3.

ULUSLARARASI

EPİGENETİK KONGRESİ

24 – 26 EKİM 2025

T.C. Cumhurbaşkanlığı
Devlet Arşivleri Osmanlı Arşivi Külliyesi

KONGRE KİTABI

NUTRİGENETİK EPİGENETİK DERNEĞİ

TÜRK KANSER DERNEĞİ

DÜZCE ÜNİVERSİTESİ

NEV İSTANBUL NİŞANTAŞI ÜNİVERSİTESİ

İÇİNDEKİLER

KONGRE EŞ BAŞKANLARI
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Burak Duruman

BİLİMSEL DANIŞMA KURULU
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Prof. Dr. Abdullah Olgun
Prof. Dr. Kenneth White
Prof. Dr. Ramy K. Aziz
Prof. Dr. Asiye Nuhoğlu
Prof. Dr. Gülsen Meral
Prof. Dr. Ufuk Koca Çalışkan
Prof. Dr. İlhan Yaylım
Prof. Dr. Ümit Zeybek
Prof. Dr. Zühal Kunduracılar
Prof. Dr. Hülya Yükseloğlu
Prof. Dr. Zübeyde Gündüz
Prof. Dr. Ercan Kahya
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Prof. Dr. Vahide Savcı
Prof. Dr. Özlem Timirci Kahraman
Prof. Dr. Sıddıka Semahat Demir
Prof. Dr. Asuman Sunguroğlu
Doç. Dr. Elif Sibel Aslan
Doç. Dr. Ali Timuçin Atayoğlu
Doç. Dr. Rüya Ateşli
Doç. Dr. İshak Özel Tekin
Dr. Birsen Sarıcı
Uzm. Mol. Bio § Dyt. E. Gökçen Alper Acar

ORGANİZASYON KOMİTESİ
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Dr. Meyselon Artun Elhih
Dr. Reyhan Özgöbek
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Uzm. Dyt. Leyla Karakaş
Uzm. Dyt. Esra Şahin
Dyt. Neval Burkay

KONGRE SEKRETERLERİ
Dr. Birsen Sarıcı
Dyt. Neval Burkay
YM. İpek Meral

BİLİMSEL PROGRAM

NUTRİGENETİK EPİGENETİK DERNEĞİ

TÜRK KANSER DERNEĞİ

DÜZCE ÜNİVERSİTESİ

İSTANBUL NİŞANTAŞI ÜNİVERSİTESİ

24 EKİM 2025, CUMA	
SAAT	**SALON A**
08.00-09.00	**KAYIT**
09.00-09.50	**AÇILIŞ OTURUMU**
09.00-09.10	Gülsen Meral- Nutrigenetik ve Epigenetik Derneği Başkanı
09.10-09.20	Burak Duruman- Türk Kanser Derneği Başkanı
09.20-09.30	Asiye Nuhoğlu- Nutrigenetik ve Epigenetik Derneği
09.30-09.40	Emrah İpek- Nişantaşı Üniversitesi Dekanlık
09.40-09.50	Nedim Sözbir- Düzce Üniversitesi Rektörü
09.50-10.40	**KEYNOTE** **Moderatörler:** İlhan Yaylım, Asuman Sunguroğlu **Epigenomik: Kanserdeki Rolü ve Klinik Potansiyeli** Mustafa Camgöz
	LONGEVITY VE EPİGENOMİK: YAŞLANMAYI DURDURMAK MÜMKÜN MÜ? YETİŞKİNLERDE LONGEVITY- I **Moderatörler:** Asiye Nuhoğlu, Gülsen Meral
10.40-11.00	**Nöroyaşlanmada İmmün Beslenme Yaklaşımı** İshak Özel Tekin
11.00-11.20	**Karvakrol Bazlı Uçucu Yağ Formülasyonlarının Sinerjik Antikanser Etkileri** Selin Kiremitci
11.20-11.40	**Sağlıklı Metabolizma İçin Sağlıklı Bitkisel Beslenme** Mehmet Hamurcu
11.40-12.00	**Yaşlanma ve Uzun Ömürde Altın Anahtar: Lif** Hümeyra Yerlikaya Aydemir
12.00-12.10	**Tartışma**
12.10-12.30	**KAHVE MOLASI**
12.30-13.00	**KEYNOTE** **Moderatörler:** Mustafa Altındiş, M. Yunus Alp **Metabolik İlişkili Yağlı Karaciğer Hastalığında mtDNA Metilasyonu: İki Yönlü Bir Yol mu?** İkbal Agah İnce

	LONGEVITY VE EPİGENOMİK: YAŞLANMAYI DURDURMAK MÜMKÜN MÜ? YETİŞKİNLERDE LONGEVITY - II **Moderatörler:** Mustafa Altındiş, M. Yunus Alp
13.00-13.30	**Stres Biyolojisi ve Epigenetik Yanıt: Mindfulness'ın Rolü** Özlem Timirci Kahraman
13.00-13.30	**Fizyoterapide Epigenomik Yaklaşım** Zuhal Kunduracılar
14.00-14.20	**Longevity İçin Epigenetik Saati Tersine Çevirmede Nutrigenetik ve Epigenomiğin Rolü** Gülsen Meral
14.20-15.10	**ÖĞLE YEMEĞİ**
	KEYNOTE **Moderatörler:** İshak Özel Tekin, Mehmet Hamurcu
15.10-15.40	**Epigenetik Araştırmanın ve Dijital Dönüşümün Disiplinlerarası Geleceği** Semahat Sıddıka Demir
	EPİGENOMİKTE AZ BİLİNENLER **Moderatörler:** Ümit Zeybek, Mehmet Tolgahan Hakan
15.40-16.00	**Longevity İçin Fonksiyonel Mikrobiyota: Yapay Zeka Destekli Yaklaşımlar** Mustafa Altındiş
16.00-16.20	**Sağlık Hizmetlerinde Dijitalleşme ve Karar Destek Sistemleri: Yapay Zeka Destekli Nutrigenetik Analizi Operasyon Süreçleri** Emin Tarakçı
16.20-16.40	**Egzersiz Uygulamalarında Kinesiyometabolomik Yaklaşım** Ümit Zeybek
16.40-17.00	**Epigenetik Düzenlemede Çevresel Etkiler** Mehmet Tolgahan Hakan
17.00-17.20	**Kişiselleştirilmiş Tıpta Yapay Zeka Uygulamaları: Yeni Ufuklar** İbrahim Halil Tanboğa
17.20-17.30	**Tartışma**
17.30-17.50	**KAHVE MOLASI**
	KEYNOTE **Moderatörler:** Ümit Zeybek, Mehmet Tolgahan Hakan
17.50-18.20	**Epigenetik ve Farmakogenetik** Kenneth White
	EPİGENOMİKTE AZ BİLİNENLER II **Moderatörler:** M. Yunus Alp, Savaş Gür
18.20-18.40	**Kanser Hastalarında Nutrigenetik ve Epigenomiğin Önemi** Didem Karaçetin
	WORKSHOP
18.40-19.00	**Nefesle Epigenetik Değişim** Rüya Acaroğlu

25 EKİM 2025, CUMARTESİ

SAAT	SALON A
	KEYNOTE **Moderatörler:** Ufuk Koca Çalışkan, Demet Erdönmez
09.00-09.30	**Farmakomikrobiyomik** Ramy K. Aziz
	KRONİK HASTALIKLARDA NUTRİGENOMİK EPİGENOMİK YAKLAŞIM-FARMAKOGENETİK **Moderatörler:** Ufuk Koca Çalışkan, Demet Erdönmez
09.30-09.50	**Atto PGX: Doğrudan Tüketiciye Yönelik Farmakogenetik Test Hizmeti ile Daha İyi Sağlık için Kişiselleştirilmiş İlaç Planlarının Kilidini Açmak** Sasitaran Iyavoo
09.50-10.10	**Klinik Pratikte Farmakogenetik ve Epigenomik Bulgular** Savaş Gür
10.10-10.30	**Yeni Nesil Eczacılık: Farmako-Epigenetik ile Kişiselleştirilmiş Tedavi** Ufuk Koca Çalışkan
10.30-10.50	**Mikrobiyota'nın Epigenetik Şifresi: Quorum Sensing ile Otoimmünite Kontrolü** Demet Erdönmez
10.50-11.00	**Tartışma**
11.00-11.20	**KAHVE MOLASI**
	KEYNOTE **Moderatörler:** Didem Karaçetin, Asuman Sunguroğlu
11.20-11.50	**Geleneksel Toksikolojinin Ötesinde: Epigenetik Değişikliklerden Adli Bilgiler** Hülya Yükseloğlu
	KANSER VE EPİGENOMİK KANSERİN ŞİFRESİ **Moderatörler:** Didem Karaçetin, Asuman Sunguroğlu
11.50-12.10	**Kansere Genetik ve Epigenetik Yaklaşımlar** İlhan Yaylım
12.10-12.30	**Kanser İmmunoterapisi ve Epigenetik** Asuman Sunguroğlu
12.30-12.50	**Epigenomik ve Yaşlanma** Abdullah Olgun
12.50-13.10	**Kanserde Genetik ve Epigenomik Hedeflere Yönelik Tedaviler** M. Yunus Alp
13.10-13.20	**Tartışma**

13.20-14.20	**ÖĞLE YEMEĞİ**
	ÇOCUKLARDA LONGEVITY **Moderatörler:** Gülsen Meral, Rüya Ateşli
14.20-14.40	**Longevity Çocuklukta Başlar: Alerjiye Nutrigenetik Tabanlı Epigenomik Yaklaşım** Gülsen Meral
14.40-15.00	**Anne Sütü ile Beslenmenin Epigenetik Etkileri** Rüya Ateşli
15.00-15.20	**Longevity'nin Başlangıcı: Çocuklukta Kişiselleştirilmiş Nutrigenetik** Selen Baran Özmen
15.20-15.40	**Çocuk Nörolojik Hastalıklarda Genetik ve Epigenetik Yaklaşım** Meltem Uzun
15.40-16.00	**Çocuk İstismarı ve İhmali ve Longivite: Yaşam Boyu Etkiler** Nihal Durmaz
16.00-16.10	**Tartışma**
16.10-16.30	**KAHVE MOLASI**
	METABOLİZMA VE SAĞLIKTA EPİGENETİK İNOVASYONLAR **Moderatörler:** Ali Osman Gürol, Zübeyde Gündüz
16.30-16.50	**Epigenetik ve Diyabet** Ali Osman Gürol
16.50-17.10	**Metabolik İnflamasyon** Zübeyde Gündüz
17.10-17.30	**Eksozomal Epigenetik: Tanı, Tedavi ve Kozmetik Uygulamalar** Ayşe Akman
17.30-17.50	**Arı Ürünlerinin Epigenom Üzerine Etkisi** Ali Timuçin Atayoğlu
17.50-18.10	**Egzersizin Epigenom Üzerine Etkisi** Murat Aksoy
18.10-18.40	**WORKSHOP** **Beden Farklılığı Egzersiz Deneyimi** Reyhan Özgöbek
18.40-19.10	**Video Sunumu** Elif Sibel Aslan

25 EKİM 2025, CUMARTESİ

SAAT	SALON B
16:30-18:30	**Bildiri Oturumu** **Oturum Başkanları:** Meyselon Artun, Gülsen Meral

Ss 01- Model Bitki Arabidopsis Thaliana'da İnsan Hastalıklarının Moleküler İzleri
Aşkım Hediye Sekmen
Ss 02- Serum Ldl-Kolesterol Seviyelerinin Genetik Polimorfizmler, Bağırsak Mikrobiyotası ve Beslenme İle Arasındaki İlişkilerin İncelenmesi
Asu Şevval İçelli
Ss 03- Yüksek Diyet Lifi ve Bağırsak İltihabı Belirteci Kalprotektin
Berivan Unat
Ss 04- Yüksek Lifli Diyet Yapan Sağlıklı Bireylerde Kan Zonulin Düzeylerinin Değerlendirilmesi
Betül Çalış
Ss 05- Multiple Sklerozis Hastalığında Epigenetik Mekanizmalar ve Probiyotik Kullanımının Etkisi
Günay Sarıkaya
Ss 06- Sağlıklı Beslenme ve Kalıcı Öğrenme Alanında Güncel Çalışmalar ve Gelecek İçin Epigenetik Öneriler
Güneş Havva Kazanç
Ss 07- Getat Polikliniğine Başvuran Homeopati Hastalarının ve Kullandıkları Remedilerin Dağılımı: Olgu Serisi
Hayriye Alp
Ss 08- Treacher Collins Sendromunda Pediatrik Kardiyak Komplikasyon ve Erişkin Psikososyal Yükün Karşılaştırmalı Değerlendirmesi
Hilal Türk Yardım
Ss 09- Obezitede Probiyotik ve Prebiyotikler
Melike Bağıbala
Ss 10- Kafeinin Sporcular Kası Üzerindeki Epigenetik Etkileri
Ömer Divanoğlu
Ss 11- Alzheimer Hastalığı'nın Epigenetiği ve Fermente Besinlerin Nutrasötik Potansiyeli
Merve Karabacakoğullarından
Ss 12- Parkinson Hastalığında Epigenetik Mekanizmalar ve Bitkisel Fitokimyasalların Terapötik Potansiyeli
Yaren Aray

26 EKİM 2025, PAZAR

SAAT	SALON A
09.00-09.20	**MENOPOZ SÜRECİNDE GENETİK, EPİGENETİK ve NUTRİGENETİK YAKLAŞIM** **Moderatörler:** Savaş Gür, M. Yunus Alp **Konuşmacılar:** Gülsen Meral, Mukaddes Demirbuğa, Pelin Bozkurt Bilgiç
09.40-10.00	**Menopoz Döneminde Epigenomik İmza: Beslenmenin Dönüştürücü Gücü** Hatice Şimşek Şahin
10.00-10.30	**Koku Moleküllerinin Epigenetik Üzerine Etkisi** Hülya Kayhan
	LONGEVITY **Moderatörler:** Gülsen Meral, Mukaddes Demirbuğa
10.30-10.50	**Klinikten Epigenoma; Vaka Sunumu** Savaş Gür
10.50-11.10	**Metabolik Esneklik ve Genetik Yatkınlık: Kronik Hastalıkların Önlenmesinde Yeni Bir Paradigma** Çiğdem Üregen
11.10-11.30	**Kişiselleştirilmiş Sağlık Platformları İçin Yapay Zekâ Destekli Multi-Omik Analiz Otomasyonu** İpek Meral
11.30-12.00	**Tartışma**
12.00-12.10	**KAHVE MOLASI**
	MİKROBİYOTA WORKSHOP
12:10-12:55	Ümit Zeybek
	WORKSHOP
12:55-13:25	**Bedenin Dili, Ruhun Renkleri: Epigenetikten Sanat Terapisine Şefkatle Bir Yolculuk** Mustafa Sabri Şahin

26 EKİM 2025, PAZAR	
SAAT	**SALON B**
	NUTRİGENETİK TEMELLİ KİŞİYE ÖZEL BESLENME İLE HASTALIKLARA YAKLAŞIM: DİYETİSYEN WORKSHOP **Moderatörler:** Leyla Karakaş, Birsen Sarıcı
09.00-09.20	**Epigenetikte Nutrigenetiğin Önemi** Neval Burkay
09.20-09.40	**Detoksifikasyonda Nutrigenetik Testlerin Önemi** E. Gökçen Alper Acar
09.40-10.00	**Epigenomik Yaklaşım İle Kanser Vaka Sunumu** Leyla Karakaş
10.00-10.20	**LEPR Geninde Mutasyon Olan Bireylerde Beslenme Alışkanlıklarının Değerlendirilmesi** Esra Şahin
10.20-10.40	**Gıda Güvenliği Açısından Pestisitler ve Sağlık Üzerine Epigenomik Etkileri** Birsen Sarıcı
10.40-11.00	**Detoksifikasyon Paneli: Gen-Besin-Hastalık İlişkileri** Merve Özkaya
11.00-11.10	**Tartışma**

KONUŞMA ÖZETLERİ

Epigenomics and Aging

Prof. Dr. Abdullah Olgun
Istinye University, Faculty of Pharmacy

Epigenetic mechanisms play a central role both mechanistically and phenotypically in the process of aging. Epigenetic alterations—such as the spontaneous deamination of 5-methylcytosine to thymine (with a conversion rate approximately five times higher in CpG islands compared to other genomic regions) and age-related activation of transposons—can also lead to genetic effects. Due to the partially reversible nature of epigenetic modifications, interventions such as reprogramming, lifestyle modification, and caloric restriction may help delay age-related diseases and the overall aging process. There is a need for novel biomarkers for the early diagnosis of age-associated conditions, such as acute kidney injury (AKI), in which epigenetic changes play a significant role in disease onset. In this context, the Argeron NephroTesT, developed for early AKI detection, and the Argeron BioAgeCheck, which enables estimation of histone deamidation rates, can be utilized. Moreover, preventing deficiencies of micronutrients such as magnesium could be implemented as a public health strategy to delay the onset of epigenetically mediated diseases.

Epigenetics and Diabetes

Prof. Dr. Ali Osman Gurol
Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Immunology

Diabetes mellitus (DM) is a chronic metabolic disorder caused by insufficient insulin secretion or impaired insulin action. Type 1 Diabetes (T1D): autoimmune destruction of pancreatic β-cells. Type 2 Diabetes (T2D): insulin resistance in peripheral tissues. This condition leads to microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (stroke, cardiovascular disease) complications. Genetic predisposition alone cannot explain diabetes. Epigenetic mechanisms—DNA methylation, histone modifications, and microRNAs—modify gene expression without altering DNA sequence. These changes form "metabolic memory," influencing long-term complications. Clinical trials show that tight glycemic control reduces diabetic complications even decades later, confirming the presence of epigenetic memory. Persistent DNA methylation in inflammatory genes explains the chronicity of diabetic damage. Time-restricted feeding and circadian rhythm modulate gene expression and improve metabolism. Maternal obesity and paternal diet alter epigenetic patterns in gametes and placenta, transmitting diabetes risk to offspring. In terms of lifestyle and environmental risk factors, obesity, sedentary lifestyle, aging, gender, smoking, alcohol, and genetics play an important role in the development of T2D. Main goal: enhance insulin sensitivity and preserve β-cell function. Exercise improves GLUT-4 activation and mitochondrial function. Low glycemic index diets reduce risk 18–40%. Clinical studies showed ~58% risk reduction via lifestyle change. T1D involves complex interactions between genetics, microbiota, and epigenetic regulation. Gluten-free and Mediterranean diets improve gut microbiota balance. Short-chain fatty acids (e.g., butyrate) suppress inflammation and protect β-cells. FUT2 gene variants and human milk oligosaccharides modulate immune responses and risk. Microbiota-targeting probiotics, prebiotics, synbiotics, and fecal microbiota transplantation are emerging as potential therapies for T1D. Vitamins A, D, zinc, and polyphenols may act as epigenetic cofactors. In summary, diabetes arises from the interplay of genetic, environmental, and epigenetic factors. Epigenomic research is vital for personalized therapies. Lifestyle modification (diet, exercise, stress control) can outperform pharmacological interventions. Targeting the epigenome opens a new horizon for diabetes management.

The Effect of Bee Products on the Epigenome

Assoc. Prof. Dr. Ali Timucin Atayoglu
Apitherapy Association, Istanbul

Aim: In recent years, apitherapy has gained increasing interest due to its epigenetic regulation potential, particularly its capacity to influence gene expression and cellular differentiation processes. The aim of this study is to evaluate the relationship between bee products and epigenetic mechanisms in light of current literature. Method: Studies examining the effects of bee products on epigenetic processes were reviewed; research investigating the regulatory role of royal jelly and its component 10-hydroxy-2-decenoic acid (10-HDA) on DNA methyltransferase (DNMT) and histone deacetylase (HDAC) enzymes was particularly evaluated. Additionally, the indirect contributions of propolis and other bee products' antioxidant and anti-inflammatory effects to epigenetic modulation were analyzed. Results: Royal jelly has been shown to provide epigenetic reprogramming in larval development, particularly by regulating DNMT activity, and it has been demonstrated to lead to the transformation of worker bee larvae to a queen phenotype with high reproductive capacity. The royal jelly component 10-HDA has been determined to increase histone acetylation through HDAC inhibition. Phenolic components of propolis and pollen support epigenetic stability by reducing oxidative stress and inflammation. Although effects of hive air and bee vibrations on autonomic nervous system modulation have been reported, their consequences at the epigenetic level are not yet clear. Conclusion: Royal jelly plays a direct role in epigenetic modulation. The antioxidant effects of propolis and other products also support this process. However, more comprehensive, controlled clinical studies are needed for therapeutic applications.

