Prof Orhan CANBOLAT, MD, PhD

https://avesis.gazi.edu.tr/ocanbolat
https://yasam.gazi.edu.tr
www.prfdrorhancanbolat.com
Prof. Dr. Orhan Canbolat – Youtube

ACADEMIC TITLES

- 2020 - Professor, Faculty of Medicine, Gazi University

- 2017 - 2020 Professor, Faculty of Medicine, Istanbul Aydin University,
- 2015 - 2016 Professor, Faculty of Medicine, University Of Higher Specialization,
- 2001 - 2013 Professor, Faculty of Medicine, Gazi University

ACADEMİC MANAGEMENT EXPERİENCE

- 2023 -.Head of Department of Medical Biochemittry , Faculty of Medicine, Gazi University
- 2020 -.Director of Health and Application Center, Gazi Universit
- 2017 - 2020 Vice Rector-Istanbul Aydin University
- 2017 - 2020 Head of Department of Medical Biochemisttry , Faculty of Medicine, Istanbul Aydin University
- 2017 - 2019 Dean Faculty of Dentistry, Istanbul Aydin University,
- 2015 - 2017 Rector, University Of Higher Specialization,
- 2003 - 2003 Deputy Chief Physician, Gazi University Faculty of Medicine Hospital

NON-ACADEMIC EXPERIENCE

2013 - 2015 General Director

- Ankara Private Koru Hospital

2003 - 2003 General Director of Health Affairs

- Social Insurance Institution, Ministry of labor and Social Security

2000 - 2002 General Director of Pharmaceuticals and Pharmacy

- Ministry of Health

COURSES

MSc - PhD

- Antimetabolite theory and nucleic acid metabolism
- Gene information - (Replication-Transcription- Genetic code, Post-transcriptional mechanisms, Translation, Post-translational mecanisms)

FACULTY OF MEDİCİNE

- Mitochondria, electron transport chain, ATP synthesis
- Gene information - (Replication-Transcription- Genetic code, Post-transcriptional mechanisms, Translation, Post-translational mecanisms)
- Nucleotide metabolism
- Citric acid cycle
- Free radical metabolism
- Enzyme and enzyme kinetics
- History of genetics.
- Renal function tests
- Science and philosophy of science

GAZI UNIVERSITY
LIFE SCIENCES APPLICATION AND RESEARCH CENTER

HISTORY

According to a regulation published in the Official Gazette on July 9, 2013, the **Molecular Biology Research and Application Centre, the Nanomedicine Research and Application Centre, and the Advanced Technologies Research and Application Centre** merged to form the Life Sciences Application and Research Centre.

MISSION

Our Centre is committed to being a leading research facility that contributes to national and international knowledge by conducting interdisciplinary research in the natural sciences to find solutions to pressing and unanswered questions in the field of life sciences. Our ultimate goal is to commercialise our research findings by creating useful patents and products, which we can then share with the world.

VISION

To serve as a national and international leader in the fields of health, engineering, and basic natural sciences by using its physical space, device infrastructure, and researcher features.

CENTRE MANAGEMENT

- Prof. Dr. Orhan CANBOLAT Director
- Prof. Dr. Mehmet Ali ERGUN Vice Director
- Prof. Dr. Mustafa ARSLAN Vice Director
- Prof. Dr. Burcu ERTIT TASTAN Coordinator
- Associate Prof. Dr. Selcen BABAOGLU AYDAS Coordinator

STEERİNG COMMİTTEE

- Prof. Dr. Orhan CANBOLAT
- Prof. Dr.Mustafa ARSLAN
- Prof. Dr. Mehmet Ali ERGUN
- Prof. Dr. Fazlı POLAT
- Prof. Dr. Cigdem ELMAS
- Prof. Dr. Suleyman ÖZÇELIK
- Associate Prof. Dr. Serdar TORT
-

