potential was evaluated by in-vitro wound healing method. Cellular cytotoxicity was evaluated by TAS-TOS analyses.

Results: In the 8505C cell line, Total antioxidant status was observed in the DXB-CRC IC50/2 group with a significant statistical increase.

THC significantly reduced the oxidative stress index in the highest combination group, especially in DXB.

It was found that the combined dose prevented migration and invasion in CAL62 cells in the first hours. There was no difference in Total Oxidant level between the combination and control groups. It was observed that the most effective dose that significantly reduced the oxidative level was DX50.

THC in ATK cells has antimetastatic potential close to Docetaxel; It was thought that docetaxel reduced oxidative stress.

Keywords: Cell Motility, Docetaxel, Curcuma Longa, Oxidative Stress, Wound Healing

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INVESTIGATION OF THE ANTIMETASTATIC POTENTIAL OF *T. SPICATA* IN HUMAN BREAST ADENOCARCINOMA CELLS COMBINED WITH STANDARD CHEMOTHERAPY

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ABSTRACT

Objective: The aim of this study was to determine the effects of hexane extract prepared from Thymbra spicata (TS) on the cytotoxic, antioxidant and metastatic process in human breast adenocarcinoma cell lines (MDA-MB-231, BT-474) in combination with the chemotherapeutic drug Paclitaxel (PAC).
Materials And Methods: IC25 and IC50 concentrations of TS and PAC in MDA-MB-231 and BT-474 cell lines were determined by the modified MTT method we developed in our laboratory. Cell motility as an indicator of metastatic potential was evaluated by in vitro wound healing method. MDA was evaluated in cellular cytotoxicity in MB 231 by TAS and TOS analyses.
Results: IC25 and IC50 concentrations of TS and PAC in MDA MB 231 and BT-474 cell lines were determined by the modified MTT method we developed in our laboratory. Cell motility as an indicator of metastatic potential was evaluated by in vitro wound healing method. MDA was evaluated in cellular cytotoxicity in MB 231 by TAS and TOS analyses.
In wound healing experiments where migration and invasion were tested: MDA MB 231; There was no statistically significant difference in the effect of PAC and TS25/PAC25 doses on cell migration. BT-474; TS and TS25/PAC25 doses were found to be effective in stopping cell migration.
Conclusion: The findings revealed the prediction that TS may be among the candidate agents in terms of giving as supportive treatment.
Keywords: Thymbra Spicata, Migration, Oxidative Stress

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EFFECT OF THYMOQUINONE IN COMBINATION WITH NIVOLUMAB ON EXPERIMENTAL RENAL CELL CANCER MODELS

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ABSTRACT

Objectives: Thymoquinone a bioactive component extracted from the seeds of Nigella sativa, has been proved to have antiinflammatory, antioxidant properties anti antitumor efficiency against breast, prostate, bladder, and renal cell cancer. We aimed to investigate the synergistic cytotoxic and apoptotic effects of thymoquinone in combination with nivolumab, an immuno-control inhibitor, and its mechanism in renal cell cancer models.
Materials and Methods: In vitro studies: Caki-1 and Renca renal cancer cell lines with mononuclear cells were cocultured and thymoquinone and nivolumab effect were analyzed by MTT and Annexin V + PI. In vivo studies: Renal cell cancer model was provided by subcutaneous injection of RENCA cells to C57BL/6, male, 8 weeks old mice in four groups. Control group, thymoquinone (1,4,7,14days,20mg/kgIP), nivolumab administered (1,6,13days10mg/kgIP), thymoquinone and nivolumab. Seven animals was randomized in each experimental group. Apoptosis, necrosis, CD4,CD8,C20,CD34,CD31,VEGF-A by immunohistochemistry, FGFR-1,PDGFRbeta,VEGFR-2,c-kit,RET,c-Met,AXL,Flt-3,TIE2, ICAM-1,VCAM-1 and E-selectin mRNA levels by quantitative real-time-PCR were evaluated on tumor tissue. Liver, kidney, brain, lung and heart tissues was evaluated for side effects. Plasma biochemistry tests were performed. Statistical analysis was be performed with Mann-Whitney U test with $p < 0.05$ value.
Results: Thymoquinone showed antitumor effect in vitro and in vivo. It also showed increase in immune cell death of nivolumab. Tumor tissue showed prominent necrosis or complete response to therapy in combination group.
Conclusions: We conclude that thymoquinone has antitumor effect on renal cell carcinoma and increases the effect of nivolumab immune, cell death effects. Besides, it does not have side effect on other organs whether alone or in combination.
Keywords: Renal Cell Cancer, Thymoquinone, Immune Check Point Inhibitors