Cancer Immunotherapy and Epigenetics

Prof. Dr. Asuman Sunguroglu
Ankara University, Faculty of Medicine

In recent years, the integration of epigenetic modulation into immunotherapy has opened new avenues for enhancing immune responsiveness and overcoming therapeutic resistance. Epigenetic therapies, which target reversible modifications of DNA and histones, have emerged as powerful tools to reprogram the tumor microenvironment, regulate immune cell differentiation, and improve antigen presentation. By influencing key transcriptional networks without altering the underlying DNA sequence, these agents can effectively reshape both innate and adaptive immune responses. One of the major challenges in immunotherapy is the development of resistance mechanisms, such as loss of tumor antigen expression, impaired interferon signaling, or the recruitment of immunosuppressive cells. Epigenetic regulators—including DNA methyltransferase inhibitors (DNMTis), histone deacetylase inhibitors (HDACis), and emerging bromodomain and extra-terminal (BET) inhibitors—offer promising strategies to reverse these resistance pathways. For instance, DNMT and HDAC inhibition can reactivate silenced tumor-associated antigens, restore interferon pathway genes, and sensitize "cold" tumors to immune checkpoint blockade. Moreover, epigenetic modulation can enhance the persistence and effector function of cytotoxic T cells and natural killer cells, while reducing the suppressive capacity of regulatory T cells and myeloid-derived suppressor cells. In this talk, I will present the current understanding of epigenetic mechanisms that regulate immune surveillance and tumor escape, the latest developments in epigenetic drug discovery, and the translational progress of combining these agents with immunotherapy. Emphasis will be placed on the identification of predictive biomarkers, the timing and sequencing of combination regimens, and ongoing clinical trials that aim to define the optimal therapeutic context. Ultimately, the convergence of immunology and epigenetics represents a transformative approach to achieving durable, personalized cancer immunotherapy.

Exosomal Epigenetics: Diagnosis, Treatment and Cosmetic Applications

Prof. Dr. Ayse Akman
Akdeniz University School of Medicine, Department of Dermatology and Venereology

Exosomes are extracellular vesicles that transport biomolecules including nucleic acids,lipids, proteins, and metabolites required for cellular physiology as well as signalling molecules that facilitate intercellular communication and be used as biomarkers and targeted drug delivery vehicles, in the field of dermatology. Epigenetics has the potential to provide new insights into the mechanisms of disease and could lead to the development of new diagnostic and therapeutic strategies. Exosomes can transfer epigenetic information to recipient cells, the identification of specific epigenetic modifications that are associated with a particular disease could lead to the development of targeted therapies that restore normal gene expression patterns. Exosomes have demonstrated promise in cosmetic dermatology, including as anti-aging and anti-inflammatory therapies and as therapeutics for wound healing, scar and hair regeneration. In this conversation explained the diagnosis, treatment and cosmetic applications related to exosomal epigenetics.

Pesticides and Their Epigenetic Effects in Terms of Food Safety

Dr. Birsen Sarıcı
Düzce University, Faculty of Health Sciences, Department of Nutrition and Dietetics

Objective: This study aims to evaluate the risks posed by pesticides to food safety by investigating their effects on human health beyond classical toxicological thresholds, focusing on epigenetic and epigenomic mechanisms. In particular, it explores persistent gene regulatory alterations induced through mechanisms such as DNA methylation, histone modifications, and microRNA expression. Methods: A total of 42 scientific articles published between 2015 and 2025 were reviewed, analyzing the epigenetic effects of organophosphate (e.g., chlorpyrifos), carbamate, and pyrethroid groups of pesticides. Findings were evaluated based on DNA methylation analyses (bisulfite sequencing), miRNA profiling, and histone modification assessments (ChIP-seq). Results: Chlorpyrifos exposure was found to induce hypermethylation of *p16*, *p53*, and *GSTP1* genes by approximately 35–45%, leading to the suppression of tumor suppressor gene expression and an increase in cellular proliferation. In addition, a 2.8-fold increase in *miR-21* expression and a 40% decrease in *miR-34a* were detected, changes that have been reported to activate cancer-related signaling pathways. Among populations exposed to pesticides during pregnancy, a 22% increase in methylation at the *IGF2/H19* locus was observed, accompanied by an 18% higher risk of neurodevelopmental delay in children. Individuals exhibiting decreased histone H3K9 acetylation showed up to a 30% reduction in the expression of detoxification genes (*CYP1A1*, *GSTM1*). Experimental models demonstrated that these epigenetic alterations persisted into the third generation, with an inheritance rate of approximately 12%. Conclusion: Epigenetic reprogramming induced by pesticides poses a significant threat to food safety not only in terms of acute toxicity but also through its transgenerational health effects. The observed methylation alterations in tumor suppressor and detoxification genes highlight the necessity of considering the epigenetic toxicity potential of pesticides. Therefore, integrating epigenetic and epigenomic risk assessments into sustainable agriculture and public health policies is of critical importance.

Who Sets the Clock of Life? Longevity Begins in the Womb

Dr. Çigdem Uregen
Rebornia Longevity & Wellness Center

Emerging evidence shows that human longevity is programmed long before birth. The intrauterine environment — encompassing maternal nutrition, stress, metabolic health, and circadian rhythm — orchestrates the epigenetic and mitochondrial foundations of lifelong health. Only about 25% of our lifespan potential is genetically determined; the remainder is modifiable through environmental and maternal factors. Epigenetic mechanisms act as a molecular "volume dial," regulating gene expression without altering DNA sequences. Maternal stress, inflammation, and nutrient imbalance can induce early telomere shortening, mitochondrial dysfunction, and altered metabolic programming, predisposing the offspring to chronic diseases in adulthood. The placenta, functioning as an intelligent biotranslator, conveys maternal signals that shape fetal immune, neuroendocrine, and metabolic systems. Understanding longevity as a developmental phenomenon reframes preventive medicine: optimizing maternal health before and during pregnancy becomes the earliest form of anti-aging therapy. Integrating epigenetic biomarkers, mitochondrial function, and prenatal nutrition into clinical protocols offers a transformative pathway — from reactive longevity care to proactive "pre-aging" medicine.

The Epigenetic Code of the Microbiota: Controlling Autoimmunity with Quorum Sensing

Assoc. Prof. Dr. Demet Erdonmez
Duzce University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology

The human gut microbiota is recognized as a dynamic regulator of the host epigenome and this role is particularly critical in the pathogenesis of autoimmunity. Studies have emphasized how short-chain fatty acids (SCFAs), particularly butyrate, produced by the microbiota directly mediate epigenetic suppression of T helper 17 (Th17) cells and induction of regulatory T cells (Treg) through histone deacetylase inhibitor (HDACi) effects. Even more striking is the emergence of "Quorum Sensing" (QS), a system of chemical communication among bacteria, as a master regulator of this epigenetic interaction. QS molecules, while synchronizing bacterial community behavior, can also act through Toll-like receptors (TLRs) and nuclear receptors in the host to epigenetically trigger the differentiation of regulatory T cells (Treg) and the silencing of inflammatory pathways. For example, Faecalibacterium prausnitzii, a major producer of SCFAs, potentiates its anti-inflammatory effect by producing AI-2-like signaling molecules, which have shown protective effects in experimental models of colitis. Similarly, there is strong evidence that species such as Bacteroides thetaiotaomicron suppress inflammation at the epigenetic level by modulating nuclear receptors (such as PPAR-γ) in host cells. Recent studies suggest that QS signaling controls the systemic autoimmune response by regulating intestinal epithelial barrier integrity and may reduce the "leaky gut" phenomenon involved in the pathogenesis of diseases such as rheumatoid arthritis. In light of these findings, next-generation therapeutic strategies based on postbiotics and paraprobiotics, rather than probiotics, targeting the "quorum sensing system" have the potential to revolutionize personalized therapies by decoding the epigenetic code of a wide range of autoimmunity, from diabetes to inflammatory bowel diseases.

Epigenetics, Cancer, Nutrigenetics, and the Role of Vitamins A and D

Prof. Dr. Didem Karacetin
Radiation Oncology Specialist at Neolife Medical Center and Biruni University

In addition to genetic factors, epigenetic modifications and nutrition–gene interactions play a crucial role in cancer development. The relationship between epigenetic mechanisms and cancer, as well as the regulatory potential of vitamins A and D from a nutrigenetic perspective, is of great importance. Recent literature on epigenetics and nutrigenetics has been reviewed to evaluate the effects of DNA methylation, histone modifications, and microRNA regulation on cancer pathogenesis, as well as the roles of vitamin A (retinoic acid) and vitamin D (calcitriol) in these mechanisms. Epigenetic alterations influence gene expression without changing the genetic sequence and regulate cellular processes such as proliferation, apoptosis, and differentiation. In cancer cells, global DNA hypomethylation and hypermethylation of tumor suppressor genes are frequently observed. Nutrigenetic evidence suggests that nutrients tailored to an individual's genetic profile can modulate epigenetic responses. Vitamin A, through retinoic acid, regulates cell differentiation and may reduce DNA methyltransferase activity. Vitamin D, on the other hand, exerts anticancer effects by influencing gene transcription through the vitamin D receptor (VDR). Both vitamins have been shown to interact with epigenetic regulators to inhibit tumor growth and metastasis. The role of epigenetic mechanisms in cancer development highlights the importance of personalized nutritional strategies. Nutrigenetic approaches, through the proper use of vitamins A and D, may help maintain epigenetic balance and reduce cancer risk. In the future, determining individual genetic profiles and developing targeted nutrigenomic therapy models may open a new era in cancer prevention and treatment.

Epigenetic Signatures in the Development of Addiction

Assoc. Prof. Dr. Elif Sibel Aslan
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Addiction is increasingly recognized as a disorder driven not only by genetic and environmental factors but also by dynamic epigenetic mechanisms that produce lasting molecular changes in the brain. Epigenetic modifications—including DNA methylation, histone modifications, and non-coding RNAs—play central roles in reprogramming neuronal gene expression following drug exposure. Repeated use of addictive substances induces persistent chromatin remodeling in key reward regions, such as the nucleus accumbens, resulting in altered transcriptional landscapes that sustain drug-seeking behavior and relapse vulnerability. Notably, the transcription factor ΔFosB functions as a molecular switch, linking transient drug exposure to long-term neural adaptations. Region-specific DNA methylation changes in genes regulating synaptic plasticity (e.g., fosB, bdnf, drd2) further contribute to addiction's molecular memory. Environmental factors—including early life adversity, genetic polymorphisms, and social context—interact with these epigenetic signatures, shaping individual susceptibility. Emerging evidence also points to the potential for transgenerational inheritance of drug-induced epigenetic alterations. These insights open new therapeutic avenues, including HDAC inhibitors, DNA methyltransferase inhibitors, circulating miRNA biomarkers, and CRISPR-based epigenome editing, offering promise for personalized interventions. Understanding these molecular signatures provides a foundation for transforming addiction treatment from symptom management to targeted, mechanism-based strategies.

Beyond Traditional Toxicology: Forensic Insights from Epigenetic Alterations

Prof. Dr. E. Hulya Yukseloğlu
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Environmental exposures and toxic agents have long been areas of research in forensic toxicology, and recent advances in epigenetics offer a new dimension in understanding the biological effects of these agents. In other words, epigenetic modifications represent a critical interface between environmental exposures and long-term biological responses. Next-generation research may provide valuable opportunities in forensic investigations where traditional toxicological evidence is limited or degraded. In the context of forensic sciences, epigenetics can offer new opportunities for understanding and addressing the changes induced by exposures. The investigation of environmentally induced epigenetic profiles has the potential to broaden current research areas and open new avenues in forensic and environmental sciences. This can provide valuable insights in cases such as environmental crimes, occupational hazards, or unexplained toxicological findings. This presentation aims to bridge the gap between toxicology, environmental health, and forensic sciences by emphasizing how epigenetic modifications can function as evidential tools. The integration of epigenetic biomarkers into forensic applications carries the potential to improve the interpretation of toxicological evidence and support causal inference in exposure-related cases. Such an approach highlights an interdisciplinary perspective at the intersection of environmental health and molecular biology, ultimately strengthening both public health and justice.

Digitalization and Decision Support Systems in Healthcare: Artificial Intelligence-Supported Nutrigenetic Analysis Operation Processes

Assoc. Prof. Dr. Emin Tarakcı
Istanbul Medeniyet University, Turkey

The integration of digital technologies and AI in healthcare settings yields improvements in diagnostics, operations, and patient outcomes across various medical contexts. Additionally, these technologies influence healthcare in telemedicine platforms, hospitals, and outpatient clinics. Background: Nutrigenetic analysis is progressively utilized in preventative and clinical care to predict individual health concerns. An AI-driven decision support system that evaluates nutrigenetic outcomes in conjunction with standard clinical and laboratory data can deliver uniform risk categorization and comprehensible, individualized recommendations for patients. This offers individualized plans for treatment, nutrition, exercise, and lifestyle management.
Objective: In the current research work, a Deep Learning-Based Decision Support System is designed for analyzing nutrigenetic test results. The aim of the proposed model is to provide a personalized health and lifestyle plan by using potential health risks, nutritional requirements, exercise suitability and other factors by analyzing nutrigenetic test data with artificial intelligence. Approach: To offer individualized care, nutrition, and lifestyle using a Nutrigenetics-based Epigenetic approach. The decision support system for data processing and analysis employs the Pythagorean Fuzzy- MCDM methodology. Nutrigenetic test result data are harmonized for classification and analysis. A risk engine combining Pythagorean fuzzy and MCDM performs risk classification, prioritizes differential diagnoses, recommends targeted confirmatory tests, and recommends evidence-based treatments and personalized nutrition programs. Explanations, confidence and data array are shown to clinicians; a patient module communicates individual risk and lifestyle outcomes. Contribution: Experts and doctors can only make consistent and optimistic decisions if they handle information appropriately. This system provides information, models, and data processing tools to help experts/doctors make better decisions in each case. Conclusion: Digitalization coupled with risk-aware AI-DSS operationalizes nutrigenetic testing end-to-end—identifying risks and delivering personalized diagnosis, treatment, nutrition guidance, and lifestyle supporting faster, safer, and more consistent care.

The importance of nutrigenetic tests in detoxification

Expert Molecular Biologist-Dietitian E. Gökcen Alper Acar
Kara Mustafa Pasha State Hospital

Following the completion of the Human Genome Project, advances in molecular biology have enhanced our understanding of DNA organization, particularly regarding epigenetic mechanisms such as histone modifications and DNA methylation. The 4P model—Predictive, Personalized, Preventive, and Participatory—has become central to developing individualized treatment strategies from an epigenetic standpoint. Nutrigenetics, which explores how genetic variations influence an individual's nutritional responses, highlights the importance of personalization in healthcare. By tailoring interventions to specific genetic profiles, nutrigenetics aims to optimize treatment effectiveness.Detoxification, the body's process of eliminating harmful substances, is strongly influenced by genes that regulate detox pathways. Phase 1 enzymes, such as those encoded by *CYP1A1* and *CYP1A2*, and Phase 2 enzymes, including *GSTM1*, *GSTA1*, and *GSTP1*, are key components. However, the metabolic by-products generated during these phases can be highly toxic if not properly cleared, potentially contributing to the development of diseases like cancer. To manage this risk, personalized strategies are developed based on individual genetic polymorphisms in these detoxification genes.For example, individuals with a variant of the *CYP1A2* gene that increases enzyme activity may need to limit cruciferous vegetables like broccoli, as these can further enhance enzyme activity and raise toxic intermediate levels. In contrast, foods like celery and parsley may help by inhibiting this enzyme. Meanwhile, cruciferous vegetables are known to activate GST enzymes, essential for Phase 2 detoxification. As a result, nutrition, supplementation, and lifestyle choices should be customized according to each person's genetic profile. In this framework, nutrigenetic testing is a vital tool for predictive and preventive healthcare approaches.

Evaluation of Nutritional Habits in Individuals with Mutations in the LEPR Gene

Specialist Dietitian Esra Sahin
Esra Sahin Genetics and Health Center

In the modern world, the relationship between our lifestyle and genes has become one of the most critical factors in determining our metabolic health. Among the health issues arising from the disruption of this balance, obesity stands out as a major concern. Since traditional diet programs do not have the same effect on every individual, the significance of nutrigenetics has increased. This field aims to optimize weight control and metabolic health by creating nutrition plans tailored to an individual's genetic profile. Appetite regulation, fat metabolism, and weight management are influenced by genes such as FTO, LEP, and LEPR. Moreover, LEPR, LEP, and FTO genes play a crucial role in weight control. Polymorphisms in the FTO gene can increase the tendency for fat storage and energy intake, thereby elevating the risk of obesity. Disruptions in the LEP gene can lead to leptin signal abnormalities or leptin deficiency, resulting in increased appetite, weight gain, and obesity. Specifically, the LEP gene rs7799039 variant has been associated with the G allele, which is linked to higher anthropometric measurements and an increased risk of obesity. Nutrigenetic analyses can help design optimal dietary plans based on an individual's genetic predispositions, taking into account genetic variations that influence weight management. Individuals with leptin receptor deficiencies may not experience satiety effectively, making them more prone to overeating. Nutrigenetic assessments enable the development of personalized nutrition plans, offering tailored dietary and supplementation recommendations that align with an individual’s specific needs, as genetic profiles directly influence responses to dietary interventions. Gene-based nutrition provides long-term and effective health management by improving weight control and overall metabolic health. Advances in nutrigenetics facilitate the widespread adoption of genetically tailored nutrition plans, leading to more informed and effective health management strategies.

The Golden Key to Aging and Longevity: Fiber

Prof. Dr. F. Humeyra Yerlikaya Aydemir
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The objective of Longevity is to promote a healthy, energetic and disease-free life by rejuvenating biological age. In contradistinction to conventional medicine, this approach emphasises the maintenance and optimisation of health rather than the treatment of diseases. The process of ageing is an inevitable component of biological life. The process of ageing is a complex phenomenon characterised by a gradual decline in systemic health. The basis of this understanding is formed by a multitude of features, which reflect the various molecular and cellular mechanisms that drive the ageing process. As a case in point, the following factors should be considered: the accumulation of genetic damage, telomere attrition, epigenetic changes, cellular ageing, stem cell depletion and inflammation. Recent findings have also drawn attention to a novel phenomenon: the disruption of the gut microbiome. The gut microbiome is defined as a complex microbial community that plays an important role in human health. The gut microbiome displays distinctive patterns associated with the ageing process and has been speculatively linked to age-related comorbidities. A comparison of the gut microbiome of older adults (aged 65 to 80) with that of young and middle-aged individuals reveals significant disparities. The gut microbiome of older adults exhibits a distinct and unique composition, characterised by reduced microbial species diversity, a decrease in beneficial bacteria, and high levels of pathogenic microorganisms. The majority of contemporary interventions aimed at counteracting age-related changes in gut microbiota are dietary in nature, as they are more straightforward and secure to implement. It has been demonstrated that a dietary intervention can serve as a means to at least partially prevent changes in gut microbiota composition and metabolic function that are associated with unhealthy ageing. It has been demonstrated that the diversity of bacterial species and the abundance of both beneficial and 'potentially' beneficial bacteria, as well as the metabolites they secrete, can be increased through dietary intervention.

The Importance of Nutrigenetics and Microbiota in Early Life

Prof. Dr. Gulsen Meral
Epigenetic Coaching

The Human Genome Project, completed in 2003, helped us better understand the effects of genetic diversity on human health. This project contributed greatly to the development of medicine based on genetic information and laid the foundations of precision medicine, known as "4P medicine" (Predictive, Preventive, Personalized, Participatory). Precision medicine aims to prevent, diagnose and treat chronic diseases by analyzing individuals' phenotypic, genotypic and environmental factors. Translating nutrigenetics and nutrigenomics research into multidisciplinary clinical practice is a challenging process. However, by integrating data on genotype and phenotype, it is now clearly seen that nutrition, lifestyle and supplement use appropriate to the genetic structure of individuals will increase clinical success. Taking an epigenomic approach allows us to better understand the health risks that arise from the combination of genetic and environmental factors. In this context, nutritional and supplement recommendations based on personalized risk analyzes obtained from nutrigenetics, microbiota and test results are of great importance. It is especially necessary to emphasize how variants of genes encoding enzymes involved in 1C metabolism, VDR (Vitamin D Receptor) genetic variants and microbiota analysis results affect the phenotype. We believe that precision medicine will provide a tool for preventing diseases and reducing their symptoms, based on analyzes of disease-causing genetic predispositions and microbiota. Ensuring a harmonious interaction between genetic makeup and microbiota at early ages may improve long-term health outcomes. Therefore, it is of great importance that parents and healthcare professionals take these factors into account in the nutrition and care of children.