ADVISORY BOARD

- Prof. Dr. Alper CEYLAN
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- Prof. Dr. Latif AYDOS
- Prof. Dr. Mehmet CAKMAK
- Prof. Dr. Ahmet OZET
- Prof. Dr. Mustafa KAVUTCU
- Associate Prof.Dr. Hasan BOSTANCI

RESEARCH GROUPS

BIOCHEMISTRY - CHEMISTRY RESEARCH GROUP	**BIOTECHNOLOGY RESEARCH GROUP**
PROF. DR. ORHAN CANBOLAT PROF. DR. MUSTAFA KAVUTÇU	PROF. DR. BELMA ASLIM PROF. DR. ZEHRANUR YUKSEKDAG DOÇ. DR. MİNE TÜRKTAŞ
TOXICOLOGY RESEARCH GROUP	**BIOINFORMATIC RESEARCH GROUP**
PROF. DR. HİKMET KATIRCIOGLU	PROF. DR. ŞEREF SAGIROĞLU DOÇ. DR. OKTAY YILDIZ PhD. YILMAZ ATAY PhD. MÜJGAN TELLI OKUR
ENVIRONMENTAL RESEARCH GROUP	**CELL IMAGING TECHNIQUES RESEARCH GROUP**
PROF. DR. SUAT KIYAK PROF. DR. ATİLLA MURATHAN PROF. DR. ZEKI AYTAÇ PROF. DR. MEHMET YILMAZ PROF. DR. A. ÇAGLAN GUNAL	PROF. DR. ÇIGDEM ELMAS PROF. DR. ZEKUYE SULUDERE DOÇ. DR. MERVE SEYMEN
EXPERIMENTAL ANIMALS RESEARCH GROUP	**PHARMACOLOGY RESEARCH GROUP**
DOÇ. DR. KURSAT DIKMEN	PROF. DR. CIMEN KARASU
CELL CULTURE RESEARCH GROUP	**CLINICAL SCIENCES RESEARCH GROUP**
PROF. DR. CIGDEM ELMAS ASSOCİATE PROF.DR. SEVCAN MAMUR	PROF. DR. MEHMET AKIF OZTURK PROF. DR. HAYRUNNISA BOLAY BELEN PROF. DR. MUSTAFA ARSLAN
NANO SCIENCES RESEARCH GROUP	**NANO-GENOTOXICOLOGY RESEARCH GROUP**
PROF. DR. UGUR TAMER PROF. DR. HUSEYIN ÇELIKKAN PROF. DR. GONCA ÇAKMAK DOÇ.DR. SERDAR TORT	PROF. DR. FATMA UNAL PROF. DR. DENIZ YUZBASIOGLU
MICROBIOLOGY RESEARCH GROUP	**MOLECULAR MEDICINE AND GENETICS RESEARCH GROUP**
PROF. DR. GULENDAM BOZDAYI	PROF. DR. MEHMET ALI ERGUN
REPRODUCTIVE MEDICAL RESEARCH GROUP	
PROF. DR. CENGIZ KARAKAYA PROF. DR. ALI ATAN Associate Prof. DR. ISMAIL GULER MD.ERHAN DEMIRDAG MD. DUYGU DAYANIR MD. FUNDA AKDULUM	

Publications 2020 -2023

- Karaboduk Kuddusi, Hasdemir Erdogan (2020). Simultaneous Determination of Quercetin and Luteolin in Mate and White Tea Samples by Voltammetry. Revue Roumaine de Chimie, 65(4), 375-385.

- Ekim Burcu, Calık Ali, Ceylan Ahmet, Sacaklı Pınar (2020). Effects of Paenibacillus xylanexedens on growth performance, intestinal histomorphology, intestinal microflora, and immune response in broiler chickens challenged with Escherichia coli K88. Poultry Science, 99(1), 214-223., Doi: 10.3382/ps/pez460.