COURSE SPEAKER ABSTRACTS

COURSE SPEAKER ABSTRACTS
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NETWORK AND PATHWAY BASED ANALYSIS OF MULTI-OMIC DATA TO ENLIGHTEN MOLECULAR MECHANISMS OF COMPLEX DISEASES

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ABSTRACT

The tremendous boost in the next generation sequencing technologies and in the "omics" technologies makes it possible to look for the coordinated behavior among different levels of biochemical activity. Irrespective of the technology used, the advent of high-throughput profiling technologies presents a new challenge, that of interpretation of these data in a meaningful manner – to uncover relationships that are not readily apparent between molecular profiles and states of health or disease. In contrast to isolated molecules, network and pathway oriented analyses are thought to better capture pathological perturbations and hence, better explain predisposition to disease. In this talk, firstly I will introduce different types of multi-omics data integration methods. Along this line, I will present existing trans-omics, merge-omics, multi-omics, panomics strategies as an example of integrative omics studies. Secondly, I will focus on network and pathway based integration techniques. In this respect, I will mention different functional enrichment analysis techniques including over-representation analysis (ORA), gene set enrichment analysis (GSEA) methods, integrative and modular enrichment analysis (MEA). Thirdly, I will summarize our approach and present how this approach can help us to identify disease-associated pathway markers. Lastly, I will conclude via discussing how these pathway markers can help us to enlighten individual disease development mechanisms and personalized targets for treatments, and hence bridging the gap between the -omics data and precision medicine.

Keywords: Multi-Omics, Network and Pathway Based–Omics Data Analysis, Functional Enrichment

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Amaç ve Kapsam

Sağlık Bilimlerinde İleri Araştırmalar Dergisi (SABİAD); bağımsız, önyargısız ve çift-kör hakemlik ilkeleri çerçevesinde yayın yapan İstanbul Üniversitesi Sağlık Bilimleri Enstitüsü'nün uluslararası ve açık erişimli bilimsel yayın organıdır. Dergi Şubat, Haziran ve Ekim aylarında olmak üzere dört ayda bir yayınlanır ve üç sayıda bir cilt tamamlanır. Yayın dili Türkçe ve İngilizcedir.

Sağlık Bilimlerinde İleri Araştırmalar Dergisi (SABİAD), tıbbın tüm alanlarında klinik ve deneysel, özgün araştırmalar, ender görülebilecek olgu sunumları, özel ve güncel konularda literatür derlemeleri ve editöre mektup yayınlamaktadır. Orijinal metot geliştirme, yeni bir girişim tekniği ve orijinal çalışmaların ön sonuçlarını içeren kısa raporlara da dergide yer verilmektedir.

Editöryal Politikalar ve Hakem Süreci

Derginin editörlük ve yayın süreçleri International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE) ve National Information Standards Organization (NISO) organizasyonlarının kılavuzlarına uygun olarak biçimlendirilmiştir ve Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice) ilkelerine uygun olarak yürütülmektedir.

Özgünlük, yüksek bilimsel kalite ve atıf potansiyelli bir makalenin yayına kabulü için en önemli kriterlerdir. Gönderilen yazıların daha önce başka bir elektronik ya da basılı dergide, kitapta veya farklı bir mecrada sunulmamış ya da yayınlanmamış olması gerekir. Toplantılarda sunulan çalışmalar için, sunum yapılan organizasyonun tam adı, tarihi, şehri ve ülkesi belirtilmelidir.

Sağlık Bilimlerinde İleri Araştırmalar Dergisi'ne (SABİAD) gönderilen tüm makaleler çift-kör hakem değerlendirme sürecinden geçmektedir. Tarafsız değerlendirme sürecini sağlamak için her makale alanlarında uzman en az iki dış-bağımsız hakem tarafından değerlendirilir. Dergi Yayın Kurulu üyeleri tarafından gönderilecek makalelerin değerlendirme süreçleri, davet edilecek dış bağımsız editörler tarafından yönetilecektir. Bütün makalelerin karar verme süreçlerinde nihai karar yetkisi Editöründür.