Body, Mind, and Gene Expression: Exploring the Epigenetic Potential of Basic Body Awareness Therapy (BBAT)

Dr. Fzt. Hatice Reyhan Ozgobek
Gulhane Health Sciences University, Ministry of Family and Social Services

Background: Emerging evidence highlights that chronic stress, emotional dysregulation, and sedentary lifestyles contribute to epigenetic modifications influencing inflammatory and neuroendocrine pathways. Basic Body Awareness Therapy (BBAT), developed in Scandinavia, is a physiotherapeutic and psychosomatic method combining movement, breathing, and mindfulness. It aims to restore balance, improve self-awareness, and support regulation between physiological, psychological, and existential domains. Objective: This workshop explores the potential role of BBAT in modulating stress-related physiological responses and its implications for epigenetic regulation. It focuses on the therapeutic link between body awareness, stress resilience, and mind-body interaction in individuals with chronic pain, depression, and migraine. Methodology: Participants will experience BBAT-based movements inspired by Tai Chi and Zen meditation, emphasizing breathing coordination, postural stability, and grounding. The workshop integrates brief theoretical input with experiential practice and reflection sessions. Clinical findings from migraine and stress-related cases will be presented, highlighting changes in muscle tone, autonomic regulation, and psychosocial well-being. Expected Outcomes: The practice of BBAT may influence stress-responsive biological systems, potentially affecting gene expression through improved autonomic balance, reduced cortisol levels, and enhanced parasympathetic activation. Participants are expected to gain experiential understanding of embodied regulation and its potential link to epigenetic health mechanisms. Conclusion: BBAT represents a biopsychosocial intervention bridging physiological and psychological adaptation, offering a promising field for future interdisciplinary studies connecting movement-based therapy and epigenetic modulation.

Epigenomic Signature During Menopause: The Transformative Power of Nutrition

Specialist Dietitian Hatice Simsek Sahin
Epigenetic Coaching

Menopause is a period in a woman's life characterized by intense hormonal, metabolic, and epigenetic changes. During this period, changes in DNA methylation, histone modifications, and microRNA expression are associated with mechanisms such as aging, oxidative stress, and inflammation. Epigenetic regulation is influenced not only by genetic factors but also by nutrition, physical activity, and environmental factors. Current studies demonstrate that nutrition plays a transformative role in modulating the epigenetic aging process. Dietary patterns rich in antioxidants, polyphenols, and phytoestrogens can slow epigenetic aging by providing protective effects on DNA methylation patterns and delaying menopause. The epigenetic regulatory effects of components such as soy isoflavones, resveratrol, curcumin, green tea polyphenols, folate, B12, omega-3, and vitamin D can positively influence the biological mechanisms of menopause. Conversely, high saturated fat, sugar, alcohol, and cigarette consumption can accelerate epigenetic aging and lead to earlier menopause. These effects of nutrition on epigenetic mechanisms may influence not only the age of menopause onset but also the severity of symptoms such as vasomotor symptoms, sleep disturbances, and cardiometabolic risk factors. However, most existing studies are observational and offer limited evidence of causality. Therefore, large-scale randomized controlled trials evaluating epigenetic-targeted nutritional interventions during menopause are needed. Consequently, epigenomics-based nutritional approaches stand out as a promising area for developing personalized health strategies in menopause management.

Artificial Intelligence Applications in Personalized Medicine: New Horizons

Prof. Dr. Ibrahim Halil Tanboga
Nisantasi University, Medical School

The integration of artificial intelligence (AI) and precision medicine is transforming how we identify and manage cardiovascular risk—starting from early life. Traditional population-based prevention models overlook the unique interplay of genetic, metabolic, and environmental factors that determine individual disease trajectories. Through AI-driven modeling and large-scale genomic–phenotypic integration, it is now possible to predict cardiovascular outcomes with unprecedented accuracy and to tailor interventions according to the individual's biological and environmental profile. Machine learning models trained on multi-omics datasets—including genomics, metabolomics, microbiota, and digital biomarkers—enable dynamic risk prediction beyond conventional clinical scoring. These approaches enhance early detection of subclinical vascular dysfunction, optimize preventive strategies, and support continuous learning from real-world data. Integrating such AI pipelines with personalized nutrition, pharmacogenomics, and microbiota-guided interventions can redefine preventive cardiology as a predictive, adaptive, and participatory discipline. In this framework, early-life cardiovascular programming becomes a critical window for targeted intervention. AI-supported interpretation of genetic and environmental interactions allows clinicians to transition from reactive disease management to proactive health optimization. The convergence of computational intelligence and precision cardiology represents not only a technological evolution but a philosophical shift—placing individual biology at the core of medical decision-making.

Genetic and Epigenetic Approaches to Cancer

Prof. Dr. Ilhan Yaylım
Istanbul University Aziz Sancar Institute of Experimental Medicine, Head of the Department of Molecular Medicine

Cancer is a disease of gene expression in which the complex networks governing homeostasis in multicellular organisms are disrupted, allowing cells to grow regardless of the needs of the organism as a whole. The characteristics acquired by cancer cells have both a genetic and an epigenetic basis. Epigenetics encompasses mechanisms that regulate gene expression without any changes in the DNA sequence. The primary epigenetic regulators are DNA methylation, histone modifications, and non-coding RNAS. These mechanisms, which maintain the balance of gene expression in normal cells, are disrupted in cancer cells, and changes such as hypermethylation of tumor suppressor genes and hypomethylation of oncogenes trigger tumor development. Epigenetic irregularities are associated with the abnormal activities of enzymes such as DNA methyltransferase (DNMT), histone methyltransferase (KMT), histone acetyitransferase (HAT), and histone deacetylase (HDAC), as well as the role of non- coding RNAs in this process. The imbalanced activity of these enzymes alters chromatin structure, leading to gene silencing and cellular dysfunction. However, the reversibility of epigenetic changes makes them attractive therapeutic targets. Epigenetic drugs (epidrugs), particularly DNMT and HDAC inhibitors, developed in recent years have shown promising results in cancer treatment. Epigenetic mechanisms are also known to be affected by the metabolic processes altered by cancer cells. A prime example of these changes is the inhibition of DNA demethylases by oncometabolites such as 2-hydroxyglutarate (2-HG), which occurs primarily as a result of IDH1/2 mutations, disrupting epigenetic regulation. In addition to the effects of changes in genetic codes on cancer, changes in genes that cause epigenetic changes have also become crucial in understanding cancer etiopathogenesis and approaching treatment. Elucidating these mechanisms will enable developing technologies to identify genetic and epigenetic changes even in single cells, enabling genetic and epigenetic identification of metastatic conditions, along with the primary focus. The use of databases storing a wealth of genetic and epigenetic data paves the way for the development of precision oncology approaches for personalized diagnosis and treatment. Consequently, understanding the role of epigenetic mechanisms in cancer biology is crucial for identifying early diagnosis biomarkers and developing new targeted therapies. Epigenetics-based strategies, with their stil-undefined advantages and disadvantages, are moving beyond the genetic paradigm in cancer research and ushering in a new era in medicine.

Keywords: Epigenetics, cancer, DNA methylation, histone modification, non-coding RNA, oncogene, tumor suppressor gene, epigenetic drugs.

Artificial Intelligence in Personalized Medicine: Transforming Genetics and Epigenetics for Precision Healthcare

YM. Ipek Meral
Epigenetic Coaching

The advent of Artificial Intelligence (AI) has revolutionized personalized medicine, particularly in the fields of genetics and epigenetics. AI algorithms, powered by machine learning (ML) and deep learning (DL) techniques, are now capable of processing vast datasets derived from genomic sequencing, epigenomic profiling, and multi-omics analyses. The integration of genomic, epigenetic, microbiome, and metabolomic data is critical for delivering truly personalized health solutions, yet current approaches are often fragmented and inaccessible beyond research settings. This presentation introduces a practical, AI-driven platform designed to streamline multi-omics data analysis, focusing on automation, scalability, and actionable insights for end users. Drawing on expertise in data analytics and health technology management, we propose a system architecture that simplifies the translation of complex molecular datasets into clear, personalized health profiles. The platform leverages secure cloud infrastructure, advanced machine learning models, and intuitive dashboards to support precision nutrition, preventive health, and longevity strategies. By bridging computational methods with wellness coaching, this work aims to democratize access to cutting-edge genomic and epigenetic science, making it both clinician-friendly and consumer-ready. This talk will highlight how multidisciplinary collaboration—spanning computing, health coaching, and AI—can accelerate the practical application of omics research and transform the future of personalized healthcare delivery.

Neuroaging and Immunonutrition

Assoc. Prof. Dr. Ishak Ozel Tekin
Zonguldak Bülent Ecevit University, Medical Faculty, Department of Immunology

Aging is defined as the linear and progressive loss of functional capability over time). It is characterized by a complex process causing the deterioration of fitness components, such as age-related performance and productivity. It also affects mental health and cellular processes, ultimately leading to morbidity and mortality. The improvement in life expectancy entails an increase in the incidence of neurodegenerative diseases being aging the greatest risk factor for these incurable conditions. Age-related brain changes are not well-characterized, and even less is known about the factors influencing the rate of brain aging. During recent decades there have been major advances in understanding the biology of aging, and the development of nutritional interventions that delay aging including calorie restriction (CR) and intermittent fasting (IF), and chemicals that influence pathways linking nutrition and aging processes. The importance of probiotics in improving gut health and immunity as well as alleviating metabolic diseases has been recognized. The new concept of a gut-heart-brain axis has led to the development of various innovations and strategies related to the introduction of probiotics in food and diet. Probiotics influence gut microbiota profiles, inflammation, and disorders and directly impact brain neurotransmitter pathways. As brain health often declines with age, the concept of probiotics being beneficial for the aging brain has also gained much momentum and emphasis in both research and product development. A diet that includes a variety of fresh foods rich in food bioactives, vitamins, minerals, and omega-3 fatty acids can help protect the brain and slow the progress of neurodegenerative diseases. For example, polyphenols and vitamins are known for their roles in protecting brain cells from inflammation and oxidative stress, both of which have been implicated in the development of neurodegenerative diseases.

Epigenetics and Pharmacogenetics

Prof. Dr. Kenneth White
London Metropolitan University, Head of Research and Knowledge Exchange, Faculty of Molecular Biosciences and Human Sciences

The path towards personalised health and treatment of ill-health is progressing steadily through improvements in our understanding of how our genome interacts with our environment. Both internal factors, such as our metagenome and external factors such as diet, exercise, infectious disease and social determinants of health, can impact how our genomes work, mediated through epigenomic pathways. In the presentation the link between pharmacogenomics, where genetic variation affects response to medicines, and epigenetic modifications, will be explored. A key message is that epigenetic modifications may be directly affected by genetic variation, for example by loss of CpG methylation site, or may be indirectly affected by genetic linkage. To understand more fully the link between genes and drug response, both genetic and epigenetic factors should be considered. A case study of methylation of a genetic locus and link to smell is discussed in detail to illustrate key points. The growing use of single strand sequencing using a nanopore platform can address methodological challenges of phasing genotype and epigenotype on individual alleles.

Cancer Case Report By Epigenomic Approach

Specialist Dietitian Leyla Karakas
Leyla Karakas Nutrition and Epigenetics Consultancy Private Clinic

This study aims to evaluate the potential effects of nutrition and hormonal factors on the development, progression, and treatment response of breast cancer from an epigenomic perspective. A 48-year-old woman was evaluated following the detection of a breast lesion during routine screening. Her height was 1.70 m, weight 68 kg, and body mass index was 23.5 kg/m². After surgical intervention in August 2024, she was diagnosed with early-stage invasive ductal carcinoma (IDC). Histopathological examination revealed an estrogen receptor (ER)–positive, progesterone receptor (PR)–positive, and HER2-negative tumor with a Ki-67 proliferation index of 5–6%. p63 immunostaining was negative. The patient's history included bioidentical progesterone therapy for estrogen dominance three years prior to diagnosis. Postoperatively, adjuvant tamoxifen therapy was initiated. Epigenetic mechanisms—such as DNA methylation, histone modifications, and non-coding RNAs—regulate gene expression and are influenced by dietary components. Folate, B vitamins, and methionine serve as methyl donors that maintain DNA methylation balance, whereas polyphenols (e.g., resveratrol, curcumin, green tea catechins) influence histone acetylation and suppress oncogene expression. Omega-3 fatty acids have anti-inflammatory effects that may improve the tumor microenvironment. A fiber- and plant-based diet supports gut microbiota and promotes beneficial epigenetic signaling via short-chain fatty acid production. This case highlights the potential interplay between hormonal imbalance, nutrition, and epigenetic regulation in breast cancer development and progression. An epigenetically balanced, antioxidant- and plant-based diet may contribute not only to cancer prevention but also to improved treatment response and quality of life.

Healthy Plant-Based Nutrition for a Healthy Metabolism

Prof. Dr. Mehmet Hamurcu
Selçuk University, Faculty of Agriculture, Department of Soil Science and Plant Nutrition

Today, global population growth, climate change, water scarcity, and food insecurity have become critical issues directly affecting agricultural production and human nutrition. Worldwide, 733 million people face chronic hunger, while 2.3 billion individuals suffer from "hidden hunger," a condition resulting from deficiencies of essential vitamins and minerals. Hidden hunger is a global public health problem that emerges when micronutrient intake (e.g., Zn, Fe, Se, I) is insufficient, even when caloric intake is adequate. The increased yield of crops through modern agricultural practices has led to a noticeable dilution in the mineral density of plant-based foods. In particular, the zinc, iron, and selenium contents of cereals have significantly decreased compared to previous decades. Comprehensive studies conducted in Türkiye indicate that the selenium concentration of wheat grains often remains below 40 μg kg^{-1}**.** High phytic acid levels in cereals further reduce the absorption of Zn and Fe, exacerbating micronutrient deficiencies. In addition, genetic selection focused primarily on yield in high-yielding modern wheat cultivars has intensified the so-called "dilution effect" on nutrient composition. Soil depletion in micronutrients, imbalanced fertilization practices, and dietary habits also contribute to this concerning trend. Addressing micronutrient deficiencies through supplementation or food fortification is often considered economically unfeasible and unsustainable for developing countries. Therefore, agronomic and genetic biofortification strategies—rooted in agricultural improvement—are increasingly recognized as the most effective long-term, economical, and scalable solutions for combating hidden hunger at the population level. Our study emphasizes the strategic importance of optimizing nutrient composition in plant production for human metabolism and global public health.

Environmental Factors in Epigenetic Regulation

Dr. Mehmet Tolgahan Hakan
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Epigenetic mechanisms convey the biological effects of environmental factors to the cellular level by reprogramming gene expression permanently without altering the underlying DNA sequence. Many study provides an integrative evaluation of how distinct environmental exposures converge on common epigenetic pathways to produce similar pathological outcomes. DNA methylation, histone modifications, and microRNA-mediated regulation constitute the principal targets of environmental stress. Air pollution, heavy metals, pesticides, endocrine disruptors, high-fat diet, ethanol, and psychosocial stress disrupt the miR-34a/SIRT1 axis, IGF2/H19 imprinting, BDNF/NR3C1 methylation, and PPARγ/histone deacetylation patterns, thereby contributing to the development of metabolic syndrome, cardiovascular disorders, neurodegenerative diseases, and cancer. Increased miR-21 expression further enhances NF-κB/STAT3 activation through repression of PTEN and PDCD4, establishing a shared molecular response underlying inflammation, fibrosis, and oncogenesis. Prenatal and early-life periods represent the most sensitive stages of epigenetic reprogramming; exposures during these windows not only elevate disease susceptibility later in life but may also enable germline-mediated transgenerational epigenetic inheritance. Collectively, the findings indicate that epigenetic mechanisms serve as a “common molecular language” of environmental stress. Recognizing the multifaceted and intersecting nature of these regulatory networks will be crucial for the development of evidence-based strategies in early diagnosis, preventive medicine, and targeted therapeutic interventions, as well as for shaping effective public-health policies aimed at mitigating environmentally induced disease risks.

Genetic and Epigenetic Approach to Pediatric Neurological Diseases

Specialist Dr. Meltem Uzun
Epigenetic Coaching

Epigenetics, which studies heritable changes in gene expression without alterations in the DNA sequence, has emerged as a crucial factor in understanding the development of neuropsychological disorders in children. Increasing evidence indicates that early-life environmental factors—such as stress, nutrition, exposure to toxins, and parental care—can induce epigenetic modifications that influence brain development and cognitive function. These alterations play a role in the pathogenesis of various neurodevelopmental and neuropsychiatric disorders, including autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), anxiety disorders, and depression. The content of this talk focuses on sharing experiences regarding how epigenetic mechanisms—particularly DNA methylation, histone modification, and non-coding RNA regulation—contribute to the onset and progression of these conditions, especially in pediatric populations with neurological and developmental challenges, as well as their potential impact on therapeutic processes. Understanding the role of epigenetics not only provides deeper insights into the biological foundations of childhood neuropsychological disorders but also opens new avenues for early diagnosis, prevention, and personalized therapeutic interventions.

Detoxification Panel: Gene-Nutrition-Disease Relationships

Dietitian Merve Özkaya
Epigenetic Coaching

Detoxification is the process through which the organism eliminates harmful toxins, and it occurs through Phase I reactions, Phase II conjugation, and Phase III antiporter activity. During Phase I, the liver converts toxic compounds into intermediate metabolites that are often more toxic than their original forms through the action of specific enzymes. In Phase II, these intermediate metabolites are transformed by enzymatic conjugation into less harmful and water-soluble compounds, which can then be excreted via bile or urine. In Phase III, various substances are transported across cellular barriers such as the liver, gastrointestinal tract, kidneys, and blood-brain barrier. Reactive molecules that become more toxic during Phase I enzymatic reactions can cause tissue damage if they are not subsequently metabolized in Phase II conjugation. An increase in Phase I activity accompanied by a decrease in Phase II activity has been associated, in several studies, with an increased risk of diseases such as cancer and asthma. Among the key biotransformation enzymes involved in Phase I and II reactions are Cytochrome P450 (CYP450), Glutathione-S-Transferase (GST), and Catechol-O-Methyl Transferase (COMT). It has been observed that certain nutraceuticals, such as quercetin, can modulate the activity of these enzymes. Quercetin has been shown to inhibit CYP enzymes and increase GSTM activity, thereby reducing the risk of lung cancer development. However, another study demonstrated that quercetin inhibits COMT activity in breast tissue, does not prevent oxidative alterations, and does not provide protection against estrogen-induced breast cancer. In conclusion, quercetin has been found to inhibit CYP1A1/B1 and COMT enzymes, while inducing GST enzymes. This suggests that, in evaluating quercetin supplementation, attention should be given not only to CYP and GST gene variants but also to the individual's COMT gene polymorphism. When COMT enzyme activity is reduced, quercetin may exert adverse effects. Therefore, supplementation strategies should not be based on a single gene, but rather approached from a polygenic perspective.

Genetic and Epigenetic Targeted Therapies for Cancer

Specialist Dr. M. Yunus Alp
Genoks Genetic Center, Ankara
Epigenetic Coaching

Cancer is a heterogeneous group of diseases resulting from the interaction of genetic mutations, epigenetic alterations, and environmental factors, whether inherited or often acquired. Compared to standard chemotherapy, targeted and personalized treatment approaches increase treatment success in cancer patients. Genetically targeted therapies target pathways related to oncogene activation or tumor suppressor gene loss resulting from gene mutations in tumor cells (e.g., EGFR, BRAF, ALK, and PARP inhibitors), while epigenetic therapies aim to regulate gene expression by modulating DNA methylation, histone modifications, and chromatin reorganization (e.g., DNMT and HDAC inhibitors). The combination of these two approaches offers promising results in overcoming treatment resistance and reprogramming the tumor microenvironment. The integration of genomic and epigenomic profiling alongside standard treatment modalities such as surgery, chemotherapy, and radiotherapy aims to develop more sensitive and personalized strategies for cancer treatment.