- Karaboduk Kuddusi (2021).Development of a voltammetric method for the determination of rapamycin in pharmaceutical samples at pretreated pencil graphite electrode. Journal of the Chinese Chemical Society, 2021, 1-9

- Karaboduk Kuddusi (2021). Modification o f s creen-printed g old e lectrode with 1 , 4 -dithiothreitol: application to sensitive volta metric determination of Sudan II. Food Quality and Safety, 5, 1-9.

- Karaboduk Hatice, Kalender Yusuf (2021). The Effects of Lead Nitrate and Mercury Chloride on Rat Liver Tissue. Fresenius Environmental Bulletin, 30, 2368 – 2379

- Orhan Canbolat, (2021). Anti Metabolite Theory, GMJ, 32(2):258-262.

- Gulsah Congur, Ulkuye Dudu Gul, Burcu Ertit Tastan, (2022). Fast, Cheap and Reliable Monitoring of Microalgae-Based Paracetamol Removal from Aquatic Environment Using Electrochemical Sensor Technology. Journal Of The Electrochemıcal Socıety169 (11).

- Burcu Ertit Tastan, Bahtiyar Bakır, Esra Yaylacı, Burcu Ekim (2022) Investigation of Physiologic and Kinetic Effects of Chicken Fertilizers on Microalgae Growth And Biomass Productivity. International Journal of Natural and Engineering Sciences E-ISSN: 2146-0086 16(1): 41-52.

- Sevcan MAMUR, Deniz Yüzbaıoglu, Sabire Nur Bülbül, Fatma Ünal, (2022). Investigation of cyto-genotoxic effects of a food sweetener Acesulfame potassium, Food and Health, 8(4): 273-283.

- Sevcan Mamur, (2022). Geraniol a natural monoterpene, identifications of cytotoxic and genotoxic effects in vitro. Journal of Essentiol Oil Research, 34 (1): 54-64.

- Sevcan Mamur, Esra Gunduzer, Melek Yaman, (2022). Toxicological aspect of bioinsecticide pyrethrum extract and expressions of apoptotic gene levels in human hepotacellular carcinoma HepG2 cells. Toxicology Mechanisms and Methods, 32(5):373-384.

Projects 2021-2024

- Project Code: 122Z742-Project Title: O.Canbolat, M.A.Ergun, G.Bozdayı, F.Canbolat, Investigation of the Effect of Ultrasound on the Nucleic Acid Structure of Sarscov2, Scientific Research Project Supported by Higher Education Institutions 2021-2022-Complated

- Project Code: 122Z742-Project Title: Developing microalgae-based sustainable CO2 reduction strategies and investigating the potential of microalgal biomass as a biodiesel, biodegradant and biosorbent-based green energy source. Project Type: TUBITAK 1001 Project-2022-2024

- **Project Code: P TSG-2022-7930-Project Title: Investigation of the effect of synthetic Ribose 5 Phosphate and synthetic nucleoside analogs containing Ribose 5 Phosphate in their structure on PRPP synthetase enzyme, which is transported into the cell with special nano systems in Breast Cancer. Project Type: Guided Project -2022-2024**

- **Project Code: TCD-2023-8358- Project Title: Investigation of epigenetic mechanisms of cytidine deaminase and pyrimidine nucleotidase enzymes in cancer cells related to gemcitabine and intracellular metabolites of gemcitabine Effect of Lupeol. Project Type: Multidisciplinary Research Project- 2023-2024**
- Project Code: TKB-2023-8525-Project Title: Determination of the effect of EF24 on the cell death response induced by Eribulin mesylate in A549 lung cancer cells. Project Type: Career Start Project-2023-2023

- Project Code: TKB-2023-8458-Project Title: Determination of the effect of EF24 on cisplatin-induced cell death response in triple negative breast cancer cells. Project Type: Career Start Project-2023-2023