Klinik ve deneysel çalışmalar, ilaç araştırmaları ve bazı olgu sunumları için World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013, www.wma.net) çerçevesinde hazırlanmış Etik Komisyon raporu gerekmektedir. Gerekli görülmesi halinde yazarlardan Etik Komisyon raporu veya eşdeğeri olan resmi bir yazı talep edilebilir. İnsanlar üzerinde yapılmış deneysel çalışmaların sonuçlarını bildiren yazılarda, çalışmanın yapıldığı kişilere uygulanacak prosedürler tümüyle açıklandıktan sonra, onaylarının alındığına dâir bir açıklamaya metin içinde yer verilmelidir. Hayvanlar üzerinde yapılan çalışmalarda ise ağrı, acı ve rahatsızlık verilmemesi için yapılmış olanlar açık ve net olarak makalede belirtilmelidir. Hasta onamları, Etik Kurul raporunun alındığı kurumun adı, onay belgesinin numarası ve tarihi ana metin dosyasında yer alan Gereç ve Yöntem başlığı altında yazılmalıdır. Hastaların kimliklerinin gizliliğini korumak yazarların sorumluluğundadır. Hastaların kimliğini açığa çıkarabilecek fotoğraflar için hastadan ya da yasal temsilcilerinden alınan imzalı izinlerin de gönderilmesi gereklidir.

Bütün makalelerin eşleşme oranı değerlendirmesi, iThenticate yazılımı aracılığıyla yapılmaktadır.

Yayın Kurulu, dergimize gönderilen çalışmalar hakkındaki intihal, atıf manipülasyonu ve veri sahteciliği iddia ve şüpheleri karşısında COPE kurallarına uygun olarak hareket edecektir.

Yazar olarak listelenen herkesin ICMJE (www.icmje.org) tarafından önerilen yazarlık koşullarını karşılaması gerekmektedir.

ICMJE, yazarların aşağıdaki 4 koşulu karşılamasını önermektedir:

1. Çalışmanın konseptine/tasarımına; ya da çalışma için verilerin toplanmasına, analiz edilmesine ve yorumlanmasına önemli katkı sağlamış olmak;
2. Yazı taslağını hazırlamış ya da önemli fikirsel içeriğin eleştirisel incelemelerini yapmış olmak;
3. Yazının yayından önceki son halini gözden geçirmiş ve onaylamış olmak;
4. Çalışmanın herhangi bir bölümünün geçerliliği ve doğruluğuna ilişkin soruların uygun şekilde sorgulandığının ve çözümlendiğinin garantisini vermek amacıyla çalışmadan her yönüyle sorumlu olmayı kabul etmek.

Bir yazar, çalışmada katkı sağladığı kısımların sorumluluğunu almasına ilaveten, diğer yazarların da

çalışmanın hangi kısımlarından sorumlu olduğunu tanımlayabilmelidir. Ayrıca, her yazar diğer yazarların katkı bütünlüğüne güven duymalıdır.

Yazar olarak belirtilen herkes yazarlığın dört koşulunu karşılamalıdır ve bu dört koşulu karşılayan her bir kişi yazar olarak tanımlanmalıdır. Dört kriterin hepsini karşılamayan kişilere makalenin başlık sayfasında teşekkür edilmelidir.

Derginin Yayın Kurulu, itiraz ve şikâyet durumlarında, COPE rehberleri kapsamında işlem uygular. Yazarlar, itiraz ve şikâyetleri için doğrudan Yayıncılık Birimi ile temasa geçebilirler. İhtiyaç duyulduğunda Yayın Kurulu'nun kendi içinde çözemediği konular için tarafsız bir temsilci atanmaktadır. İtiraz ve şikâyetler için karar verme süreçlerinde nihai kararı Baş Editör verecektir.

Sağlık Bilimlerinde İleri Araştırmalar Dergisi her makalenin https://dergipark.org.tr/tr/pub/sabiad adresinden erişebileceğiniz Telif Hakkı Anlaşması Formu ile beraber gönderilmesini talep eder. Yazarlar, basılı ya da elektronik formatta yer alan resimler, tablolar ya da diğer her türlü içerik dâhil daha önce yayınlanmış bir alıntıyı kullanırken telif hakkı sahibinden izin almalıdırlar. Bu konudaki yasal, mali ve cezai sorumluluk yazar(lar)a aittir.