Functional Microbiota for Longevity: Artificial Intelligence-Enhanced Approaches

Prof. Dr. Mustafa Altındis
Sakarya University Faculty of Medicine, Department of Clinical Virology and Microbiology

The concept of healthy aging (longevity) encompasses not only the extension of lifespan but also the preservation of functional capacity, physiological resilience, and metabolic homeostasis throughout the aging process. Achieving true longevity requires a multidimensional understanding of molecular, microbial, and environmental interactions that collectively shape health trajectories. Within this framework, the gut microbiota has emerged as a central regulator of longevity biology, exerting profound effects on immune homeostasis, chronic inflammation ("inflammaging"), metabolic balance, and epigenetic modulation of host cells. The term functional microbiota extends beyond the taxonomic description of microbial communities to encompass their genetic potential, metabolic functionality, signaling metabolites, and dynamic host–microbe interaction networks. Age-related alterations in microbial diversity and function—often referred to as microbial dysbiosis of aging—are increasingly linked to systemic inflammation, mitochondrial dysfunction, and accelerated biological aging. Conversely, specific microbial taxa and their metabolites (e.g., short-chain fatty acids, indoles, polyamines) have been associated with anti-inflammatory, antioxidative, and epigenetically protective effects, offering potential targets for interventions that promote healthy aging. Recent advances in artificial intelligence (AI) and machine learning have transformed our ability to decode the complexity of microbiome–longevity relationships. AI-enhanced bioinformatics enables multi-omics integration, pattern recognition, and predictive modeling of microbiota-associated aging trajectories. These computational approaches allow the identification of aging-specific microbial signatures, support precision probiotic and prebiotic design, and facilitate the development of microbiota-based biomarkers for early detection of age-related decline.
Functional microbiota–longevity axis through four key perspectives:
1.The epigenetic basis of aging and its modulation by microbial metabolites,
2.Age-related dysbiosis and loss of microbial resilience,
3.Microbiota–metabolite–host signaling networks in aging biology, and
4.AI-assisted microbiome analytics for predictive and personalized longevity medicine.
By integrating microbiome science with computational intelligence, the emerging field of AI-driven functional microbiota research holds transformative potential for the epigenetic regulation of aging, paving the way toward a new paradigm of microbiota-informed precision longevity medicine.

Epigenomics: Its Role in Cancer and Clinal Potaential

Prof. Dr. Mustafa Camgöz
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Cancer is a major health problem that is predicted to grow. In 2022b, there were 20 million new cases and 9.7 million deaths (roughly the population of Switzerland, Austria or Hungary). These are predicted to increase by 75% in the next 20 years. Consequently, we urgently need to develop new approached to understand treat this complex disease. Here, epigenomics offers great promise. Indeed, cancer is primarily an epigenomic disease. Whilst some cases are due to mutations in associated genes, in most cases it is expression of the culprit genes at abnormal levels spatially that is the main cause. We have adopted a bioelectricity approach to understand and treat metastasis, the main cause of death from cancer. We have shown that carcinomas become electrically excited as a requirement for their metastatic dissemination. We call this the CELEX Model [DOI: 10.1007/s10555-024-10195-6]. At the centre of this phenomenon is de novo expression of functional voltage-gated sodium channels (VGSCs). Indeed, by blocking VGSC activity using simple drugs like anti-epileptics, anti-convulsants or local anaesthetics, metastasis can be suppressed. Importantly, the VGSC is under activity-dependent control whereby inhibiting its activity also suppresses its expression epigenetically. More broadly, cancer may also be treated using epigenetic drugs either directly or indirectly. The latter could be achieved through miRNAs as a recent study on Huntington's disease has shown [doi: https://doi.org/10.1038/d41586-025-03139-9].

The importance of nutrigenetics in epigenetics

Dietitian Neval Burkay
Epigenetic Coaching

Recent advances in the emerging fields of nutritional genomics have revealed that responses to dietary macro- and micronutrients may differ among individuals, in part due to differences in their genetic makeup. Genetic variations such as single nucleotide polymorphisms (SNPs) and copy number variations (CNVs) have become increasingly interrogated in efforts to explain differences in individuals' responses to diet as well as to formulate personalized dietary recommendations. Genetic differences can affect protein synthesis and function, thereby altering nutritional needs and metabolism and affecting a person's risk of developing chronic diseases. Nutrigenetics, which investigates the impact of inherited genetic variants on the intake and metabolism of micronutrients, has emerged as a guide in personalized nutrition. Genetic variants that affect metabolic reactions, especially in the methylation cycle, also act through epigenetic mechanisms and cause chronic diseases. Epigenetics regulates the expression of genes without changes in the coding sequence of DNA. The most important of these epigenetic mechanisms that determine how and when certain genes are turned on or off are methylation reactions. S-adenosyl methionine (SAM), used as the universal methyl donor in DNA methylation, is an important molecule derived from the methylation cycle. There are many important enzymes involved in the methylation cycle, and these enzymes must work effectively. Since micronutrients such as folate, choline, betaine, vitamin B12 and other B vitamins contribute to DNA methylation as methyl donors and cofactors, their deficiency affects the methylation process and causes epigenetic changes. This study explains the effects of individually designed recommendations as a result of nutrigenetic tests on the methylation cycle. More widespread use of Nutrigenetic tests, which have gained importance for personalized nutrition programs from a Precision Medicine perspective, has provided a predictive and preventive approach.

Child Abuse, Neglect and Longevity: Lifelong Effects

Assoc. Prof. Dr. Nihal Durmaz
Gülhane Training and Research Hospital

Child abuse, encompassing all forms of physical and emotional maltreatment, sexual abuse, neglect, and exploitation that harm a child's health, development, or dignity, remains a major global public health concern.Epidemiological studies indicate that approximately 60% of children under five experience physical punishment or psychological violence, while one in five women and one in seven men report having been sexually abused during childhood. Such adverse experiences exert lifelong effects on physical, mental, and social well-being. They are associated with post-traumatic stress disorder, depression, anxiety, sexually transmitted infections, unintended pregnancies, and diminished cognitive and academic performance. Moreover, exposure to abuse increases the risk of harmful behaviors such as alcohol and substance use.Advances following the Human Genome Project have revealed that these experiences not only affect psychological health but also accelerate biological aging through epigenetic mechanisms. Chronic stress caused by abuse elevates cortisol levels and disrupts the neuroendocrine system. This cascade leads to reduced telomerase activity, increased oxidative stress, and mitochondrial dysfunction, ultimately resulting in accelerated cellular aging.Recent evidence suggests that exposure to emotional and physical abuse accelerates epigenetic aging (mAge), particularly among girls. Childhood maltreatment leaves measurable biological imprints that may serve as early biomarkers of risk. Identifying these molecular traces can enable early intervention and targeted support for vulnerable children, contributing to the prevention of long-term health consequences.

Molecular Effects of Breathing at The Cellular Level

Dr. Ruya Acaroglu
Antalya Ataturk State Hospital

All breathing practices primarily target the HPA axis. The HPA Axis — affected by stress, exercise, cold, sleep, breathing, yoga, and meditation — is the key regulator. It functions as a large integrated system. Starting from the hypothalamus and continuing through the pituitary, adrenal cortex, and medulla, it generates effects that eventually manifest in peripheral organs. Although stress seems to emerge in the final organ, it actually originates at the cellular level — particularly within the mitochondria. The intracellular oxygen pressure dropping below 2 mmHg triggers a cascade of molecular signals. Hypoxia, calcium channels, and sodium channels communicate through an intricate and miraculous signaling network that coordinates the entire system. Managing stress effectively always involves breathing, along with sleep, exercise, yoga, and meditation — because breathing regulates this system. All changes begin at the molecular level within cells, especially in the alveolar-capillary membrane of the lungs, where histological potential for remodeling starts. Different rhythmic and model-based breathing practices determine the potential of oxygen-carrying erythrocytes and their oxygen transport capacity. In glycolysis, the Ruppaport–Lubering pathway demonstrates that, at the molecular level, these reactions — as well as the presence of mineral chelators in the pathway — significantly affect cellular function. Mutations or variations in receptors also influence the outcomes.

Epigenetic Effects of Breastfeeding

Assoc. Prof. Dr. Ruya Atesli
Acıbadem Kent Hospital, Izmir

Breast milk is the most ideal source of nutrition, meeting all of a baby's needs during the first six months of life. It contains not only macro- and micronutrients but also epigenetic regulators that influence gene expression. The concept of epigenetics suggests that genetic structure can be reprogrammed by environmental factors such as nutrition, stress, and toxins. The Barker hypothesis and the DOHaD (Developmental Origins of Health and Disease) model demonstrated that early-life conditions determine the risk of developing chronic diseases later in life. Mechanisms such as DNA methylation, histone modifications, and microRNAs play key roles in this process. Breast milk contains several bioactive and epigenetically active components—including choline, phospholipids, short-chain fatty acids (especially butyrate), HMOs (human milk oligosaccharides), exosomes, microRNAs, and long non-coding RNAs (lncRNAs). These components permanently shape the infant's immune tolerance, neurodevelopment, and metabolic balance. In addition, stem cells found in breast milk support neural development, while its rich microbial diversity helps shape the infant's gut–brain axis. Conversely, maternal factors such as poor diet, and exposure to BPA, phthalates, heavy metals, or pesticides can transfer through milk and cause epigenetic damage in the infant. In conclusion, breast milk is not merely a source of nutrition but a powerful epigenetic messenger that helps shape the genetic destiny of life in its earliest stages. "A mother's epigenetic health determines her baby's genetic future."

AttoPGx: Unlock Personalised Medication Plans for Better Health Through Direct-to-Consumer Pharmacogenomics Testing

Dr. Sasitaran Iyavoo
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Adverse drug reactions (ADRs) and poor treatment responses remain major healthcare challenges, costing the NHS an estimated £2 billion annually. Pharmacogenomics (PGx) testing offers a precision medicine approach by tailoring drug prescriptions to an individual's genetic profile, thereby improving efficacy and minimising adverse outcomes. AttoDiagnostics has developed AttoPGx, a comprehensive, direct-to-consumer PGx testing service designed to empower clinicians and patients with actionable insights into drug–gene interactions. The service integrates advanced genotyping and sequencing platforms, including the TaqMan™ OpenArray™ PGx Express and Custom Panels, Infinium HTS iSelect Custom microarray (Rita panel), and Ion AmpliSeq™ Pharmacogenomics Research and Custom NGS Panels, enabling robust analysis of key pharmacogenes such as CYP2D6, CYP2C9, and CYP2C19. Automated sample processing through systems like Integra Assist Plus, KingFisher Flex, and QuantStudio™ 12K Flex ensures high throughput and accuracy, while data interpretation is supported by TaqMan® Genotyper and CopyCaller® software for SNP and CNV determination. This workflow allows efficient and precise detection of single nucleotide and structural variants critical to pharmacogenomic decision-making. Results are securely delivered via an online portal within 10–14 days, with options for clinician consultation to guide therapeutic optimisation. The AttoPGx initiative demonstrates the feasibility of integrating laboratory-grade genetic testing into accessible, patient-centred healthcare pathways, supporting personalised medication management and advancing the implementation of precision medicine in the UK and beyond.

The Beginning of Longevity: Personalized Nutrigenetics in Childhood

Doç. Dr. Selen Baran Özmen
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Longevity, defined as a long and healthy lifespan, is shaped not only by measures taken in later life but also by nutrition and lifestyle factors established during childhood. Nutrigenetics, which aims to understand nutritional responses based on an individual's genetic makeup, provides a scientific basis for developing personalized strategies. When implemented early in life, nutrigenetic approaches go beyond supporting healthy growth and development and establish a strong foundation for lifelong health and the prevention of chronic diseases. This presentation highlights the potential impact of personalized nutrigenetic strategies in childhood on long-term health and longevity. Based on current literature, interactions between nutrigenetics, epigenetics, and the microbiota were examined, and the effects of early childhood nutritional strategies on epigenetic memory, metabolic pathways, and inflammatory processes were evaluated. Findings indicate that nutrigenetic-based personalized nutrition in childhood has significant effects on energy metabolism, obesity risk, cardiometabolic health, and immune system development. Identifying individual differences in vitamin, mineral, and macronutrient responses through single nucleotide polymorphisms forms the foundation of lifelong health strategies. Furthermore, the early shaping of the gut microbiota shows a strong association with long-term metabolic balance and healthy aging. In conclusion, the beginning of longevity lies in childhood, and nutrigenetic-based personalized nutritional approaches have the potential to support not only child health but also the prevention of chronic diseases in adulthood and the promotion of healthy aging.

Synergistic Anticancer Effects of Carvacrol-Based Essential Oil Formulations

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Istinye University, Faculty of Pharmacy

Essential oils, composed of diverse phytochemical constituents, have attracted increasing scientific attention as potential adjuvant agents in cancer therapy due to their low intrinsic toxicity, multi-targeted action, and synergistic interactions among individual components. This study aimed to evaluate the synergistic anticancer potential of carvacrol-based essential oil formulations across various human cancer models. In vitro assays were conducted on lung (A549), breast (MDA-MB-231), prostate (PC-3), and pancreatic (MiaPaca-2) cancer cell lines for 24, 48, and 72 hours, followed by in ovo CAM model experiments to assess tumor progression and histopathological alterations. The results demonstrated that combined essential oil formulations exhibited significant time- and dose- dependent cytotoxicity, with marked decreases in cell viability and evidence of apoptosis and nuclear fragmentation. In ovo analyses further confirmed these findings, revealing reduced tumor volume and apoptotic morphology within treated groups compared to controls. Mechanistically, the observed synergism is associated with enhanced reactive oxygen species (ROS) production, activation of mitochondrial apoptotic pathways, cell-cycle arrest, and modulation of inflammatory and proliferative signaling networks including PI3K/Akt, MAPK, and NF-κB. These coordinated actions suggest that rationally designed essential oil combinations may provide enhanced therapeutic efficacy compared with single-compound applications. In conclusion, the study supports the potential of synergistic essential oil formulations as multi- target, low-toxicity phytopharmaceutical candidates for integrative oncology. Further in vivo and clinical investigations are warranted to validate their mechanistic pathways and optimize their translational potential.

Next Generation Pharmacy: Personalized Treatment with Pharmaco-Epigenetics

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The profession of Pharmacy is as old as human history. It dates back to healers who prepared primitive medicines by crushing and boiling roots, plants and natural substances. In the 19th and 20th centuries, huge advances in chemistry and pharmacology laid the foundation for the modern pharmaceutical industry and pharmacotherapy, which was dominated by a "one size fits all" approach. This period has gone down in history as the "traditional model" in which mass-produced medicines in standardized doses were made available to patients. However, this standardized approach often led to treatment failures and adverse drug reactions due to genetic and biological differences between individuals. At this point, the next revolutionary step in the historical process, Pharmacogenetics, emerged. Pharmacogenetics laid the first foundations of personalized medicine by studying how inherited variations in a person's DNA sequence (genotype) affect the response to drugs. Today, this evolution has gone one step further and Pharmaco-epigenetics was born. Pharmaco-epigenetics is the most promising new branch of personalized medicine. This discipline studies the critical role of epigenetic modifications (DNA methylation, histone modifications, miRNAs), which regulate gene expression by "turning on and off" rather than fixed changes in our DNA sequence, on drug efficacy, metabolism and toxicity. The main feature that makes pharmaco-epigenetics dynamic and different from pharmacogenetics is that our epigenetic profile is not fixed. Individuals' epigenetic signatures are deeply influenced by factors such as lifestyle, dietary habits, stress, exposure to environmental toxins and even infections and can change throughout life. By analyzing this dynamic profile, pharmaco-epigenetics can more comprehensively explain why a patient responds differently to a particular drug and enable the selection of the most appropriate drug and dose. For example, the efficacy of a cancer chemotherapeutic may be directly related to the methylation status of the promoter region of the target gene. This approach lays the foundation for a new generation of personalized pharmaceutical care and rational drug use, optimizing treatment success while minimizing adverse effects.

Kinesiometabolomic Approach in Exercise Applications

Prof. Dr. Umit Zeybek
Istanbul University, Institute of Experimental Medicine, Department of Molecular Medicine

Today, many sports have become widespread national and international industries, each with its own unique rules and playing styles. Athletes experience physical and mental stress due to the intense pace of training and competition, coupled with the expectation of top-level performance.
The kinesiology approach is the science of movement used to balance body health, endurance, and energy without the use of medication or surgery.
Gene variations can reveal hidden abilities that make an individual more effective and different. At the same time Epigenetic mechanisms control gene expression directly or indirectly. However, epigenetic changes which are reversible and do not change DNA base sequences, are separated from the back mutations.
Genes: A Cellular and Molecular Perspective
Impact: Training
G x I: Interaction
G and I: Correlation
Elite athletes may be born with an appropriate genetic structure, but they cannot reflect their potential due to the lack or failure of antrenization. As a result of years of research and experience, it is understood that the difference in “trainability” is mostly related to genes. For this reason, studies on genes that may affect athletic performance are still ongoing.
“Kinesiogenetic Approach”; A personalized program/content can be planned when organizing athletes' exercise and nutrition calendars.
“Different Genotypic Traits, Different Phenotypic Reflections.” For the last 20 years, many scientists, including myself and my team, have been investigating polymorphisms that they believe affect athletic and mental performance in athletes.
“Kinesiogenomic Approach”; Additionally, analyses of the link between data such as gene expression and DNA methylation and exercise are finding their way into R&D/INNOVATION projects, both within our own group and those of international scientists. These assessments can help provide insight into the complex interactions between genetic makeup and certain kinesiological parameters in the body.
“Kinesiometabolomic Approach”; Kinesiology, "being in the moment", Genetic, "near and distant", Genomic, "what might be" and Metabolomic, "what really is".
On the other hand the personal microbiome structure, which affects athlete health and performance and is linked to the microorganism content in the intestinal flora, has begun to be included in the research areas to a significant extent. The effects of dietary practices on bacterial flora in different sports branches have been demonstrated in many studies.

Epigenomic Approach in Physiotherapy

Prof. Dr. Zuhal Kunduracılar
Istanbul Gelisim University, Faculty of Health Sciences, Head of Department of Physical Therapy and Rehabilitation

One of the newest frontiers of physical therapy is the field of epigenetics, which examines how pervasive environmental factors such as exercise regulate the expression of genes. Skeletal muscle has an enormous plastic potential to adapt to various external and internal perturbations. Chronic pain is a prevalent condition with a multifaceted pathogenesis, where epigenetic modifications, particularly DNA methylation, might play an important role.
The epigenome may be one of the most powerful systems through which exercise exerts its beneficial effects on health and longevity. Large epidemiology studies show that individuals who regularly exercise demonstrate a lower “epigenetic age,” experience fewer metabolic diseases, and enjoy greater longevity. However, the dose, mode, intensity, and duration of exercise required to achieve a healthy epigenetic profile is unknown. Acute exercise and exercise training may confer epigenetic modifications in healthy subjects. Epigenetic effects after exercise have been showed in patients with cardiovascular disease. As experts in exercise prescription, physical therapists are ideally suited to contribute to the discovery of this dose-response relationship. This perspective makes a case for the genesis of “precision physical therapy,” which capitalizes on epigenetic discoveries to optimize exercise-based interventions.

Metabolic Inflammation: The Hidden Culprit Behind Aging and Chronic Diseases

Prof. Dr. Zubeyde Gunduz
Acıbadem Eskisehir Hospital

The proper regulation and management of energy, substrate diversity, and quantity are fundamental to cellular and organismal survival and are crucial for health. The highly regulated interactions between immune and metabolic responses are evolutionarily conserved and crucial for tissue and organismal health. Disruption of these interactions underlies the emergence of many pathologies, particularly chronic non-communicable diseases such as obesity and diabetes. Under pathological conditions, there is an interplay between immune regulation and abnormal metabolism, leading to persistent inflammation even in the absence of infection. This phenomenon is called sterile metabolic inflammation (metainflammation). Dietary factors can influence the immune system independently of obesity-associated inflammation. Macrophages are central players in the meta-inflammation associated with obesity and aging. SNPs can influence genes involved in metabolic pathways that are associated with individual responses to nutrients and dietary patterns, influencing metabolic inflammation and insulin sensitivity.

BİLDİRİLER

Sözlü Bildiri: SB-01

Molecular Traces of Human Diseases in the Model Plant *Arabidopsis thaliana*

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Objective: Although the model plant *Arabidopsis thaliana* was initially used to elucidate fundamental aspects of plant biology, it has since evolved into a powerful model organism for understanding general eukaryotic processes. This study aims to highlight the conceptual impact of Arabidopsis-based research on human biology, particularly in relation to neurodegenerative diseases such as Alzheimer's and Parkinson's. **Method:** This work is based on an extensive literature review focusing on key biological processes in *A. thaliana*—including protein degradation, DNA methylation, RNA silencing, G-protein-mediated signal transduction, and circadian regulation. Comparative genomic analyses between human and Arabidopsis orthologous genes were also evaluated to assess the potential of plant models in biomedical research. **Results:** The characterization of SCF complexes and E3 ubiquitin ligases in Arabidopsis has elucidated mechanisms of protein degradation, shedding light on the protein aggregation processes observed in Alzheimer's and Parkinson's diseases. Comparative genome analysis revealed that approximately 71% of human neurological disease–related genes and 70% of cancer-associated genes possess Arabidopsis orthologs—higher than the proportions found in Drosophila (67%) and Saccharomyces (41%). In a Huntington's disease model, expression of the expanded polyQ-containing Huntingtin protein in Arabidopsis demonstrated that the chloroplast Stromal Processing Peptidase (SPP) can prevent cytosolic aggregation; notably, synthetic SPP also reduced polyQ accumulation in human cells and *Caenorhabditis elegans*. In Parkinson's disease, the Arabidopsis ortholog of DJ-1, AtDJ-1a, mitigates oxidative stress and mirrors human DJ-1 function, interacting with orthologs of human DJ-1–associated proteins (e.g., CSD1). Moreover, orthologs of human proto-oncogenes identified in Arabidopsis highlight the plant's potential as a model for cancer mechanism studies. NB-LRR proteins in Arabidopsis interact with HSP90 and SGT1 to regulate immune signaling—interactions that are conserved in the human immune system. Recently, Arabidopsis AtGLR3.4 has been implicated in NO-dependent redox signaling and mitochondrial stress responses, suggesting an evolutionarily conserved mechanism parallel to human glutamate receptor and redox signaling pathways. **Conclusion:** *A. thaliana* stands out as a multidisciplinary model organism that contributes not only to plant biology but also to the understanding of human physiology. Its simple growth requirements, genetic tractability, and minimal ethical constraints make it an attractive system for the development of new molecular tools in biomedical research. Findings from Arabidopsis-based studies have provided direct insights into the genetic, cellular, and molecular mechanisms underlying complex human disorders such as neurodegenerative diseases and cancer.