- Project Code: TKB-2023-8564-Project Title: Effect of ozone therapy and vitamin C on heart tissue in myocardial ischemia reperfusion injury model in rats with diabetes mellitus by streptozotocin. Project Type: Career Start Project-2023-2024

- Project Code: TCD-2023-7867-Project Title: Effect of pesticide application on siderophore gene expression level in Bacillus subtilis subsp inaquosorum DY5, which produces siderophores with agronomic and probiotic importance. Project Type: Multidisciplinary Research Project
- **External Joint Research Project- Project Title: The relationship of cisplatin resistance or toxicity with apoptosis and autophagy processes and the role of glutathione metabolism in triple-negative breast cancer. 2023-2025**
- **External Joint Research Project-Project Title: The relationship between cisplatin resistance or toxicity in HELA cells, apoptosis and autophagy, and the role of free radical metabolism enzymes. 2023-2025**

COURSES, SEMINARS AND CONFERENCES: 2021-2023

- 1st Gazi University And Kazakh National Medical University Named After S.D. Asfendıyarov Health Sciences Congress, 1-2 December 2021, Ankara
- International Seminars On Health Science, Webinar, “Molecular Mechanisms of Melatonin and Its Clinical Applications” Speaker: Prof. Dr. Darío Acuña-Castroviejo, 02.07.2021, Ankara
- International Seminars On Health Science, Webinar, “How Cells Sense and Adapt to Oxygen Sensitivity” Speaker: Prof. Dr. Joachim Fandrey'in (Medical Faculty - Vice Dean University of Duisburg-Essen), 08.06.2021, Ankara
- Experimental Ischemia Reperfusion Models Course 1- 25–26 September 2021
- Applied Basic Cell Culture Techniques Course - 19-21 September 2022
- Experimental Ischemia Reperfusion Models Course 2- 26–27 March 2022
- 2nd Gazi University And Asfendıyarov Kazakh National Medical University Health Sciences Congress, May 26-27, 2022, Almaty/Kazakhstan.
- International Seminars On Health Science, Webinar, “Contribution of Genetic Variants to Early-Onset Breast Cancer" Speaker: Dr. Zhunussova Gulnur, 03.03.2022, ANKARA
- Life Sciences Application and Research Center 2022-2023 Academic Year Seminars, “Potential cancer biomarkers: Circular RNAs (circRNAs)” Assoc. Dr. Hacer İlke Önen, 01.11.2022.
- Life Sciences Application and Research Center 2022-2023 Academic Year Seminars, “The Role of Raman Spectroscopy in Life Sciences” Assoc. Dr. Mehmet Yesiltas, 19.10.2022.
- Life Sciences Application and Research Center 2022-2023 Academic Year Seminars, “Biofilm formation and removal”, Dr. Faculty Member Tuğba Kılıç, 03.10.2022.
- Life Sciences Application and Research Center 2022-2023 Academic Year Seminars, "Stem Cells in Dentistry", Dr. Faculty Member Ayşegül Mendi, 16.01.2023.
- Life Sciences Application and Research Center 2022-2023 Academic Year Seminars, "The Role of Bacterial Quorum Sensing (QS) in Virulence and QS Inhibition" Dr. Faculty Member Elif Burcu Bali, 02.01.2023.
- Life Sciences Application and Research Center 2022-2023 Academic Year Seminars, “On Medicine”, Prof.Dr. Orhan Canbolat, 23.03.2023.