Dergide yayınlanan makalelerde ifade edilen görüşler ve fikirler Sağlık Bilimlerinde İleri Araştırmalar Dergisi, Editör, Editör Yardımcıları, Yayın Kurulu ve Yayıncı'nın değil, yazar(lar)ın bakış açılarını yansıtır. Editör, Editör Yardımcıları, Yayın Kurulu ve Yayıncı, bu gibi durumlar için hiçbir sorumluluk ya da yükümlülük kabul etmemektedir. Yayınlanan içerik ile ilgili tüm sorumluluk yazarlara aittir.

Yayın Politikası

Dergi yayın etiğinde en yüksek standartlara bağlıdır ve Committee on Publication Ethics (COPE), Directory of Open Access Journals (DOAJ), Open Access Scholarly Publishers Association (OASPA) ve World Association of Medical Editors (WAME) tarafından yayınlanan etik yayıncılık ilkelerini benimser; Principles of Transparency and Best Practice in Scholarly Publishing başlığı altında ifade edilen ilkeler için: https://publicationethics.org/resources/guidelines-new/principles-transparency-and-best-practice-scholarly-publishing

Gönderilen makaleler derginin amaç ve kapsamına uygun olmalıdır. Orijinal, yayınlanmamış ve başka bir dergide değerlendirme sürecinde olmayan, her bir yazar tarafından içeriği ve gönderimi onaylanmış yazılar değerlendirmeye kabul edilir.

Makale yayınlanmak üzere Dergiye gönderildikten sonra yazarlardan hiçbirinin ismi, tüm yazarların yazılı izni olmadan yazar listesinden silinemez ve yeni bir isim yazar olarak eklenemez ve yazar sırası değiştirilemez.

İntihal, duplikasyon, sahte yazarlık/inkar edilen yazarlık, araştrma/veri fabrikasyonu, makale dilimleme, dilimleyerek yayın, telif hakları ihlali ve çıkar çatışmasının gizlenmesi, etik dışı davranışlar olarak kabul edilir. Kabul edilen etik standartlara uygun olmayan tüm makaleler yayından çıkarılır. Buna yayından sonra tespit edilen olası kuraldışı, uygunsuzluklar içeren makaleler de dahildir.

İntihal

Ön kontrolden geçirilen makaleler, iThenticate yazılımı kullanılarak intihal için taranır. İntihal/kendi kendine intihal tespit edilirse yazarlar bilgilendirilir. Editörler, gerekli olması halinde makaleyi değerlendirme ya da üretim sürecinin çeşitli aşamalarında intihal kontrolüne tabi tutabilirler. Yüksek benzerlik oranları, bir makalenin kabul edilmeden önce ve hatta kabul edildikten sonra reddedilmesine neden olabilir. Makalenin türüne bağlı olarak, bunun oranın %15 veya %20'den az olması beklenir.

Çift Kör Hakemlik

İntihal kontrolünden sonra, uygun olan makaleler baş editör tarafından orijinallik, metodoloji, işlenen konunun önemi ve dergi kapsamı ile uyumluluğu açısından değerlendirilir. Editör, makalelerin adil bir şekilde çift taraflı kör hakemlikten geçmesini sağlar ve makale biçimsel esaslara uygun ise, gelen yazıyı yurtiçinden ve /veya yurtdışından en az iki hakemin değerlendirmesine sunar, hakemler gerek gördüğü takdirde yazıda istenen değişiklikler yazarlar tarafından yapıldıktan sonra yayınlanmasına onay verir.

Açık Erişim İlkesi

Dergi açık erişimlidir ve derginin tüm içeriği okura ya da okurun dahil olduğu kuruma ücretsiz olarak sunulur. Okurlar, ticari amaç haricinde, yayıncı ya da yazardan izin almadan dergi makalelerinin tam metnini okuyabilir, indirebilir, kopyalayabilir, arayabilir ve link sağlayabilir. Bu BOAI açık erişim tanımıyla uyumludur.