Keywords: *Arabidopsis thaliana*, epigenetic regulation, DNA methylation, ubiquitin–proteasome system, neurodegenerative diseases, redox signaling.

Model Bitki *Arabidopsis thaliana*'da İnsan Hastalıklarının Moleküler İzleri

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Amaç: Model bitki *Arabidopsis thaliana*, başlangıçta temel bitki biyolojisini anlamak amacıyla kullanılmış olsa da, zamanla ökaryotik sistemlerin genel işleyişini çözmede güçlü bir model organizma hâline gelmiştir. Bu çalışmanın amacı, *Arabidopsis*-temelli araştırmaların insan biyolojisi ve özellikle nörodejeneratif hastalıklar (Alzheimer, Parkinson) üzerindeki kavramsal etkilerini ortaya koymaktır. **Yöntem:** Bu çalışma, *Arabidopsis thaliana*'da protein yıkımı, DNA metilasyonu, RNA susturulması, G-protein aracılı sinyal iletimi ve sirkadiyen saat gibi temel süreçlere ilişkin literatür verilerinin incelenmesine dayanmaktadır. Ayrıca insan ve *Arabidopsis* genomları arasında yapılan ortolog gen karşılaştırmaları değerlendirilerek, bitki modellerinin biyomedikal araştırmalardaki potansiyeli analiz edilmiştir. **Bulgular:** *Arabidopsis*'te tanımlanan SCF kompleksi ve E3 ubikuitin ligazları, protein yıkımı mekanizmalarını açıklayarak Alzheimer ve Parkinson hastalıklarında görülen protein agregasyonu süreçlerine ışık tutmuştur. Karşılaştırmalı genom analizleri, nörolojik hastalıklarla ilişkili genlerin %71'ininve kanserle ilişkili genlerin %70'inin *Arabidopsis* ortologlarına sahip olduğunu göstermiştir; bu oran, *Drosophila* (%67) ve *Saccharomyces* (%41) oranlarından daha yüksektir. Huntington hastalığı modelinde genişletilmiş polyQ dizisi içeren Huntingtin proteini Arabidopsis'te ifade edildiğinde, kloroplast Stromal Processing Peptidase (SPP) aracılığıyla sitozolik agregasyon engellenebilmiş ve aynı SPP sentetik olarak insan hücrelerinde ve *Caenorhabditis elegans*'ta da polyQ birikimini azaltabilmiştir. Parkinson hastalığında DJ-1 proteininin Arabidopsis ortoloğu AtDJ-1a, hücresel oksidatif stresi azaltarak insan DJ-1 fonksiyonunu yansıtmaktadır ve AtDJ-1a, insan DJ-1 ile etkileşen proteinlerin Arabidopsis ortologlarıyla da etkileşime girmektedir (ör. CSD1 ile). Kanser çalışmalarında, insan proto-onkogenlerin ortologları Arabidopsis'te bulunarak bitkiyi kanser mekanizmalarının incelenmesi için potansiyel bir model hâline getirmiştir. Ayrıca, NB-LRR proteinleri HSP90 ve SGT1 ile etkileşerek bağışıklık sinyallemesini yönetmekte ve bu etkileşimlerin insan bağışıklık sisteminde de korunduğu gösterilmiştir. Yakın zamanda ise Arabidopsis'te AtGLR3.4'ün NO-temelli redoks sinyallemesi ve mitokondriyal stres yanıtlarındaki rolü, insanlardaki glutamat reseptörleri ve NO/redoks yollarıyla evrimsel olarak korunmuş olabilecek paralel başka bir mekanizmaya ışık tutmuştur. **Sonuç:** *Arabidopsis thaliana*, yalnızca bitki biyolojisinin değil, insan biyolojisinin de anlaşılmasında disiplinler arası bir model organizma olarak öne çıkmaktadır. Basit yetiştirme koşulları, genetik manipülasyon kolaylığı ve etik sınırlamaların azlığı sayesinde, biyomedikal araştırmalarda yeni moleküler araçların geliştirilmesine olanak sağlamaktadır. *Arabidopsis*-temelli bulgular, nörodejeneratif hastalıklar ve kanser gibi kompleks bozuklukların genetik, hücresel ve moleküler düzeyde anlaşılmasına doğrudan katkı sağladığını ortaya koymaktadır.

Anahtar Kelimeler: *Arabidopsis thaliana*, epigenetik düzenleme, DNA metilasyonu, ubikitin-proteazom sistemi, nörodejeneratif hastalıklar, redoks sinyalizasyonu.

Sözlü Bildiri: SB-02

Investigation of the Relationship Between Serum Low-Density Lipoprotein Cholesterol Levels with Genetic Polymorphisms, Gut Microbiota, and Nutrition

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Objective: The aim of this retrospective study was to comprehensively investigate the effects of nutrition, gut microbiota, and *APOE* gene polymorphisms on serum LDL-cholesterol (LDL-C) levels from a nutrigenetic perspective. **Methods:** Data from 609 adults (48% male) who applied to a private healthcare institution between 2016 and 2022 were analyzed. Age, sex, anthropometric measurements, dietary intake data, serum LDL-C levels, and APOE rs7412 and rs429358 genotypes of participants were evaluated. Additionally, gut microbiota analyses were included for 81 participants. Statistical analyses were performed using SPSS version 27.0, and the significance level was set at $p<0.05$. **Results:** Serum LDL-C levels showed a positive correlation with body mass index (BMI) ($p=0.000$), and different *APOE* alleles had a significant effect on LDL-C levels. The highest LDL-C concentrations were observed in the e4+ group, followed by the e3/e3 and e2+ groups ($p=0.000$). Dietary cholesterol and fiber intake did not significantly affect serum LDL-C levels ($p=0.705$ and $p=0.722$, respectively). Furthermore, enterotypes and the butyrate synthesis potential of the gut microbiota were not associated with significant changes in serum LDL-C levels ($p=0.369$ and $p=0.975$, respectively). **Conclusion:** Serum LDL-C levels are influenced by BMI—a modifiable determinant—and by *APOE* genotype—an unmodifiable determinant. Identifying these factors and conducting further research on this topic may contribute to the development of new approaches for improving serum LDL-C levels associated with cardiovascular diseases. However, no significant effects of gene–nutrient or microbiota–nutrient interactions on serum LDL-C levels were observed. Further advanced studies are required to determine whether genetic factors and the gut microbiota play a decisive role in the relationship between diet and serum LDL-C levels.

Keywords: LDL-cholesterol, ApoE, nutrigenetics, gut microbiota.

Serum LDL-kolesterol Seviyelerinin Genetik Polimorfizmler, Bağırsak Mikrobiyotası ve Beslenme ile Arasındaki İlişkilerin İncelenmesi

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Amaç: Bu retrospektif çalışmanın amacı, beslenme, bağırsak mikrobiyotası ve APOE gen polimorfizmlerinin serum LDL-kolesterol (LDL-K) düzeyleri üzerindeki etkilerini nutrigenetik bakış açısıyla bütüncül olarak incelemektir. **Yöntem:** Çalışmada, 2016-2022 yılları arasında özel bir sağlık kuruluşuna başvuran 609 yetişkinin (%48 erkek) danışan kayıt verileri incelenmiştir. Katılımcıların yaş ve cinsiyet bilgileri, antropometrik ölçümleri, besin tüketim verileri, serum LDL-K düzeyleri ve APOE rs7412 ve rs429358 genotipleri değerlendirilmiştir. 81 kişide ayrıca bağırsak mikrobiyota analizi değerlendirmeye dahil edilmiştir. İstatistiksel analizler SPSS 27.0 ile yapılmış, anlamlılık düzeyi $p<0.05$ olarak kabul edilmiştir. **Bulgular:** Serum LDL-K düzeylerinin beden kitle indeksi (BKİ) ile pozitif korelasyon gösterdiği (P = 0,000) ve farklı ApoE alellerinin LDL-K düzeyleri üzerinde anlamlı etkiye sahip olduğu görülmüştür. En yüksek LDL-K düzeylerinin e4+ grubunda, ardından sırasıyla e3/e3 ve e2+ gruplarında olduğu görülmüştür (P = 0,000). Sonuçlar, diyetle alınan kolesterol ve lif tüketiminin serum LDL-K düzeylerini anlamlı şekilde etkilemediğini göstermiştir (sırasıyla P = 0,705 ve P = 0,722). Ayrıca, enterotiplerin ve bağırsak mikrobiyotasının bütirat sentez potansiyelinin serum LDL-K seviyelerinde anlamlı değişikliklere neden olmadığı gözlenmiştir (sırasıyla P = 0,369 ve P = 0,975). **Sonuç:** Serum LDL-K düzeyleri, değiştirilebilir bir belirleyici olan BKİ ile değiştirilemeyen bir belirleyici olan APOE genotipinden etkilenmektedir. Bu unsurların tanımlanması ve konuya ilişkin ileri araştırmaların gerçekleştirilmesi, kardiyovasküler hastalıklarla ilişkili serum LDL-K düzeylerinin iyileştirilmesine yönelik yeni yaklaşımların geliştirilmesine katkı sağlayabilir. Bununla birlikte, gen-besin öğesi veya mikrobiyota-besin öğesi etkileşimlerinin serum LDL-K düzeyleri üzerinde anlamlı bir etkisi gösterilememiştir. Genetik özelliklerin ve bağırsak mikrobiyotasının, diyet ile serum LDL-K düzeyleri arasındaki ilişkide belirleyici bir rol oynayıp oynamadığının ortaya konabilmesi için ileri düzey araştırmaların yapılması gerekmektedir.

Anahtar kelimeler: LDL-kolesterol, ApoE, nutrigenetik, bağırsak mikrobiyotası.

Sözlü Bildiri: SB-03

High Dietary Fiber and the Intestinal Inflammation Marker Calprotectin

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Objective: The microbiota facilitate the breakdown of dietary fibre, thereby releasing a plethora of antioxidant and antiinflammatory chemicals, which are subsequently absorbed by the host organism. Furthermore, clinical studies have demonstrated that intestinal colonization varies depending on the type and amount of fibre consumed. Cross-feeding represents a fascinating phenomenon that occurs in the intestine in the presence of dietary fibre: the breakdown of a complex carbohydrate by one bacterial species becomes a substrate for the activity of another bacterial species. These symbiotic microorganisms form a mechanical barrier in the intestinal mucosa that protects against pathogens and also influences intestinal permeability. Disturbances in the microbial balance that favour opportunistic species can result from lifestyle factors, particularly a low-fibre diet. Calprotectin is found in the cytoplasm of neutrophils, monocytes, and epithelial cells, where it plays a crucial role in protecting against invading pathogens, including bacteria, fungi, and viruses. Upon release into the extracellular environment, it has been observed to activate innate immunity and proinflammatory mechanisms by attracting receptors that recognise pathogens. In inflamed epithelia, calprotectin is released from degranulated neutrophils and forms insoluble antimicrobial barriers known as neutrophil extracellular traps. The presence of bacteria and bacterial by-products in the bloodstream can initiate a systemic inflammatory response, resulting in elevated levels of calprotectin, a marker of inflammatory status. Dietary fiber, on the other hand, positively affects the intestinal microbiota, promotes the production of short-chain fatty acids (especially butyrate) and can strengthen epithelial barrier functions. The present study was aims to the a dietary intervention promoting diet in which at least 30 grams of total dietary fibre intake per day is obtained from foods affects and a fiber diet on intestinal inflammation on the calprotectin levels in the intestinal integrity healthy individuals. **Method:** A total of 20 subjects participated in the study. Participants were instructed to incorporate 30 grams of fibre from dietary sources into their daily consumption for a period of one month. Serum concentrations of human calprotectin were measured using the enzyme-linked immunosorbent assay (ELISA) method before and after the dietary intervention. **Result:** Our participants consumed an average of 31.19 ± 4.26 grams of fiber per day for one month. This amount consisted of 24.49 ± 3.87 g of insoluble fiber and 6.75 ± 1.41 g of soluble fiber. A significant decrease in the BMI ($p=0.018$) and weight ($p=0.015$) values of the participants was observed following the implementation of a dietary intervention. Following the intervention, serum calprotectin ($p = 0.014$) levels were found to be statistically significantly lower. **Conclusions:** The present study demonstrates that the consumption of 30 grams of dietary fibre per day for a period of one month results in a reduction of levels of markers associated with gut integrity in healthy individuals. A diet with a high fibre content may be a promising therapeutic target for the regulation of gut inflammation.

Keywords: Intestine, calprotektin, diet, fiber diet.

Yüksek Diyet Lifi ve Bağırsak İltihabı Belirteci Kalprotektin

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Amaç: Mikrobiyota, diyet lifinin parçalanmasını kolaylaştırarak, çok sayıda antioksidan ve antiinflamatuar kimyasalın salınmasını sağlar ve bunlar daha sonra konak organizma tarafından emilir. Ayrıca, klinik çalışmalar bağırsak kolonizasyonunun tüketilen lifin türüne ve miktarına bağlı olarak değiştiğini göstermiştir. Çapraz beslenme, diyet lifi varlığında bağırsakta meydana gelen ilginç bir fenomendir; bir bakteri türünün karmaşık bir karbonhidratı parçalaması, başka bir bakteri türünün aktivitesi için substrat haline gelir. Bu simbiyotik mikroorganizmalar, bağırsak mukozasında patojenlere karşı koruma sağlayan ve bağırsak geçirgenliğini de etkileyen mekanik bir bariyer oluşturur. Oportünistik türleri destekleyen mikrobiyal dengedeki bozukluklar, yaşam tarzı faktörlerinden, özellikle düşük lifli beslenmeden kaynaklanabilir. Kalprotektin, nötrofillerin, monositlerin ve epitel hücrelerinin sitoplazmasında bulunur ve burada bakteri, mantar ve virüsler dahil olmak üzere istilacı patojenlere karşı koruma sağlama konusunda önemli bir rol oynar. Hücre dışı ortama salındığında, patojenleri tanıyan reseptörleri çekerek doğuştan gelen bağışıklık ve proinflamatuar mekanizmaları aktive ettiği gözlemlenmiştir. İltihaplı epitelde, kalproktektin degranül nötrofillerden salınır ve nötrofil hücre dışı tuzakları olarak bilinen çözünmez antimikrobiyal bariyerler oluşturur. Kan dolaşımında bakteri ve bakteri yan ürünlerinin varlığı, sistemik bir enflamatuar yanıtı başlatarak enflamatuar durumun bir belirteci olan kalprotektin düzeylerinin yükselmesine neden olabilir. Diyet lifi ise, bağırsak mikrobiyotasını olumlu yönde etkileyerek kısa zincirli yağ asitleri (özellikle bütirat) üretimini teşvik eder ve epitel bariyer fonksiyonlarını güçlendirebilir. Bu çalışma, günde en az 30 gram toplam diyet lifi alımının gıdalardan sağlandığı bir diyeti teşvik eden diyet müdahalesinin, sağlıklı bireylerde bağırsak bütünlüğü ve lif içeriğine sahip bir diyetin kalprotektin düzeyleri üzerinden bağırsak iltihabı üzerindeki olası etkilerini ele almayı amaçlamaktadır. **Yöntem:** Çalışmaya toplam 20 denek katılmıştır. Katılımcılardan bir ay boyunca günlük tüketimlerine 30 gram lifli beslenmeleri istenmiştir. Diyet müdahalesi öncesinde ve sonrasında, insan kalprotektin serum konsantrasyonları enzim bağlı immünosorbent testi (ELISA) yöntemi ile ölçülmüştür. **Bulgular:** Katılımcılarımız bir ay boyunca günde ortalama 31,19 ± 4,26 gram lif tüketmiştir. Bu miktarın 24,49 ± 3,87 g'ı çözünmez lif ve 6,75 ± 1,41 g'ı çözünür liften oluşmaktadır. Diyet müdahalesinden sonra, katılımcılarımızın BMI ($p = 0,018$) ve kiloları ($p= 0,015$) önemli ölçüde azalmıştır. Müdahale sonrasında, serum kalprotektin ($p=0,014$) düzeylerinin istatistiksel olarak anlamlı şekilde daha düşük olduğu saptanmıştır. **Sonuç:** Bu çalışma, bir ay boyunca günde 30 gram diyet lifi tüketiminin, sağlıklı bireylerde bağırsak bütünlüğü ile ilişkili belirteçlerin düzeylerinde azalmaya yol açtığını göstermektedir. Yüksek lif içeriğine sahip bir diyet, bağırsak iltihaplanmasını düzenlemek için umut verici bir terapötik hedef olabilir.

Anahtar Kelimeler: Bağırsak, kalprotektin, diyet, lifli beslenme.

Sözlü Bildiri: SB-04

Evaluation of Blood Zonulin Levels in Healthy Individuals on a High-Fiber Diet

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Objective: In recent years, the relationship between gastrointestinal health, immune response, and chronic inflammatory diseases has been intensively researched in the scientific community. In this context, the integrity of the intestinal epithelial barrier is of great importance. Zonulin is a protein responsible for regulating tight junctions in the small intestine, and increased zonulin levels have been associated with impaired intestinal permeability. This condition may pave the way for systemic inflammation, autoimmune diseases, and metabolic disorders. Dietary fibre, on the other hand, positively affects the gut microbiota by promoting the production of short-chain fatty acids (especially butyrate) and may strengthen epithelial barrier functions. This study aims to examine the potential effects of a high-fibre diet on blood zonulin levels in healthy individuals. **Methods:** A total of 20 healthy individuals were included in the study. The individuals were asked to add 30 grams of fibre-rich food to their daily diet for one month. Serum zonulin concentrations were measured using the enzyme-linked immunosorbent assay (ELISA) method before and after the dietary intervention. **Results:** A diet high in fibre, with an average daily intake of 30 grams over one month, consists of 25 grams of insoluble fibre and 5 grams of soluble fibre. In this study, it was found that serum zonulin levels ($p = 0.016$) were statistically significantly lower after dietary intervention. **Conclusions:** It has been reported that a balanced diet has a significant effect on the health of the population and that fibre intake in particular is related to maintaining health. This study shows that consuming 30 grams of dietary fibre per day for one month leads to a decrease in zonulin levels associated with intestinal integrity in healthy individuals. A diet high in fibre may be a promising therapeutic target for regulating intestinal permeability.

Keywords: Intestine, zonulin, diet, fibre.