THE LABORATORY DEVICE - II

BIOCHEMISTRY-CHEMISTRY

- 1. GC-MS (Agilent)
- 2. GC-MS (Shimadzu)
- 3. HPLC (Agilent)
- 4. HPLC (Shimadzu)
- 5. DSC (Shimadzu)
- 6. TGA (Thermogravimetric Analyzer- Shimadzu)
- 7. FTIR
- 8. Spectrophotometer (Shimadzu)
- 9. XRF (X-Ray Fluorescent Spectrophotometer- Shimadzu)
- 10. ICP-OES (Perkin Elmer)
- 11. AAS (Perkin Elmer)
- 12. Zetasizer (Malvern)
- High Speed Floor Type Centrifuge (Thermo Scientific Brand)

MOLECULAR BIOLOGY

- 1. DNA Sequence Analysis Device (Applied Biosystems)
- 2. Real Time PCR Device (Applied Biosystems)
- 3. Real Time PCR Device (Qiagen)
- 4. Gradient PCR Device (Applied Biosystems)
- 5. Gradient PCR Device (Applied Biosystems)
- 6. Gradient PCR Device (SensoQuest)
- 7. Horizontal electrophoresis
- 8. Vertical electrophoresis
- 9. Gel Imaging and Analysis System (UVP)

THE LABORATORY DEVICE - I

MICROSCOPY AND SPECTROSCOPY

- Atomic Force Microscope (AFM-WITec)
- RAMAN spectroscopy (WITec)
- Transmission Electron Microscope (TEM) (FEI TECNAI, 120Kv)
- Ultramicrotome Leica (EM UC6)
- Microtome (EM Trimmer- Leica)
- Cryostat Leica (CM1900)
- Light Microscope Automatic Tracker (Leica, TP 1020)
- Laser Scanning Confocal Microscope System Leica (TCS SP2)
- Inverted Microscope with Fluorescent Attachment (Leica, DMI4000B)
- Fluorescent Microscope (Leica, DMIL LED)
- Light (Binocular) Microscope
- Inverted Microscope (Leica, DMIL LED)

MICROBIOLOGY

- Lyophilizer (CHRIST)
- Colony Counter (Synbiosis Brand)
- Pure Water and Ultra Pure Water Device
- Air Conditioning Cabinet
- Carbon Dioxide Incubator
- Bacteriological Oven10.
- Microbiology Lyophilizer (CHRIST)
- Colony counter (Synbiosis Brand)

CELL CULTURE LABORATORIES

There are two cell culture laboratories. In these laboratories, researchers use current cytotoxicity test methods on healthy and cancer cell lines to determine the effects and functions of a specific substance (nanoparticles, plant extracts, drugs, food additives, and many chemical substances). In addition, DNA and RNA studies in cell culture, as well as apoptosis and necrosis studies, are performed to determine cell death.

1. The Clean Room
2. Incubator with Humidity Control
3. Cabinet for Biosafety
4. Inverted Microscope
5. Binocular Microscope
6. Transport and Storage Unit for Liquid Nitrogen

EXPERIMENTAL ANIMAL PRODUCTION AND RESEARCH LABORATORY

It has a work permit approved by the Ministry of Agriculture and Forestry for mice, rats, guinea pigs, rabbits and poultry.

It divided into separate sections for poultry and rat-mouse-guinea pig-rabbit. Experimentalanimals are produced in its laboratories. There are study rooms to be used in research.

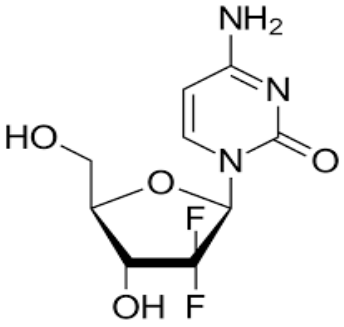
LAPOROSCOPIC AND ROBOTIC SURGERY EDUCATION AND RESEARCH UNIT

Five high-tech surgery rooms are available within the laboratory. The use of laparoscopic and robotic surgery on test subjects is feasible.