Makale Hazırlama
Makaleler, ICMJE-Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals (updated in December 2015 - http://www.icmje.org/icmje-recommendations.pdf) ile uyumlu olarak hazırlanmalıdır. Randomize çalışmalar CONSORT, gözlemsel çalışmalar STROBE, tanısal değerli çalışmalar STARD, sistematik derleme ve meta-analizler PRISMA, hayvan deneyli çalışmalar ARRIVE ve randomize olmayan davranış ve halk sağlığıyla ilgili çalışmalar TREND kılavuzlarına uyumlu olmalıdır.

Makaleler sadece https://dergipark.org.tr/tr/pub/sabiad adresinde yer alan derginin online makale yükleme ve değerlendirme sistemi üzerinden gönderilebilir. Farklı mecralardan gönderilen makaleler değerlendirilmeye alınmayacaktır.

Gönderilen makalelerin dergi yazım kurallarına uygunluğu ilk olarak Yayıncılık Birimi tarafından kontrol edilecek, derginin yazım kurallarına uygun hazırlanmamış makaleleri teknik düzeltme talepleri ile birlikte yazarlarına geri gönderilecektir.

Yazar(lar)ın aşağıdakileri sunmaları gerekir:

Telif Hakları Formu

Kapak sayfası: Gönderilen tüm makalelerle birlikte ayrı bir kapak sayfası da gönderilmelidir. Bu sayfada;

- Makalenin Türkçe ve İngilizce başlığı ve 50 karakteri geçmeyen Türkçe ve İngilizce kısa başlığı,
- Yazarların isimleri, kurumları, eğitim dereceleri ve ORCID numaraları
- Finansal destek bilgisi ve diğer destek kaynakları hakkında detaylı bilgi,
- Sorumlu yazarın ismi, adresi, telefonu (cep telefonu dâhil), faks numarası ve e-posta adresi,
- Makale hazırlama sürecine katkıda bulunan ama yazarlık kriterlerini karşılamayan bireylerle ilgili bilgileri içermelidir.

Özet: Editöre Mektup türündeki yazılar dışında kalan tüm makalelerin Türkçe ve İngilizce özetleri olmalıdır. Özgün Araştırma makalelerinin özetleri "Amaç", "Gereç ve Yöntem", "Bulgular" ve "Sonuç" alt başlıklarını içerecek biçimde hazırlanmalıdır. Olgu sunumu ve derleme türündeki yazıların Özet bölümlerinde alt başlıklar yazılmamalıdır.

Anahtar Sözcükler: Tüm makaleler en az 3 en fazla 6 anahtar kelimeyle birlikte gönderilmeli, anahtar sözcükler özetin hemen altına yazılmalıdır. Kısaltmalar anahtar sözcük olarak kullanılmamalıdır. Anahtar sözcükler National Library of Medicine (NLM) tarafından hazırlanan Medical Subject Headings (MeSH) veritabanından seçilmelidir.

Makale Türleri

Özgün Araştırma: Ana metin; "Giriş", "Gereç ve Yöntem", "Bulgular" ve "Tartışma" alt başlıklarından oluşmalıdır.

Özgün Araştırmalarla ilgili sınırlandırmalar için lütfen Tablo 1'i inceleyiniz.

Sonucu desteklemek için istatistiksel analiz genellikle gereklidir. İstatistiksel analiz, tıbbi dergilerdeki istatistik verileri bildirme kurallarına göre yapılmalıdır (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983: 7; 1489-93). İstatiksel analiz ile ilgili bilgi, Gereç ve Yöntemler bölümü içinde ayrı bir alt başlık olarak yazılmalı ve kullanılan yazılım kesinlikle tanımlanmalıdır.

Birimler, uluslararası birim sistemi olan International System of Units (SI)'a uygun olarak hazırlanmalıdır.

Editöryel Yorum: Dergide yayınlanan bir araştırmanın, o konunun uzmanı olan veya üst düzeyde değerlendirme yapan bir hakem tarafından kısaca yorumlanması amacını taşımaktadır. Yazar(lar), dergi tarafından seçilip davet edilir. Özet, anahtar sözcük, tablo, şekil, resim ve diğer görseller kullanılmaz.