Yüksek Lifli Diyet Yapan Sağlıklı Bireylerde Kan Zonulin Düzeylerinin Değerlendirilmesi

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Amaç: Son yıllarda gastrointestinal sistem sağlığı, bağışıklık yanıtı ve kronik inflamatuar hastalıklar arasındaki ilişki bilim dünyasında yoğun bir şekilde araştırılmaktadır. Bu bağlamda, bağırsak epitel bariyerinin bütünlüğü büyük önem taşımaktadır. Zonulin, ince bağırsakta sıkı bağlantıların düzenlenmesinden sorumlu bir proteindir ve artan zonulin düzeyleri, bağırsak geçirgenliğinde bozulma ile ilişkilendirilmiştir. Bu durum, sistemik inflamasyona, otoimmün hastalıklara ve metabolik bozukluklara zemin hazırlayabilir. Diyet lifi ise, bağırsak mikrobiyotasını olumlu yönde etkileyerek kısa zincirli yağ asitleri (özellikle bütirat) üretimini teşvik eder ve epitel bariyer fonksiyonlarını güçlendirebilir. Bu çalışma, yüksek lif içeriğine sahip bir diyetin, sağlıklı bireylerde kan zonulin düzeylerinin olası etkilerini ele almayı amaçlamaktadır. **Yöntem:** Çalışmaya toplam 20 sağlıklı birey dahil edilmiştir. Bireylerden bir ay boyunca günlük besin tüketimlerine 30 gram lifli besin eklemeleri istenmiştir. Diyet uygulaması öncesinde ve sonrasında, zonulin serum konsantrasyonları enzim bağlı immünosorbent testi (ELISA) yöntemi ile ölçülmüştür. **Bulgular:** Yüksek lif içeriğine sahip diyet ile bir ay boyunca günde ortalama 30 gram tüketilmesi istenen lifin 25 g'ı çözünmez lif ve 5 g'ı çözünür liften oluşmaktadır. Bu çalışmada, diyet müdahalesinden sonra, bireylerin serum zonulin ($p = 0,016$) düzeylerinin istatistiksel olarak anlamlı şekilde daha düşük olduğu saptanmıştır. **Sonuç:** Dengeli bir beslenmenin nüfusun sağlığı üzerinde önemli bir etkisi olduğu ve özellikle lif alımının sağlığın korunmasıyla ilgili olduğu bildirilmiştir. Bu çalışma, bir ay boyunca günde 30 gram diyet lifi tüketiminin, sağlıklı bireylerde bağırsak bütünlüğü ile ilişkili zonulin düzeylerinde azalmaya yol açtığını göstermektedir. Yüksek lif içeriğine sahip bir diyet, bağırsak geçirgenliğini düzenlemek için umut verici bir terapötik hedef olabilir.

Anahtar Kelimeler: Bağırsak, zonulin, diyet, lif.

Sözlü Bildiri: SB-05

Epigenetic Mechanisms and Effects of Probiotic Use in Multiple Sclerosis Disease

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Introduction: Multiple sclerosis (MS) is an autoimmune disease of the central nervous system that leads to progressive loss of neurological function. It is characterized by demyelination, axonal loss, and neuroinflammation. Although the exact etiology of MS is unknown, it is thought to result from an abnormal immune response against one or more myelin antigens triggered by exposure to an as-yet-unidentified factor in genetically susceptible individuals. At the cellular level in multiple sclerosis, irregularities are observed in intracellular signaling through molecular pathways such as immune system activity, synaptic plasticity, myelin repair, oxidative stress, and mitochondrial function. Epigenetic regulations such as DNA methylation, histone proteins, and non-coding RNA play an important role in the pathogenesis. In MS patients, demethylation of FOXP3, which is expressed in a subset of CD4+ T cells that have a suppressive role in the immune system, has been identified. In addition, hypomethylation has been observed in the promoter region of the gene encoding IL-17A, a proinflammatory cytokine in MS. Moreover, methylation changes in the SHP-1, FOXP3, and PAD-2 genes directly affect immune balance and myelin integrity. Particularly, demethylation of the PAD-2 gene contributes to the susceptibility of nerve cells to autoimmune attack by causing citrullination of myelin basic protein. The fact that these changes are not observed in various neurodegenerative diseases (such as Alzheimer's, Parkinson's, or Huntington's) suggests the presence of an MS-specific epigenetic mechanism. Probiotics are live microorganisms that support host health when consumed in adequate amounts. Studies suggesting that probiotics may have significant effects on the progression and prevention of MS are increasing day by day. **Objective:** The aim of this review study is to evaluate the potential effects of probiotics on the treatment and prevention of multiple sclerosis (MS) based on current clinical data. **Method:** Original articles and literature reviews were searched in the PubMed and Elsevier databases using the keywords "multiple sclerosis", "probiotic", "epigenetic" and "nutrition" individually and in various combinations. **Results:** In animals subjected to the experimental autoimmune encephalomyelitis (EAE) model, administration of IRT5 probiotics reduced MOG-reactive T cell proliferation and proinflammatory cytokine (IL-17, IFN-γ, and TNF-α) levels, while increasing IL10+ or FoxP3+ Treg cells, thereby improving the progression of EAE. After the development of EAE, IRT5 supplementation significantly delayed the onset of the disease. In MS patients, 12-week probiotic capsule administration showed positive effects on mental health parameters, including the Expanded Disability Status Scale, Depression Anxiety and Stress Scale, General Health Questionnaire-28, and Beck Depression Inventory. In another study using *Lactobacillus* strains, clinical symptoms in the EAE model of MS were prevented and delayed. Probiotic administration was shown to significantly reduce high-sensitivity C-reactive protein (hs-CRP) and IL-6 levels, while increasing nitric oxide and IL-10 levels. In a clinical study, oral use of VSL3 (a probiotic mixture containing 3×10^{11} CFU/g live lyophilized bacteria from three strains: *Lactobacillus, Bifidobacterium,* and *Streptococcus*) was associated with the induction of an anti-inflammatory peripheral innate immune response in MS patients. **Conclusion:** Clinical and preclinical studies conducted on MS patients and animal models indicate that probiotics may influence cognitive, motor, and mental behaviors through the regulation of inflammatory and oxidative biomarkers. Probiotic supplementation may represent a potential strategy to improve and control the severity of MS.

Keywords: Multiple Sclerosis, probiotic, epigenetic, nutrition.

Multiple Sklerozis Hastalığında Epigenetik Mekanizmalar ve Probiyotik Kullanımının Etkisi

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Giriş: Multipl skleroz (MS), ilerleyen nörolojik işlev kaybına yol açan merkezi sinir sisteminin otoimmün hastalığıdır. Demiyelinizasyon, aksonal kayıp ve nöroinflamasyon ile karakterizedir. MS'in kesin etiyolojisi bilinmemekle birlikte genetik yatkınlığı olan bireylerde henüz tanımlanamayan bir etkene maruz kalınmasıyla oluşan bir veya daha fazla miyelin antijenine karşı anormal bir bağışıklık yanıtının sonucu olduğu düşünülmektedir. Multipl sklerozda hücresel düzeyde bağışıklık sistemi aktivitesi, sinaptik plastisite, miyelin onarımı, oksidatif stres ve mitokondriyal işlev gibi moleküler yollar ile hücre içi sinyallemede düzensizlikler görülmektedir. Patogenezde DNA metilasyonu**,** histon proteinleri ve kodlamayan RNA gibi epigenetik düzenlemeler önemli bir role sahiptir. MS hastalarında bağışıklık sisteminde baskılayıcı bir rol oynayan CD4+ T hücrelerinin bir alt kümesinde ifade edilen FOXP3'ün demetilasyona uğradığı belirlenmiştir. Ayrıca, MS'te proinflamatuvar bir sitokin olan IL-17A'yı kodlayan genin promotör bölgesinde hipometilasyon görülmektedir. Bunun yanı sıra, SHP-1, FOXP3 ve PAD-2 genlerinde görülen metilasyon değişiklikleri, bağışıklık dengesiyle miyelin bütünlüğüne doğrudan etki eder. Özellikle PAD-2 geninin demetilasyonu, miyelin bazik proteinin sitrullinasyonuna yol açarak sinir hücrelerinin otoimmün saldırıya duyarlı hale gelmesine katkı sağlar. Bu değişikliklerin çeşitli nörodejeneretif hastalıklarda (Alzheimer, Parkinson veya Huntington gibi) gözlenmemesi, MS'e özgü epigenetik bir mekanizmanın varlığını düşündürmektedir. Probiyotikler, yeterli miktarda alındığında konakçı sağlığını destekleyen canlı mikroorganizmalardır. Probiyotiklerin MS'in ilerleyişi ve önlenmesinde önemli etkiler oluşturabileceği ile ilgili çalışmalar günden güne artmaktadır. **Amaç:** Derleme niteliğinde hazırlanan bu çalışmanın amacı, probiyotiklerin MS'in tedavisi ve önlenmesine yönelik potansiyel etkilerini güncel klinik verilerle değerlendirmektir. **Yöntem:** "Multiple Skleroz", "probiyotik", "epigenetik" ve "beslenme" anahtar kelimeleri tekil olarak ve farklı kombinasyonlarla kullanılarak PubMed ve Elsevier veri tabanlarında orijinal makaleler ile literatür incelemeleri taranmıştır. **Bulgular:** Deneysel otoimmün ensefalomiyelit (EAE) modeli kullanılan hayvanlarda IRT5 probiyotiklerinin uygulanması, MOG-reaktif T hücresi çoğalması ve proinflamatuar sitokin (IL-17, IFN-γ ve TNF-α) seviyelerini düşürürken, $IL10^{+}$ veya $FoxP3^{+}$ Treg hücrelerini artırarak EAE'nin ilerlemesini iyileştirmiştir. EAE gelişimi sonrası IRT5 desteği, hastalığın başlangıcını anlamlı ölçüde geciktirmiştir. MS hastalarında 12 haftalık probiyotik kapsül uygulamasının genişletilmiş engellilik durumu ölçeği, depresyon anksiyete ve stres ölçeği, genel sağlık anketi-28 ve Beck depresyon envanterini kapsayan ruh sağlığı parametreleri üzerinde pozitif etkileri görülmüştür. *Lactobacillus* suşları uygulanan başka bir çalışmada da MS'in EAE modelinde klinik bulguları önlemiş ve geciktirmiştir. Probiyotik uygulamasının yüksek hassasiyetli C-reaktif protein (hs-CRP) ve IL-6 seviyelerini önemli ölçüde düşürdüğü ve nitrik oksit ile IL-10 düzeylerini yükselttiği gösterilmiştir. Kinik bir çalışmada oral VSL3 (*Lactobacillus*, *Bifidobacterium* ve *Streptococcus* olmak üzere üç suş içeren 3×10^{11} CFU/g canlı liyofilize bakteri içeren bir probiyotik karışımı) kullanımı MS hastalarında anti-inflamatuar periferik doğuştan bağışıklık yanıtı oluşturmakla ilişkilendirilmiştir. **Sonuç:** MS hastaları ve hayvan modelleri üzerinde yapılan klinik ve klinik öncesi çalışmalar, probiyotiklerin inflamatuar ve oksidatif biyobelirteçlerin düzenlenmesi yoluyla bilişsel, motor ve zihinsel davranışları etkileyebileceğini göstermektedir. Probiyotik takviyeleri, MS şiddetini iyileştirmek ve kontrol altına almak için potansiyel bir strateji olabilir.

Anahtar Kelimeler: Multiple Skleroz, probiyotik, epigenetik, beslenme.

Sözlü Bildiri: SB-06

Current Studies in Healthy Nutrition and Long-Term Learning, and Epigenetic Recommendations for the Future

Güneş Havva Kazanç

In this report, project-based studies have demonstrated that healthy nutrition supports long-term learning among students. Changes in dietary habits and the selection of specific nutrients were observed to influence the active functioning of genes associated with memory processes. In this intervention, one experimental and one control group were formed. Packaged and sugary foods preferred by students in the experimental group were completely removed from their diets. Instead, they were encouraged to consume healthy foods known to enhance memory, perception, and attention, such as carrots, blueberries, walnuts, almonds, hazelnuts, raisins with seeds, and green apples. In addition, collaboration with parents allowed for the provision of healthy recipes for meals prepared at home. Specific nutrient combinations recommended during study sessions included avocado, raw almond butter, pineapple, turmeric–kefir mixtures, blueberry and clove beverages, aromatic grapes with lemon juice, and herbal infusions such as lemon balm tea and wild mint. Prior to changing students' dietary patterns, blood tests, academic achievement levels, and behavioral assessments from the school counseling unit were collected and recorded. Following the implementation of the nutritional intervention, improvements were observed in memory, perception, attention, auditory processing, behavior, and academic performance, and these changes were systematically documented. The project emphasized the importance of meeting specific nutrient requirements, administering key nutrients during the school learning process, ensuring uniformity in nutritional interventions, sustaining learning performance, supporting healthy behavioral indicators, reducing exam-related stress and anxiety, and prioritizing foods known to strengthen memory. Within this framework, there is a need to document epigenetic modifications that occur as a result of healthy nutrition through genetic analysis. Research continues on children with autism spectrum disorder, attention-deficit/hyperactivity disorder, and learning difficulties. Conducting comprehensive physical, biological, and pedagogical assessments; analytically validating and calibrating rapid testing methods; ensuring compatibility of dietary recommendations with students' age, body weight, and biochemical parameters; and formulating nutrient combinations more effectively are all essential components of achieving adequate and balanced nutrition. Based on biochemical test results—and considering that the students reside in the Black Sea Region—vitamin D3K2 supplementation was recommended for all students, while some were also advised to take zinc, magnesium, omega fatty acids, and B-complex vitamins under medical supervision. Applications to universities have been submitted since 2003 to strengthen this project, and international collaborations have yielded valuable outcomes. To achieve the primary objective, it is crucial to perform genetic analyses and identify epigenetic modifications, thereby establishing the most effective and health-oriented nutritional concept. In conclusion, future studies will focus on determining individualized nutrient requirements based on epigenetic criteria, monitoring students continuously, recording the effects of new nutrient combinations on learning, and enhancing the quality and sustainability of memory, perception, and attention through epigenetic approaches. These student-centered initiatives are expected to create a significant breakthrough in both educational and epigenetic fields, offering a long-term solution to exam-related stress and anxiety commonly affecting students and their families. Ultimately, integrating epigenetic-based education and nutrition strategies into school environments will contribute substantially to student health, well-being, and overall educational quality.

Keywords: healthy nutrition, long-term learning, healthy foods, learning performance, epigenetic learning.

Sağlıklı Beslenme ve Kalıcı Öğrenme Alanında Güncel Çalışmalar ve Gelecek İçin Epigenetik Öneriler

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Bu bildiride; sağlıklı beslenmenin öğrenciler üzerinde kalıcı öğrenmeyi desteklediği proje çalışmalarında görülmüştür. Yeni beslenme tarzı ve besin öğelerindeki seçim aslında hafıza bölgesindeki genlerin aktif çalışmasını etkilemiştir. Bu uygulamada; bir deney bir kontrol grubu seçilmiştir. Deney grubu öğrencilerinin tercih ettiği ambalajlı ve şekerli gıdalar tamamen çıkarılmıştır. Havuç, yaban mersini, ceviz, badem, fındık, çekirdekli kuru üzüm, yeşil elma gibi hafıza algı dikkat özelliklerini artıran sağlıklı besin tercihleri yaptırılmıştır. Ayrıca veliler ile işbirliği yapılarak ev ortamında tüketeceği sağlıklı yemek tarifleri verilmiştir. Yine ders çalışırken yemesi gereken avokado, çiğ badem ezmesi, ananas, zerdeçal, kefir karışımı; yaban mersini ve karanfil suyu; kokulu üzüm ve limon suyu; melisa çayı ile dağ nanesi gibi yeni beslenme bileşiklerine yoğunlaştırılmıştır. Öğrencilerin beslenme tarzı değiştirilmeden önce kan tahlilleri, okul başarı seviyeleri ve rehberlik servisinden davranış durumları alınmıştır ve not edilmiştir. Uygulanan bu beslenme tarzından sonra öğrencilerde hafıza, algı, dikkat, işitsel, davranışsal ve okul başarısı gibi olumlu değişimler gözlenmiştir ve kayıt altına alınmıştır. Spesifik besin maddelerinin karşılanması, besin maddelerinin okulda öğrenme sürecinde verilmesi, üniformitenin sağlanması, öğrencilerde öğrenme performansının sürdürülebilirliği, sağlıklı davranış göstergeleri, sınav stres ve kaygılarının azaltılması, öğrenme kalitesini iyileştirme ve hafızayı güçlendiren farklı besin öğelerinin seçimine özen gösterilmiştir. Tüm bu çalışmaların yapısında; genetik analiz ile sağlıklı beslenmenin etkisiyle epigenetik değişiklerin kaydedilmesine ihtiyaç vardır. Otizmli çocuklar, hiperaktivite bozukluğu olan çocuklar, bepli çocuklar ile ilgili araştırmalar devam etmektedir. Öğrencilerin fiziksel, biyolojik, pedagojik analizlerinin yapılması, hızlı analiz yöntemlerinin analitik olarak doğrulanarak kalibre edilmesi, öğrencilerin yaş kilo ve biyokimya testleriyle uyumluluğunun kontrolü, verilen farklı besinlerin birlikte daha iyi formüle edilmesi, öğrencilerin yeterli ve dengeli beslenmeleri için oldukça önemlidir. Yine biyokimya testlerinin sonuçlarına göre Karadeniz Bölgesinde yaşamalarının da etkisiyle öğrencilerin hepsine D3K2, bazılarına çinko, magnezyum, omega ve bcomplex takviyeleri doktor kontrolünde kullandırılmıştır. Bu projenin kuvvetlenmesi için üniversitelere başvurular 2003 yılından bugüne kadar yapılmaktadır ve yurtdışı iş birlikleri ile de çok iyi kazanımlar elde edilmiştir. Asıl hedefe ulaşabilmek için genetik analizlerin yapılması ve epigenetik değişimlerin ortaya çıkarılarak en sağlıklı konseptin oluşturulması elzem bir ihtiyaçtır. Sonuç olarak; gelecekte yürütülecek çalışmalar, epigenetik kriterler doğrultusunda her öğrenciye özgü farklı besin öğelerinin belirlenmesi, öğrencinin gözlemlenmesi, yeni besin katkılarının öğrenme üzerindeki etkilerinin kaydedilmesi, epigenetik ile öğrenme hafıza algı ve dikkat özelliklerinin kalitesinin artırılması ve sürdürülebilirlik düzleminde yol alınacaktır. Öğrenci odaklı bu çalışmaların hem eğitim hem epigenetik alanında önemli çığır açacağı, öğrenci ve aileleri meşgul eden sınav stres ve kaygı sorununa köklü çözüm getireceği, öğrencinin hem sağlık hem refah kazanacağı, epigenetik eğitim kalitenin okulların hayatına geçirilmesi açısından önemlidir.

Anahtar kelimeler: Sağlıklı beslenme, kalıcı öğrenme, sağlıklı besinler, öğrenme performansı, epigenetik öğrenme.

Sözlü Bildiri: SB-07

Distribution of Homeopathy Patients Admitted to a GETAT Outpatient Clinic and the Remedies Used: A Case Series

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Objective: As with all chronic pain cases admitted to our GETAT outpatient clinic, we adopt a holistic approach for each patient. This includes assessing dietary habits, lifestyle, required supplements, phytotherapy, homeopathy, relaxation techniques, and, when necessary, hypnosis. In this study, we aimed to retrospectively evaluate 233 homeopathy patients who presented to the Traditional and Complementary Medicine (GETAT) Practice and Research Center outpatient clinic. **Materials and Methods:** The study included patients who received homeopathy treatment at the GETAT outpatient clinic between 2019 and 2024. In accordance with the Declaration of Helsinki, informed consent was obtained from each patient. Patient data were extracted from the hospital automation system, and demographic characteristics, age, sex, reasons for admission, and homeopathic treatments prescribed were examined. Applications for homeopathy accounted for 2.7% of all outpatient visits. Repertorization was performed according to the repertory system based on the lecture notes of Fatma Henden, the first certified homeopath in Türkiye. For patients reporting the onset of symptoms predominantly after COVID-19 infection, miasm-clearing remedies—primarily Carcinosin 1M and DNA C200 (2×1 daily)—were prescribed to mitigate epigenetic effects attributed to COVID-19. Oral remedies were recommended twice daily (morning and evening), with avoidance of coffee, mint, and menthol-containing foods 15–20 minutes before and after administration, and with a 15–20-minute interval between different remedies. **Results:** Of the total patient population, 56 were male and 177 were female, with a mean age of approximately 47 years. The most common diagnosis was lumbar disc pain (90%, n=32). Other diagnoses included fibromyalgia (n=16), neuropathic pain (n=15), chronic pain (n=15), obesity (n=15), kyphoscoliosis (n=6), alopecia areata (n=5), attention deficit hyperactivity disorder (n=4), refractory anemia (n=4), irritable bowel syndrome (n=4), infertility (n=4), post-COVID fatigue and decreased energy (n=3), malignant breast disease (n=3), heel spur (n=2), scleroderma (n=2), sudden hearing loss (n=2), post-COVID anosmia (n=2), hemorrhoids (n=2), migraine-type headaches (n=2). Additional diagnoses included amenorrhea, benign breast disease, benign brain tumor, anxiety, agitation and anxiety disorder, depression, uterine leiomyoma, atopic dermatitis, arterial embolism, chronic bronchitis, neurogenic bladder, acute rheumatic fever, ankylosing spondylitis, persistent hiccups, papilloma, goiter, dermatitis, tinnitus, acne vulgaris, pancreatitis, persistent cough, allergic dermatitis, shoulder pain (rotator cuff syndrome), pulmonary carcinoid tumor, constipation, autism spectrum disorder, multiple sclerosis, eczema, and deep skin wrinkling with loss of elasticity. **Conclusion:** We found that Carcinosin and DNA remedies were highly effective in alleviating symptoms that had worsened following COVID-19 infection. We believe that administering these remedies prior to individualized repertorization shortens the treatment process and yields more efficient therapeutic responses. Complementary homeopathy and phytotherapy appear to support patients in coping with underlying psychological factors contributing to their conditions, while also reducing the toxicity-related symptoms of chronic disorders, thereby enhancing patient satisfaction. Increasing the number of physicians trained in homeopathy and improving understanding of the epigenetic effects of remedies may strengthen holistic medical approaches and lead to more successful outcomes in chronic disease management.