Epigenetic processes of gemcitabine and intracellular metabolites of cytidine deaminase enzymes in cancer cells; lupeol impact - I

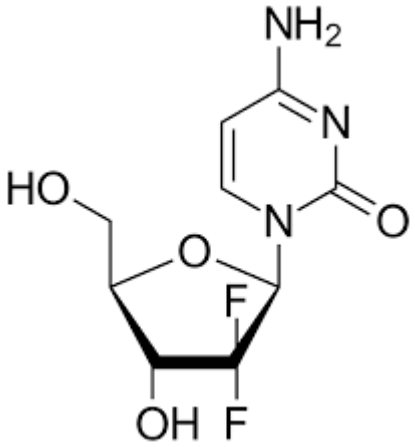
- Three distinct enzymes, each encoded by a unique set of genes and performing distinct tasks, make up the cytidine deaminase family.
- **Cytidine deaminase (or CDA**) catalyses the hydrolytic deamination of cytidine and deoxycytidine to uridine and deoxyuridine, respectively, as part of the pyrimidine rescue pathway. CDA, which relies mostly on its free cytidine as a substrate, plays a crucial function in the control of the cancer cell's nucleotide pool.
- **Proteins belonging to the APOBEC family of cytidine deaminases** are responsible for editing apolipoprotein B mRNA. When it comes to innate immunity, APOBECs are crucial for warding off viruses and retrotransposons.
- One of the most important regulators of B-cell diversity is **activation-induced cytidine deaminase (AID).** Initiating processes of class transition recombination and somatic hypermutation, AID helps to generate a reserve of varied and high-affinity immunoglobulin isotypes, making it a major player in adaptive immunity.

- A Eroglu O Canbolat, S Demirci, H Kocaoglu, Y Eryavuz, H Akgül, Activities of adenosine deaminase and 5'-nucleotidase in cancerous and noncancerous human colorectal tissues, Med Oncol, 2000 Nov;17(4):319-24.
- I Durak 1, Y Bedük, M Kavutcu, O Süzer, O Yaman, H S Oztürk, O Canbolat, S Ulutepe, Activity of the enzymes participating in purine metabolism of cancerous and noncancerous human kidney tissues,Cancer Invest,1997;15(3):212-6.
- I Durak, N Ormeci, O Akyol, O Canbolat, M Kavutçu, M Bülbül,Adenosine deaminase, 5'-nucleotidase, xanthine oxidase, superoxide dismutase, and catalase activities in gastric juices from patients with gastric cancer, ulcer, and atrophic gastritis, Dig Dis Sci.,1994 Apr;39(4):721-8.
- O Canbolat, I Durak, R Cetin, M Kavutcu, S Demirci, S Oztürk, Activities of adenosine deaminase, 5'-nucleotidase, guanase, and cytidine deaminase enzymes in cancerous and non-cancerous human breast tissues., Breast Cancer Res Treat,1996;37(2):189-93.
- I Durak, R Cetin, O Canbolat, D Cetin, Z Yurtarslani, A Unal, Adenosine deaminase, 5'-nucleotidase, guanase and cytidine deaminase activities in gastric tissues from patients with gastric, Cancer Lett,1994 Sep 15;84(2):199-202.
- I Durak 1, A C Işik, O Canbolat, O Akyol, M Kavutçu, Adenosine deaminase, 5' nucleotidase, xanthine oxidase, superoxide dismutase, and catalase activities in cancerous and noncancerous human laryngeal tissues, Free Radic Biol Med, 1993 Dec;15(6):681-4.



Epigenetic processes of gemcitabine and intracellular metabolites of cytidine deaminase enzymes in cancer cells; lupeol impact- II

- **Gemcitabine** is a potent and specific analogue of deoxycytidine.After uptake into malignant cells, gemcitabine, a cytidine analog, is phosphorylated by deoxycytidine kinase to form **gemcitabine monophosphate**, which is then converted to its active compounds gemcitabine **diphosphate (dFdCDP) and gemcitabine triphosphate (dFdCTP).**
- Active metabolites are nucleosides that mediate the antitumor effects of gemcitabine. **dFdCTP competes with deoxycytidine triphosphate (dCTP) for incorporation into DNA, thereby competitively inhibiting DNA chain elongation.**
- Post-synthesis defects of the enzyme, mutations in the gene region of the enzyme may be responsible for individual drug resistance or toxicity.