Davetli Derleme: Konunun alanında birikimi olan ve bu birikimleri uluslararası literatüre yayın ve atıf sayısı olarak yansımış uzmanlar tarafından hazırlanmış yazılar değerlendirmeye alınır. Yazar(lar) dergi tarafından da davet edilebilir. Bir bilgi ya da konunun klinikte kullanılması için vardığı son düzeyi anlatan, tartışan, değerlendiren ve gelecekte yapılacak çalışmalara yön veren bir düzeyde hazırlanmalıdır. Ana metin; "Giriş", "Klinik ve Araştırma Etkileri" ve "Sonuç" bölümlerini içermelidir. Derleme türündeki yazılarla ilgili kısıtlamalar için lütfen Tablo 1'i inceleyiniz.

Olgu Sunumu: Olgu sunumları için sınırlı sayıda yer ayrılmakta ve sadece ender görülen, tanı ve tedavisi güç olan hastalıklarla ilgili, yeni bir yöntemi tarif eden, kitaplarda yer verilmeyen bilgiler yansıtan, ilgi çekici ve öğretici özelliği olan olgular yayına kabul edilmektedir. Ana metin; "Giriş", "Olgu Sunumu", "Tartışma" ve Sonuç" alt başlıklarını içermelidir. Olgu Sunumlarıyla ilgili kısıtlamalar için lütfen Tablo 1'i inceleyiniz.

Editöre Mektup: Yazar(lar), dergide daha önce yayınlanan bir yazının önemini, gözden kaçan bir ayrıntısını ya da eksik kısımlarını tartışabilir. Ayrıca derginin kapsamına giren alanlarda okurların ilgisini çekebilecek konular ve özellikle eğitici olgular hakkında da Editöre Mektup formatında yazılar yayınlanabilir. Okuyucular da yayınlanan yazılar hakkında yorum formatında Editöre Mektup yazılarını sunabilirler. Bu metinde, özet, anahtar sözcük, tablo, şekil, resim ve diğer görseller kullanılmaz. Ana metin alt başlıksız olmalıdır. Hakkında mektup yazılan yayına ilişkin cilt, yıl, sayı, sayfa numaraları, yazı başlığı ve yazar(lar)ın adları açık bir şekilde belirtilmeli, kaynak listesinde yazılmalı ve metin içinde atıfta bulunulmalıdır.

Tablolar

Tablolar ana dosyaya eklenmeli, kaynak listesi sonrasında sunulmalı, ana metin içerisindeki geçiş sıralarına uygun olarak numaralandırılmalıdır. Tabloların üzerinde tanımlayıcı bir başlık yeralmalı ve tablo içerisinde geçen kısaltmaların açılımları tablo altına yazılmalıdır. Tablolar Microsoft Office Word dosyası içinde "Tablo Ekle" komutu kullanılarak hazırlanmalı ve kolay okunabilir şekilde düzenlenmelidir. Tablolarda sunulan veriler ana metinde sunulan verilerin tekrarı olmamalı; verileri destekleyici nitelikte olmalıdır.

Tablo 1: Makale türleri için kısıtlamalar

Makale türü	Sözcük limiti	Özet sözcük limiti	Kaynak limiti	Tablo limiti	Resim limiti
Özgün Araştırma	3500	250 (Alt başlıklı)	50	6	7 ya da toplamda 15 resim
Davetli Derleme	5000	250	50	6	10 ya da toplamda 20 resim
Olgu Sunumu	1000	200	15	Tablo yok	10 ya da toplamda 20 resim
Editöre Mektup	500	Uygulanamaz	5	Tablo yok	Resim yok

Resim ve Resim Altyazıları
Resimler, grafikler ve fotoğraflar (TIFF ya da JPEG formatında) ayrı dosyalar halinde sisteme yüklenmelidir. Görseller bir Word dosyası dokümanı ya da ana metin içerisinde sunulmamalıdır. Alt birimlere ayrılan görseller olduğunda, alt birimler tek bir görsel içerisinde verilmemelidir. Her bir alt birim sisteme, ayrı bir dosya olarak yüklenmelidir. Resimler alt birimleri belli etmek amacıyla etiketlenmemelidir (a, b, c vb.). Resimlerde altyazıları desteklemek için kalın ve ince oklar, ok başı, yıldızlar, asteriksler ve benzer işaretler kullanılabilir. Makalenin geri kalanında olduğu gibi resimlerde kör olmalıdır. Bu sebeple, resimlerde yer alan kişi ve kurum bilgilerine kesinlikle yer verilmemelidir.. Görsellerin minimum çözünürlüğü 300 DPI olmalıdır. Değerlendirme sürecindeki aksaklıkları önlemek için gönderilen tüm görsellerin çözünürlüğü net ve büyük boyutlu (minimum boyutlar 100x100 mm) olmalıdır. Resim altyazıları ana metnin sonunda yer almalıdır.