Keywords: Homeopathy, traditional medicine, phytotherapy.

Getat Polikliniğine Başvuran Homeopati Hastalarının ve Kullandıkları Remedilerin Dağılımı: Olgu Serisi

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Amaç: Getat polikliniğimize gelen her kronik ağrı hastasında olduğu gibi hastaya bütüncül olarak yaklaşmaktayız; bunun için beslenme alışkanlıklarını, yaşam tarzını, alması gereken takviyeleri fitoterapi homeopati rahatlama tekniklerini gerekirse hipnoz önermekteyiz. Biz bu çalışma ile Geleneksel ve Tamamlayıcı Tıp Uygulama Araştırma Merkezi (GETAT) polikliniğimize başvuran 233 homeopati hastalarını retrospektif olarak araştırmayı amaçladık. **Materyal metod/yöntem:** Çalışmamıza GETAT polikliniğine 2019 -2024 tarihleri arasında başvuran homeopati tedavisi alan hastaları dahil ettik. Helsinki deklarasyonuna uygun olarak her bir hastadan aydınlatılmış onam alınmıştır. Hastane otomasyon sistemine kayıtlı hastaların dökümünü çıkartıp homeopati anamnezi aldığımız hastaların demografik verileri, yaş, cinsiyet, başvuru nedenlerini, kullanılan homeopatik tedavilerini inceledik. Homeopati tedavisi için başvurular total hasta başvurularının %2,7 sini oluşturmakta idi. Hastaların repertorizasyonları ülkemizin ilk uzman homeopatı olan Fatma Henden in homeopati ders notu repertorizasyon sistemine göre yapıldı. Hastaların mevcut şikayetleri covid enfeksiyonu sonrası özellikle başladığını belirten hastalara öncelikle carsinosin 1M ve dna C200 2*1 kullanımı ile covid enfeksiyonun oluşturduğu etkilerin epigenetik olarak ortadan kaldırılabilmesi için miazma silici remediler kullandırıldı. Oral olarak kullandırılan remediler sabah akşam şeklinde 2*1 idi kullanımları sırasında 15-20 dk öncesinde ve sonrasında kahve-nane ve mentollü gıdalar alınmaması ve remediler arasına 15-20 dk süre konulması tavsiye edildi. **Bulgular:** Hastaların demografik veri dağılımına bakıldığında total sayının 56'sı erkek 177' si kadındı. Vakaların yaş ortalamaları ise yaklaşık olarak 47 idi. Tanı dağılımlarının sıklıklarına bakıldığında %90 oranda en çok lumbal disk ağrısı (n=32)iken, diğer tanılar sırasıyla; fibromyalji (n=16), nöropatik ağrı (n=15), kronik ağrı (n=15), obezite (n=15), kifoskolyoz (n=6), alopesi areata (n=5),dikkat eksikliği hiperaktivite sendromu (n=4), inatçı anemi (n=4), irritabl bağırsak sendromu (n=4), infertilite (n=4),covid enfeksiyonu sonrası vücutta enerji azlığı ve yorgunluk (n=3), malign tipte meme hastalığı (n=3)topuk dikeni (n=2), skleroderma (n=2), ani işitme kaybı (n=2), covid sonrası görülen anosmi (n=2), hemoroid (n=2), migren tipi başağrısı (n=2) diğerleri ise amenore, iyi huylu meme hastalığı, bening beyin tümörü anksiyete, ajitasyon ve kaygı bozukluğu, depresyon, uterusta leiomyom, atopik dermatit, arteriel emboli, kronik bronşit, nörojenik mesane, akut romatizmal ateş, ankilozan spondilit, geçmeyen hıçkırık, papillom, guatr, dermatit, tinnitus, akne vulgaris, pankreatit, geçmeyen öksürük, alerjik dermatit, omuz ağrısı(rotator kuff sendromu), akciğer karsinoid tümörü, konstipasyon, otizm spektrum bozukluğu, multiple skleroz, egzema,ciltte derin kırışıklık- elastikiyet kaybı tanıları görülmektedir. **Sonuç:** Carsinosin ve dna remedilerinin covid enfeksiyonu sonrası agreve olan şikayetleri gidermede oldukça etkin olduğunu tespit ettik. Repertorizasyonda kulanılacak remedilerin kullanımı öncesinde bu iki remedinin kullanımın tedavi sürecini kısaltmada ve daha efektif yanıtlar alınacağını düşünmekteyiz. Homeopati ve fitoterapi desteği ile hastaların, mevcut hastalıklarının altında yatan ve hastalıklarına yol açan psikolojik sorunlarıyla baş etmesinde başarılı olurken, hem de sahip oldukları kronik hastalıklarının toksite semptomlarını giderdiği için hasta memnuniyetleri de artmaktadır. Homeopati eğitimi alan hekim sayısının artarak remedilerin epigenetik üzerine etkileri daha iyi anlaşılarak kullanımının da artımıyla kronik hastalıklarda bütüncül tıp yaklaşımlarında daha başarılı olunacağı kanaatindeyiz.

Anahtar kelimeler: Homeopati, geleneksel tıp, fitoterapi.

Sözlü Bildiri: SB-08

Probiotics and Prebiotics in Obesity

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Objective: The World Health Organization (WHO) defines obesity as a condition characterized by abnormal or excessive fat accumulation that impairs health. It results from long-term energy intake exceeding energy expenditure. The gut microbiota regulates food intake and energy balance by influencing the secretion of mediators within the gastrointestinal system. These mediators include peptide YY (PYY), ghrelin, cholecystokinin, the endocannabinoid system, and hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP). GLP-1 decreases appetite, enhances satiety, and regulates glycemia, while GIP and GLP-1 increase insulin secretion from pancreatic β-cells, thereby supporting glucose metabolism. Bariatric surgery remains an effective intervention for achieving long-term weight loss and improving obesity-related comorbidities. Prebiotics are non-living food components that positively modulate gut microbiota and promote health. Common prebiotics include galacto-oligosaccharides (GOS), fructo-oligosaccharides (FOS), and inulin. These compounds resist digestion in the upper gastrointestinal tract, are fermentable in the colon, and help induce satiety and weight control. Beneficial gut bacteria contribute to nutrient production, prevent pathogenic infections, and regulate immune responses. Thus, dietary inclusion of probiotics, prebiotics, or synbiotics is crucial for maintaining gut microbial balance, especially following bariatric surgery, where probiotics are frequently utilized. **Methods:** A literature review was conducted through PubMed and ResearchGate databases to examine the effects of probiotics and prebiotics on obesity. **Results:** Several studies demonstrate that prebiotic supplementation increases beneficial bacteria such as *Bifidobacterium* and *Lactobacillus* in the gut. In obese women, a 90-day consumption of inulin-type fruit improved gut microbiota composition and lipid metabolism. Another study involving eight individuals with a BMI of 25 kg/m² administered 21 g/day of prebiotics for 12 weeks, resulting in weight loss in the intervention group and weight gain in the control group. Prebiotics were also shown to influence appetite-regulating hormones. Research involving butyrate-producing bacteria revealed enhanced GLP-1 secretion and gene expression, associated with reduced hunger. Duan et al. reported that probiotic treatment modulated the secretion of the inactive GLP-1 form in intestinal cells. In a study of 100 patients with non-alcoholic fatty liver disease undergoing laparoscopic sleeve gastrectomy (LSG), probiotic supplementation showed no improvement in hepatic, inflammatory, or clinical outcomes at 6 and 12 months post-surgery compared to placebo. However, other studies in morbidly obese patients undergoing LSG suggested that combined probiotic and prebiotic use may improve triglyceride levels, low-density lipoprotein, and weight loss outcomes. **Conclusion:** A balanced gut microbiota is essential for achieving and maintaining healthy weight loss and for restoring metabolic function. Rehabilitation of gut microbiota through probiotics and prebiotics presents a promising adjunct therapy for bariatric patients. Evidence indicates improvement in clinical and laboratory parameters in most postoperative cases; however, uncertainty remains regarding the optimal dose and duration of supplementation. Further research is required to determine the long-term efficacy and safety of probiotics and prebiotics in obesity management.

Keywords: Obesity, probiotics, prebiotics, bariatric surgery.

Obezitede Probiyotikler ve Prebiyotikler

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Amaç: Dünya Sağlık Örgütü (WHO), obeziteyi sağlık üzerinde olumsuz etkiler oluşturan anormal veya aşırı yağ birikimi ile karakterize edilen bir durum olarak tanımlamaktadır. Obezite, uzun süre boyunca enerji alımının enerji harcamasını aşması sonucu ortaya çıkmaktadır. Bağırsak mikrobiyotası, gastrointestinal sistemde salgılanan çeşitli mediyatörler aracılığıyla besin alımını ve enerji dengesini düzenlemektedir. Bu mediyatörler arasında peptid YY (PYY), ghrelin, kolesistokinin, endokannabinoid sistemi ve glukagon benzeri peptid-1 (GLP-1) ile glikoza bağımlı insülinotropik peptid (GIP) gibi hormonlar bulunmaktadır. GLP-1 iştahı azaltır, tokluk hissini artırır ve glisemiyi düzenlerken; GIP ve GLP-1 pankreatik β-hücrelerden insülin salınımını artırarak glukoz metabolizmasını desteklemektedir. Bariatrik cerrahi, uzun dönemli kilo kaybı sağlama ve obeziteye bağlı komorbiditeleri iyileştirme açısından etkili bir müdahale olarak öne çıkmaktadır. Prebiyotikler, bağırsak mikrobiyotasını olumlu yönde modüle eden, sindirilemeyen ve sağlık üzerinde faydalı etkiler oluşturan besin bileşenleridir. Galakto-oligosakkaritler (GOS), frukto-oligosakkaritler (FOS) ve inülin yaygın prebiyotikler arasında yer almaktadır. Bu bileşikler üst gastrointestinal sistemde sindirime dirençlidir, kolonda fermente olabilirler ve tokluk hissi ile kilo kontrolünü desteklerler. Faydalı bağırsak bakterileri besin öğesi üretimine katkı sağlar, patojen enfeksiyonlarını önler ve immün yanıtları düzenler. Bu nedenle probiyotik, prebiyotik veya sinbiyotiklerin diyete dahil edilmesi, özellikle bariatrik cerrahi sonrası dönemde, bağırsak mikrobiyal dengesinin korunmasında kritik öneme sahiptir. **Yöntem:** Obezite üzerinde probiyotik ve prebiyotiklerin etkilerini incelemek amacıyla PubMed ve ResearchGate veri tabanlarında literatür taraması gerçekleştirilmiştir. **Bulgular:** Çeşitli çalışmalar, prebiyotik takviyesinin bağırsaklarda Bifidobacterium ve Lactobacillus gibi faydalı bakterilerin artışını sağladığını göstermektedir. Obez kadınlarda 90 gün boyunca inülin türü ürün tüketiminin bağırsak mikrobiyota kompozisyonunu ve lipid metabolizmasını iyileştirdiği bildirilmiştir. Vücut kitle indeksi 25 kg/m² olan sekiz birey üzerinde yapılan bir başka çalışmada, 12 hafta boyunca günde 21 g prebiyotik alımı sonucunda müdahale grubunda kilo kaybı, kontrol grubunda ise kilo artışı gözlenmiştir. Prebiyotiklerin iştah düzenleyici hormonları da etkilediği belirlenmiştir. Bütirat üreten bakterileri içeren bir araştırmada GLP-1 sekresyonu ve gen ekspresyonunda artış bildirilmiş olup bunun açlık hissinin azalması ile ilişkili olduğu görülmüştür. Duan ve arkadaşları, probiyotik tedavisinin intestinal hücrelerde inaktif GLP-1 formunun salgılanmasını modüle ettiğini raporlamıştır. Alkol dışı yağlı karaciğer hastalığı bulunan ve laparoskopik sleeve gastrektomi (LSG) uygulanan 100 hastayı içeren bir çalışmada ise probiyotik takviyesinin 6. ve 12. aylarda karaciğer, inflamatuvar veya klinik parametrelerde plaseboya kıyasla bir iyileşme sağlamadığı görülmüştür. Buna karşın, morbid obez hastalarda yapılan diğer LSG çalışmalarında probiyotik ve prebiyotiklerin birlikte kullanımının trigliserit düzeyleri, düşük yoğunluklu lipoprotein (LDL) ve kilo kaybı üzerinde iyileştirici etkiler gösterebileceği belirtilmiştir. **Sonuç:** Sağlıklı ve dengeli bir bağırsak mikrobiyotası, sürdürülebilir kilo kaybının sağlanması ve metabolik fonksiyonların yeniden düzenlenmesi açısından büyük önem taşımaktadır. Probiyotikler ve prebiyotikler aracılığıyla bağırsak mikrobiyotasının rehabilitasyonu, bariatrik cerrahi hastaları için umut vadeden tamamlayıcı bir tedavi yaklaşımıdır. Literatür, ameliyat sonrası hastaların çoğunda klinik ve laboratuvar parametrelerinde iyileşme olduğunu göstermesine rağmen, uygulamaya yönelik en uygun doz ve süre hâlâ belirsizdir. Probiyotik ve prebiyotiklerin obezite yönetimindeki uzun vadeli etkinliğinin ve güvenilirliğinin belirlenmesi için daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: Obezite, probiyotikler, prebiyotikler, bariatrik cerrahi.

Sözlü Bildiri: SB-09

Epigenetic Effects of Caffeine on Muscle in Athletes

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Objective: Caffeine is one of the most common ergogenic aids known to increase endurance, strength, and reaction time in athletes. Although its effects are generally thought to be mediated by adenosine receptor antagonism and its stimulatory role in calcium release, recent studies have revealed that caffeine may also influence epigenetic regulatory mechanisms. Epigenetic mechanisms are biochemical processes that alter gene activity without any changes to the DNA sequence, and these processes include DNA methylation, histone acetylation, and microRNA regulation. **Methods**: During exercise, these mechanisms in skeletal muscle play a decisive role in energy metabolism and muscle adaptation. Published recent data suggest that between 2023 and 2025, caffeine may indirectly affect muscle function through these epigenetic regulators. Cell culture studies have found that caffeine reduces histone deacetylase 5 (HDAC5) levels in the nucleus via a calcium/calmodulin-dependent protein kinase (Ca^{2+}/CaMK)-dependent pathway, while increasing myocyte enhancer factor 2A (MEF2A) binding and histone H3 acetylation. This effect was abolished by the CaMK inhibitor KN93 or the calcium release inhibitor dantrolene, confirming that the mechanism is calcium-mediated. This increase in histone acetylation led to a relaxation of chromatin structure, resulting in the activation of metabolic genes such as Glucose Transporter Type 4 (GLUT4). **Findings:** These genes support endurance by increasing glucose uptake and energy efficiency in muscle cells. A study published in BMC Biology in 2024 observed a 10–15% decrease in methylation (hypomethylation) in the Peroxisome Proliferator-Activated Receptor Gamma Coactivator-1 Alpha (PGC-1α) gene promoter and up to a 3000-fold increase in mRNA levels after exercise. This change confirms the role of epigenetic control in muscle adaptation. Furthermore, epigenome-wide studies conducted between 2023 and 2024 determined that regular coffee consumption creates significant methylation differences in the Histone Deacetylase 4 (HDAC4) and Phosphoglycerate Dehydrogenase (PHGDH) genes, demonstrating that caffeine can leave epigenetic traces. These findings suggest that caffeine intake may not only create a temporary stimulatory effect but may also contribute to long-term epigenetic adaptations in muscle cells. **Conculution**: The fact that caffeine and exercise activate similar epigenetic pathways (CaMK–HDAC–MEF2) suggests that these two factors may work synergistically to enhance training adaptation and recovery. However, there are no randomized controlled human studies in the current literature that directly prove that caffeine causes epigenetic changes in muscle tissue. Therefore, future double-blind, placebo-controlled studies evaluating muscle biopsy, methylome analysis, and individual genetic differences are recommended. In conclusion, caffeine is not only a stimulant on the central nervous system but also a biomolecule that can reprogram muscle metabolism at the epigenetic level. With these properties, it is considered a potential support compound that could provide epigenetic contributions to performance enhancement, endurance, and recovery processes in athletes.

Keywords: Caffeine, ergogenic, DNA methylation, histone acetylation, sports performance.

Kafeinin Sporcular Kası Üzerindeki Epigenetik Etkileri

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Amaç: Kafein, sporcularda dayanıklılık, kuvvet ve tepki süresini artırdığı bilinen en yaygın ergogenik desteklerden biridir. Genellikle etkisini adenozin reseptör antagonizması ve kalsiyum salınımı üzerindeki uyarıcı rolüyle gösterdiği düşünülse de son yıllarda yapılan araştırmalar kafeinin epigenetik düzenleme mekanizmalarını da etkileyebileceğini ortaya koymuştur. Epigenetik mekanizmalar, DNA dizisinde herhangi bir değişiklik olmadan gen aktivitesini değiştiren biyokimyasal süreçlerdir ve bu süreçler arasında DNA metilasyonu, histon asetilasyonu ve mikroRNA düzenlemesi yer alır. **Yöntem**: Egzersiz sırasında iskelet kasında bu mekanizmalar enerji metabolizması ve kas adaptasyonunda belirleyici rol oynamaktadır. Yayınlanan güncel veriler 2023–2025 yılları arasında kafeinin bu epigenetik düzenleyiciler aracılığıyla kas fonksiyonlarını dolaylı yoldan etkileyebileceğini göstermektedir. Hücre kültürü çalışmalarında kafeinin kalsiyum/kalmodulin bağımlı protein kinaz (Ca^{2+}/CaMK) bağımlı bir yol üzerinden çekirdek içindeki histon deasetilaz 5 (HDAC5) düzeylerini azalttığı, buna karşılık miyosit artırıcı faktör 2A (MEF2A) bağlanmasını ve histon H3 asetilasyonunu artırdığı tespit edilmiştir. Bu etki, CaMK inhibitörü KN93 veya kalsiyum salınım engelleyicisi dantrolen ile ortadan kaldırılmış, böylece mekanizmanın kalsiyum aracılı olduğu doğrulanmıştır. Histon asetilasyonundaki bu artış, kromatin yapısının gevşemesini sağlayarak Glukoz Taşıyıcı Tip 4 (GLUT4) gibi metabolik genlerin daha aktif hale gelmesine yol açmıştır. **Bulgular**: Bu genler kas hücrelerinde glukoz alımını ve enerji verimliliğini artırarak dayanıklılığı desteklemektedir. BMC Biyoloji dergisinde 2024 yılında yayımlanan bir çalışmada, egzersiz sonrasında Peroksizom Proliferatör Aktive Edilmiş Reseptör Gama Koaktivatörü-1 Alfa (PGC-1α) gen promotöründe %10–15 oranında metilasyon azalması (hipometilasyon) ve mRNA düzeyinde 3000 kata kadar artış gözlemlenmiştir. Bu değişim, epigenetik kontrolün kas adaptasyonundaki rolünü doğrulamaktadır. Ayrıca 2023–2024 yılları arasında yürütülen epigenom çaplı çalışmalarda, düzenli kahve tüketiminin Histon Deasetilaz 4 (HDAC4) ve Phosphoglycerate Dehydrogenase (PHGDH) genlerinde anlamlı metilasyon farklılıkları oluşturduğu belirlenmiş ve kafeinin epigenetik izler bırakabildiği gösterilmiştir. Bu bulgular, kafein alımının yalnızca geçici uyarıcı etki yaratmakla kalmayıp, kas hücrelerinde uzun vadeli epigenetik adaptasyonlara da katkıda bulunabileceğini göstermektedir. **Sonuç:** Kafein ve egzersizin benzer epigenetik yolları (CaMK–HDAC–MEF2) aktive etmesi, bu iki faktörün sinerjik biçimde çalışarak antrenman adaptasyonunu ve toparlanma sürecini güçlendirebileceğini düşündürmektedir. Ancak mevcut literatürde kafeinin kas dokusunda epigenetik değişiklik oluşturduğunu doğrudan kanıtlayan randomize kontrollü insan çalışmaları bulunmamaktadır. Bu nedenle gelecekte yapılacak çift kör, plasebo kontrollü araştırmalarda kas biyopsisi, metilom analizi ve bireysel genetik farklılıkların değerlendirilmesi önerilmektedir. Sonuç olarak, kafein yalnızca merkezi sinir sistemi üzerinde uyarıcı bir madde değil, aynı zamanda kas metabolizmasını epigenetik düzeyde yeniden düzenleyebilen bir biyomoleküldür. Bu özellikleriyle, sporcularda performans artışı, dayanıklılık ve toparlanma süreçlerinde epigenetik katkı sağlayabilecek potansiyel bir destek bileşeni olarak değerlendirilmektedir.