Translational Medicine

Demonstrating the function of cytidine deaminase in the metabolism of gemcitabine and its metabolites in numerous types of cancer cells

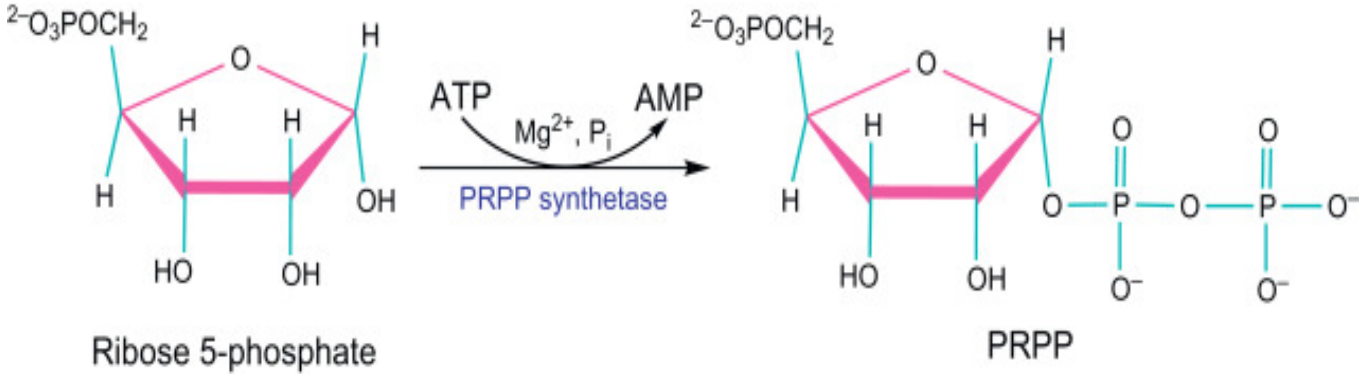
Clarifying the protein-mRNA-DNA connection.

Lipol's mechanism in cancer cell lines

HeLa cervical cancer and HT-29 colon cancer cell line, Assays for cell viability, Caspase-3 activity, autophagy and biochemical analyses

Investigation of the molecular effects of nucleotides containing synthetic Ribose 5 Phosphate or synthetic Ribose 5 Phosphate transferred into the cell with special nanosystems in breast cancer - I

The enzyme phosphoribosyl pyrophosphate synthetase (Prps) synthesizes phosphoribosyl pyrophosphate (PRPP) using Ribose 5-phosphate (R5P). PRPP is the main regulatory molecule located in **the de novo and salvage pathway of purine and pyrimidine nucleotides.**



Ribose 5-phosphate PRPP

The anti-metabolite theory is predicated on the idea that modifying the substrates of important enzymes involved in the metabolism of nucleotides or nucleic acids, or integrating synthetic nucleotide analogues into the structure of DNA and RNA, is the way to achieve the desired effect.

Canboat O. Anti metabolite theory, GMJ,32, 2, 258-262, 2021

Investigation of the molecular effects of nucleotides containing synthetic Ribose 5 Phosphate or synthetic Ribose 5 Phosphate transferred into the cell with special nanosystems in breast cancer -II

- Synthetic analogs of R-5P and nucleosides containing synthetic R-5P are planned to be transported to epithelial cells of human breast cancer MCF7 (ER+) and (MCF12A) with special nanocarrier systems.

- The effects of synthetic R5P analogs on breast cancer MCF7 (ER+) and immortal human breast epithelial cells (MCF12A), cell death pathways (apoptosis, autophagy and necrosis) and cell cycle will be determined.