Makale içerisinde geçen tüm kısaltmalar, ana metin ve özette ayrı ayrı olmak üzere ilk kez kullanıldıkları yerde açıklanarak kısaltma açıklamanın ardından parantez içerisinde verilmelidir.

Ana metin içerisinde cihaz, yazılım, ilaç vb. ürünlerden bahsedildiğinde ürünün ismi, üreticisi, üretildiği şehir ve ülke bilgisini içeren tüm bilgiler parantez içinde verilmelidir; "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)".

Tüm kaynaklar, tablolar ve resimlere ana metin içerisinde uygun olan yerlere sırayla numara verilerek atıf yapılmalıdır.

Özgün araştırmaların kısıtlılıkları, engelleri ve yetersizlikleri Sonuç paragrafı öncesi "Tartışma" bölümünde yer almalıdır.

Revizyonlar
Yazar(lar) makalelerin revizyon dosyalarını gönderirken, ana metin üzerinde yaptıkları değişiklikleri işaretlemeli, ek olarak, hakemler tarafından öne sürülen önerilerle ilgili notlarını "Hakemlere Cevap" dosyasında göndermelidir. Hakemlere Cevap dosyasında her bir hakemin yorumunun ardından yazarın cevabı gelmeli ve değişikliklerin yapıldığı satır numaraları da ayrıca belirtilmelidir. Revize edilen makaleler karar mektubunu takip eden 30 gün içerisinde dergiye gönderilmelidir. Makalenin revize versiyonu belirtilen süre içerisinde yüklenemezse, revizyon seçeneği iptal olabilir. Yazar(lar) ın revizyon için ek süreye ihtiyaç duyması durumunda uzatma taleplerini ilk 30 gün sona ermeden dergiye iletmeleri gerekmektedir.

Yayına kabul edilen makaleler dil bilgisi, noktalama ve biçim açısından kontrol edilir. Yayın süreci tamamlanan makaleler, yayın planına dâhil edildikleri sayıyla birlikte yayınlanmadan önce erken çevrimiçi formatında dergi web sitesinde yayına alınır. Kabul edilen makalelerin baskıya hazır PDF dosyaları sorumlu yazarlara iletilir ve yayın onaylarının 2 gün içerisinde dergiye iletilmesi istenir.

Kaynaklar
Atıf yapılırken en son ve en güncel yayınlar tercih edilmelidir. Atıf yapılan erken çevrimiçi makalelerin DOI numaraları mutlaka sağlanmalıdır. Kaynakların doğruluğundan yazar(lar) sorumludur. Dergi isimleri Index Medicus/Medline/PubMed'de yer alan dergi kısaltmaları ile uyumlu olarak kısaltılmalıdır. Altı ya da daha az yazar olduğunda tüm yazar isimleri listelenmelidir. Eğer 7 ya da daha fazla yazar varsa ilk 6 yazar yazıldıktan sonra "et al." yazılmalıdır. Ana metinde kaynaklara atıf yapılırken parantez içinde Arap rakamları kullanılmalıdır. Farklı yayın türleri için kaynak stilleri aşağıdaki örneklerde sunulmuştur:

Dergi makalesi: Blasco V, Colavolpe JC, Antonini F, Zieleskiewicz L, Nafati C, Albanèse J, et al. Long-term outcome in kidney recipients from donors treated with hydroxyethylstarch 130/0.4 and hydroxyethylstarch 200/0.6. Br J Anaesth 2015;115(5):797-8.

Kitap bölümü: Sherry S. Detection of thrombi. In: Strauss HE, Pitt B, James AE, editors. Cardiovascular Medicine. St Louis: Mosby; 1974.p.273-85.

Tek yazarlı kitap: Cohn PF. Silent myocardial ischemia and infarction. 3rd ed. New York: Marcel Dekker; 1993.

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