- NMR (1D, 2D), HPLC, Raman spectroscopy, Electron microscopy, SDS-PAGE-Western blot techniques will be used in the project.
- All laboratory techniques of the study, including cell culture, will be carried out in our research center. Synthetic analogs of PRPP synthase and carrier systems will be synthesized by the research group.
- The project has a high potential to move to experimental animal models, clinical pharmacology and clinical research studies in the next step.

Cisplatin-induced Autophagy or Apoptosis and Radical Metabolism; from protein to gene - I

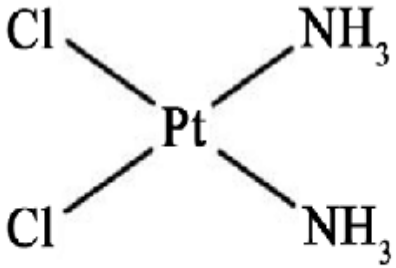
- Cisplatin (CDDP) is a platinum compound with two amide and two chloride ligands.
- Cisplatin is commonly used to treat malignancies of the testicles, ovaries, cervix, bladder, head and neck, and small cell lung.
- Despite significant clinical success, tumour cell drug resistance has hampered CDDP's clinical use for decades.
- Monoadducts create intra-stand and inter-stand crosslinks as a result of the interaction between CDDP and DNA bases.
- When the level of DNA damage caused by CDDP surpasses the repair capacity, cells die and the **apoptotic signalling pathway is activated**, which is frequently used in studies into tumour resistance to platinum-based drugs.
- In certain cancer cells, **autophagy plays a significant role in chemotherapy resistance.** Cisplatin causes an increase in the expression of Beclin-1, an autophagy regulating protein. Beclin-1 functions as an autophagy initiator. This causes the Atg12-Atg5 complex, Atg3 and Atg7 complex to assemble, resulting in the creation of the autophagosome vesicle, which selectively retains the injured cell.

Studies have shown that cisplatin can cause DNA damage, mitochondrial dysfunction and increase the **production of reactive oxygen species (ROS)**

High levels of hydroxyl radicals have been shown to induce the formation of autophagosomes and autolysosomes in cisplatin-treated

Detection of the relationship between the oxygen radical detoxifying SOD1 and SOD2 enzymes and **apoptosis and autophagy** may support the idea that antioxidants can be used clinically.

Drug resistance and toxicity may result from changes in intracellular glutathione levels and the activity of glutathione-dependent enzymes such glutathione peroxidase and glutathione reductase, or from mutations in the genetic composition of these enzymes.



Cisplatin

Durak İ., Öztürk H., Kavutçu M., Individual M., Yel M., Güven T., Canbolat O.,Protective role of antioxidant vitamins on adriamycin-induced free radical generation and cardiotoxicity in guinea pigs. Cancer Research Therapy & Control, 5, 2, 133-141, 1998

Radical Metabolism and Cisplatin-induced Autophagy or Apoptosis; from protein to gene - II

The relationship between apoptotic and autophagic responses and potential protein inhibition or activation with DNA mutations in cisplatin- and EF24-treated HeLa cervical cancer cells will be studied.

Biochemistry; SOD1, SOD2, GsHPx, GR, GST, Glutathione

Cell Culture; HeLa cervical cancer cell line

Cell Viability Assay

Determination of the amount of lactate dehydrogenase (LDH)

Apoptosis- Determination of Caspase-3 Activity

Determination of Autophagy - p62 Evaluation Experiment

Protein Isolation and Western Blot Analysis

DNA extraction and sequencing analysis

Several mutations in the SOD1 gene have been identified. One of them is a 50-base deletion (1,684 bp upstream of the ATG start codon). This variant has been proven to reduce mRNA expression levels.Using a DNA isolation kit, genomic DNA (gDNA) will be extracted from cultivated HeLa cells. PCR will be used to amplify gene sections using primers specific to the SOD1 exons.

The PCR products will be purified and sequence amplified using PCR. Following the purification of the sequencing products, they will be put into the DNA sequencing instrument and the findings will be analysed.