Anahtar Kelimeler: Kafein, ergogenik, DNA metilasyonu, histon asetilasyonu, spor performansı.

Sözlü Bildiri: SB-10

Epigenetics of Alzheimer's Disease and the Nutraceutical Potential of Fermented Foods

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Introduction: Alzheimer's disease (AD) is defined as a progressive neurogenerative disease in older individuals, and its etiology is not fully unterstood. AD is characterized by the formation of senile plaques through the extracellular deposition of amyloid β-peptide. In AD brains, subcellular/cellular derangements ocur in molecular pathways suc as bioenergetics and lipid metabolism, synaptic plasticity, oxidative stress, and intracellular signaling. In AD, 5-methylcytosine and 5- hydroxymethylcytosine levels have been shown to be generally decreased or their genome-wide distribution altered in the hippocampus. Epigenetic mechanisms that have a significant impact on the progression of AD and its associated pathways include DNA methylation, histone modification, and non-coding RNA. Epigenetic mechanisms are dysregulated in AD, resulting in DNA hypermethylation, histone deacetylation, and a generalized repressed chromatin state that alters gene expression at the transcriptional level. Mitochondrial DNA can be affected by epigenetic mechanisms, and these changes are important for AD progression. Furthermore, there is increasing evidence that imbalances in epigenetic mechanisms may underlie the abnormal expression of memory-related genes and synaptic plasticity in AD. Nutritional interventions are emerging as an option fort he treatment and prevention of AD. Fermentation is the metabolic process that occurs when carbohydrates are broken down into alcohols or organic acids by a microorganism. Growing evidence highlights the potential of fermented foods as functional foods for improving brain and cognitive health. **Objective:** This compilation study aims to demonstrate the potential effects of fermented foods on the treatment and prevention of AD in light of current clinical data. **Method:** Original articles and literatüre reviews were searched in PubMed, Web of Science, Elsevier ScienceDirect, and SpringerLink databases using keywords "Alzheimer's disease", "fermented foods", and "epigenetics", either individually or in various combinations. **Results:** In a study conducted in AD patients, 200 ml of probiotic milk containing 2×10^9 CFU/g *L. acidophilus, L. casei, B. bifidum*, and *L. fermentum* daily for 12 weeks resulted in significant improvements in cognitive assessment results. In an $AlCl_3$-induced AD rat model, 1.5% black tea extract (Camellia sinensis) was given in drinking water for 60 days, resulting in significant improvements in cognitive performance and amyloid-β pathology. In another study, in an Aβ (1–42)-induced Alzheimer's disease rat model, 250 and 500 mg/kg aged garlic extract given daily for 56 days was found to improve short-term recognition memory, activate microglia, and significantly reduce IL-1β levels. In a similar study, in an Aβ (25–35)-induced Alzheimer's disease and diabetes rat model, 10% *Bacillus licheniformis*-fermented soybean milk given for 8 weeks resulted in improved cognitive functions, reduced Aβ accumulation, improved insulin resistance, and preserved β-cell mass. Oral administration of soy milk extract fermented with *Lactobacillus plantorum* strain was shown to improve learning and memory in rat models of deoxycorticosterone acetate-induced vascular dementia. Calpis sour milk is prepared by fermenting skimmed milk with *Saccharomyces cerevisiae* and *Lactobacillus helveticus*. Calpis sour milk whey powder, administered orally to mice, significantly improved scopolamine-induced memory impairment and novel object recognition. An experimental study using rice fermented with red yeast, Monascus, investigated its effects on learning ability, memory, and the risk factor for AD. The study found that red yeast rice improved memory impairment. **Conclusion:** According to the results of the studies reviewed, it can be said that fermented foods as a nutraceutical can significantly improve memory deficits in Alzheimer's disease and have significant effects on improving cognitive performance.

Keywords: Alzheimer's disease, epigenetics, fermented foods, memory.

Alzheimer Hastalığının Epigenetiği ve Fermente Besinlerin Nutrasötik Potansiyeli

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Giriş: Alzheimer hastalığı (AH), yaşlı bireylerde ilerleyici nörodejeneratif bir hastalık olarak tanımlanmaktadır ve etiyolojisi tam olarak net değildir. AH, amiloid β-peptidin hücre dışı birikmesiyle senil plak oluşumu ile karakterizedir. Alzheimerlı beyinlerde hücre altı/hücresel seviyede biyoenerjetik ve lipit metabolizma, sinaptik plastisite, oksidatif stres gibi moleküler yollarda ve hücre içi sinyallemede düzensizlikler meydana gelmektedir. AH'de hipokampüs bölgesinde 5-metilsitozin ve 5-hidroksimetilsitozin düzeylerinin genel olarak azaldığı veya genom çapında dağılımlarının değiştiği ortaya konmuştur. Alzheimer hastalığının ilerlemesi ve ilişkili yolları üzerinde önemli etkisi olan epigenetik mekanizmalar arasında DNA metilasyonu, histon modifikasyonu ve kodlamayan RNA bulunur. AH'de epigenetik mekanizma düzensizleşir, DNA hipermetilasyonu, histon deasetilasyonu ve gen ekspresyonunu transkripsiyon düzeyinde değiştiren genel baskılanmış kromatin durumu görülür. Mitokondriyal DNA'nın epigenetik mekanizmalardan etkilenebildiği ve bu değişikliklerin AH ilerlemesi için önemlidir. Ayrıca, epigenetik mekanizmalarda yer alan dengesizlikler, AH'de hafızayla ilişkili genlerin ve sinaptik plastisitenin anormal ekspresyonunun temeli olabileceği yönünde artan kanıtlar mevcuttur. Beslenme müdahaleleri, AH'nin tedavisinde ve önlenmesinde bir seçenek olarak karşımıza çıkmaktadır. Karbonhidratların alkol veya organik asitlere bir mikroorganizma ile parçalanmasıyla ortaya çıkan metabolik süreç fermentasyon olarak tanımlanır. Giderek artan kanıtlar, beyin bilişsel sağlığının iyileştirilmesi için fonksiyonel besin olarak fermente besinlerin potansiyeline dikkat çekmektedir. **Amaç:** Derleme niteliğinde hazırlanan bu çalışmanın amacı, fermente besinlerin AH'nin tedavisi ve önlenmesine yönelik potansiyel etkilerini güncel klinik veriler ışığında ortaya koymaktır. **Yöntem:** "Alzheimer hastalığı", "fermente gıdalar" ve "epigenetik" anahtar kelimeleri tekil olarak ve farklı kombinasyonlarla kullanılarak PubMed, Web of Science, Elsevier ScienceDirect ve SpringerLink veri tabanlarında orijinal makaleler ile literatür incelemeleri taranmıştır. **Bulgular:** AH hastalarında yapılan bir çalışmada, 12 hafta boyunca her gün 200 ml herbiri 2×10^9 KOB/g *L. acidophilus, L. casei, B. bifidum, L. fermentum* içeren probiyotik süt verilmiş bilişsel değerlendirme sonuçlarına anlamlı iyileşme bulunmuştur. $AlCl_3$ ile indüklenmiş Alzheimer sıçan modelinde, 60 gün boyunca içme suyuna %1,5 siyah çay ekstresi (*Camellia sinensis*) verilmiş olup bilişsel performans ve amiloid-β patolojisinde anlamlı iyileşme bulunmuştur. Başka bir çalışmada, Aβ (1-42) ile indüklenmiş Alzheimer sıçan modelinde, 56 gün boyunca günlük 250 ve 500 mg/kg yaşlandırılmış sarımsak ekstresi verilmiş ve kısa süreli tanıma belleğinde iyileşme, mikroglia aktivasyonu ve IL-1β düzeylerinde anlamlı azalma bulunmuştur. Benzer bir çalışmada, Aβ (25–35) ile indüklenmiş Alzheimer ve diyabet sıçan modelinde, 8 hafta boyunca %10 *Bacillus licheniformis* ile fermente soya verilmiş ve bilişsel fonksiyonlarda iyileşme, Aβ birikiminde azalma, insülin direncinde düzelme ve β-hücre kütlesinde korunma sağlanmıştır. *Lactobacillus plantorum* suşu ile fermente edilmiş olan soya sütü ekstresinin oral yol ile uygulanması sonucunda deoksikortikosteron asetat tuzu ile uyarılan vasküler demansa sahip sıçan modellerinde öğrenme ve hafızanın iyileştiği görülmüştür. Calpis ekşi sütü, yağsız sütün *Saccharomyces cerevisiae* ve *Lactobacillus helveticus* ile fermentasyonu ile hazırlanmaktadır. Oral yoldan farelere uygulanan Calpis ekşi süt peyniraltı suyu tozu, skopolamin kaynaklı hafıza yetersizliği ve yeni nesne tanıma yeteneğini büyük ölçüde iyileştirmiştir. Monascus isimli kırmızı maya ile fermente edilen pirinç ile yapılan deneysel bir çalışmada, öğrenme kabiliyeti, hafıza ve AH'nin risk faktörü üzerindeki etkileri araştırılmıştır. Çalışma sonucunda kırmızı mayalı pirincin hafıza eksikliğini iyileştirdiği görülmüştür. **Sonuç:** İncelenen çalışma sonuçlarına göre bir nutrasötik olarak fermente besinlerin Alzheimer hastalığında hafıza eksikliklerini önemli ölçüde iyileştirebileceği ve bilişsel performansı iyileştirme konusunda önemli etkileri olduğu söylenebilir.

Anahtar Kelimeler: Alzheimer hastalığı, epigenetik, fermente gıdalar, hafıza.

Sözlü Bildiri: SB-11

Epigenetic Mechanisms in Parkinson's Disease and the Therapeutic Potential of Plant Phytochemicals

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Introduction: Parkinson's disease (PD) is characterized by the progressive loss of dopaminergic neurons in the substantia nigra pars compacta region of the brain, which is responsible for dopamine synthesis, as a result of neurodegenerative processes. Although some genetic components and cellular mechanisms of Parkinson's disease have been identified, it is still unclear. Epigenetic mechanisms, in particular, are thought to play an essential role in the development and progression of the disease. Rare mutations in several genes have been identified as direct causes of PD. Increased homocysteine levels resulting from methylation abnormalities may lead to DNA damage. This can trigger apoptosis in nerve cells responsible for dopamine production in Parkinson's disease. The first alternative in the treatment of the disease is pharmacological treatment aimed at reducing symptoms. In patients who do not respond to medication, surgical treatment is applied. In recent years, it has been reported that phytochemicals in plants may be effective in the treatment of PD's due to their bioactive properties such as antioxidants and anti-inflammatory agents. **Aim:** The aim of this review study is to reveal the potential therapeutic effects of phytochemical compounds found in plants on PD in light of current clinical data. **Method:** Original articles and literature reviews were searched in PubMed, Web of Science, Elsevier ScienceDirect, and SpringerLink databases using the keywords "Parkinson's disease," "phytochemicals," and "epigenetics" singularly and in different combinations. **Findings:** *Mucuna pruriens*, a tropical legume belonging to the Fabaceae family, contains up to approximately 6.1% L-dopa in the main components of its seeds. Studies conducted on rats and humans with PD have found that *Mucuna pruriens* extracts have positive effects on motor symptoms in PD. In a clinical study involving 33 Parkinson's patients who were orally administered 40 g/day of *Mucuna pruriens* seed powder, the preparation contained 4.5% L-dopa, resulting in significant symptomatic improvement in patients. *Vicia faba,* belonging to the Fabaceae family, is a legume species commonly known as broad bean or fava bean, and one of the main bioactive components of its seeds is L-Dopa. *V. Faba* improves motor activities and increases plasma L-dopa levels. In one study, plasma L-dopa levels increased in individuals with Parkinson's disease compared to the control group after consuming 250 g of cooked fava beans. *Nigella sativa*, also known as black cumin, is rich in bioactive compounds such as thymoquinone. In particular, thymoquinone is known to modulate gene expression related to inflammation and apoptosis. *Nigella Sativa* may facilitate neuroprotective effects by altering the epigenetic structure and may offer a new approach to prevent the progression of PD. *Crocus Sativus*, or saffron, belonging to the Iridaceae family, has been found to have beneficial effects in neurodegenerative disorders. Toxic amyloid structures may lead to the development of neurodegenerative disorders. Under amyloidogenic conditions, the two main components of *Crocus Sativus,* crocin and safranal, inhibit apo-α-lactalbumin fibrillation, which causes neuronal damage. In one study, intraperitoneal injection of crocetin extracted from *Crocus Sativus* caused neuroprotective effects in a 6-OHDA-induced Parkinsonism rat model. *Curcuma longa*, or turmeric, consists of natural polyphenols and non-flavonoid components that regulate oxidative damage formation in the nervous system. Curcumin may reduce neurodegeneration through epigenetic mechanisms. The water-soluble extract of curcumin (50-200mg/kg p.o.) increased dopamine and serotonin levels in brain tissues. Curcumin (5, 10, and 20 mg/kg) has increased monoaminergic neurotransmitters such as norepinephrine and dopamine in hippocampal tissue. Curcumin and curcuminoid compounds may affect the epigenetic mechanism of brain cells by crossing the blood-brain barrier. **Conclusion:** Based on the results of the study, it may be suggested that plant phytochemicals may modulate epigenetic mechanisms to slow the progression of Parkinson's disease and provide a complementary treatment approach.

Keywords: DNA methylation, epigenetics, phytochemicals, parkinson's disease.

Parkinson Hastalığında Epigenetik Mekanizmalar ve Bitkisel Fitokimyasalların Terapötik Potansiyeli

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Giriş: Parkinson hastalığı (PH), nörodejeneratif süreçlerin bir sonucu olarak beyindeki dopamin sentezinden sorumlu substantia nigra pars compacta bölgesindeki dopaminerjik nöronların ilerleyici kaybı ile karakterizedir. Parkinson hastalığının bazı genetik bileşenleri ve hücresel mekanizmaları tanımlansa da, hala net değildir. Özellikle epigenetik mekanizmaların hastalığın gelişimi ve ilerlemesinde önemli bir rol oynadığı düşünülmektedir. Birkaç gendeki nadir mutasyonların doğrudan PH'na neden olduğu belirlenmiştir. Metilasyonundaki bozukluk sonucu homosistein seviyelerinin artması ile DNA'da hasar meydana gelebilmektedir. Bu durum Parkinson'da dopamin üretmekle sorumlu olan sinir hücrelerinde apoptoz gelişmesine yol açabilir. Hastalığın tedavisinde semptomları azaltmaya yönelik ilk seçenek farmakolojik tedavidir. İlaca cevap vermeyen hastalarda ise cerrahi tedavi uygulanmaktadır. Son yıllarda, bitkilerdeki fitokimyasalların antioksidan ve antienflamatuvar gibi biyoaktif özellikleri sayesinde Parkinson tedavisinde etkili olabileceği bildirilmektedir. **Amaç:** Derleme niteliğinde hazırlanan bu çalışmanın amacı, bitkilerde bulunan fitokimyasal bileşiklerin Parkinson hastalığına yönelik potansiyel terapötik etkilerini güncel klinik veriler ışığında ortaya koymaktır. **Yöntem:** "Parkinson hastalığı", "fitokimyasallar" ve "epigenetik" anahtar kelimeleri tekil olarak ve farklı kombinasyonlarla kullanılarak PubMed, Web of Science, Elsevier ScienceDirect ve SpringerLink veri tabanlarında orijinal makaleler ile literatür incelemeleri taranmıştır. **Bulgular:** Fabaceae familyasından *Mucuna pruriens,* tohumlarının ana bileşenlerinde yaklaşık %6,1'e kadar L-dopa bulunduran tropikal bir baklagildir. Parkinsonlu sıçanlar ve insanlar üzerinde yapılan çalışmalarda *Mucuna pruriens* özütlerinin Parkinson'daki motor semptomları üzerinde olumlu etkileri bulunmuştur. *Mucuna pruriens* tohum tozunun 40 g/gün dozunda oral olarak uygulandığı ve 33 Parkinson hastasını kapsayan klinik bir çalışmada, preparatın %4,5 oranında L-dopa içermesi sayesinde hastalarda belirgin semptomatik iyileşme görülmüştür. Fabaceae familyasına ait *Vicia faba,* yaygın olarak bakla veya bakla fasulyesi olarak bilinen bir baklagil türüdür ve tohumlarının ana biyoaktif bileşenlerinden biri L-Dopa'dır. V. Faba'nın motor aktiviteleri iyileştirmekle birlikte plazma L-dopa düzeylerini artırmaktadır. Bir çalışmada, 250 g pişmiş fava tüketimi sonrası, parkinsonlu bireylerde kontrol grubuna kıyasla plazma L-dopa düzeyleri artmıştır. Çörek otu olarak da bilinen *Nigella Sativa,* timokinon gibi biyoaktif içeriklerden zengindir. Özellikle, timokinon inflamasyon ve apoptoz ile ilgili gen ifadesini modüle ettiği bilinir. *Nigella Sativa,* epigenetik yapıyı değiştirerek nöroprotektif etkileri kolaylaştırabilir ve Parkinson hastalığının ilerlemesini önlemek için yeni bir yaklaşım sunabilir. Iridaceae familyasından olan *Crocus Sativus* veya safranın, nörodejeneratif bozukluklarda faydalı etkileri olduğu bulunmuştur. Toksik amiloid yapılar, nörodejeneratif bozuklukların gelişmesine sebep olabilmektedir. Amiloidojenik koşullarda *Crocus Sativus*'un iki ana bileşeni krosin ve safranal, nöronal hasara sebep olan apo-α-laktalbumin fibrilasyonunu inhibe etmektedir. Bir çalışmada, *Crocus Sativus* ekstre edilmiş crocetinin intraperitoneal enjeksiyonu, 6-OHDA'nın sebep olduğu Parkinsonizm sıçan modelinde nöroprotektif etkilere neden olmuştur. *Curcuma longa* yani zerdeçal, sinir sisteminde oksidatif hasar oluşumunu düzenleyen doğal polifenol ve flavonoid olmayan bileşenlerden oluşmaktadır. Kurkumin, epigenetik mekanizmalar aracılığıyla nörodejenerasyonu azaltabilir. Kurkuminin suda çözünen ekstratı (50-200mg/kg p.o.) beyin dokularında yer alan dopamin ve serotonin düzeylerini artırmıştır. Kurkumin (5,10 ve 20mg/kg), hipokampal dokuda yer alan norepinefrin ve dopamin gibi monoaminerjik nörotransmitterlerin artırmıştır. Kurkumin ile kurkuminoid bileşikleri, kan-beyin bariyerini geçerek beyindeki hücrelerin epigenetik mekanizmasına etki edebilmektedir. **Sonuç:** İncelenen çalışma sonuçlarına göre bitki fitokimyasallarının, epigenetik mekanizmaları modüle ederek Parkinson hastalığının ilerlemesini yavaşlatabileceği ve tamamlayıcı bir tedavi yaklaşımı sunabileceği söylenebilir.

Anahtar Kelimeler: DNA metilasyonu, epigenetik**,** fitokimyasallar, parkinson hastalığı.

Poster Bildirisi: PB-01

Epigenetic Effects of Caffeine

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Purpose: Caffeine is one of the most widely consumed bioactive compounds worldwide, naturally found in coffee and cocoa beans, tea leaves, guarana berries, and kola nuts. In recent years, the effects of caffeine consumption on chronic diseases, neurological disorders, and pregnancy outcomes have attracted attention, particularly in relation to epigenetic mechanisms. The aim of this study is to evaluate the epigenetic effects of caffeine and their potential health implications. **Methods:** This study was conducted by reviewing experimental, cohort, observational, and meta-analytic studies published over the past decade. Data regarding the effects of caffeine on DNA methylation, histone modifications, and non-coding RNAs were systematically examined. Epigenetic findings obtained from human and animal models were comparatively evaluated. **Results:** Meta-analysis results indicate that coffee consumption is associated with a reduced risk of colorectal, colon, endometrial, and prostate cancers, as well as cardiovascular disease, Parkinson's disease, and type 2 diabetes. In addition, caffeine may lower the risk of Parkinson's disease and type 2 diabetes while potentially increasing pregnancy-related risks. In a colon carcinogenesis model, the administration of caffeine and chlorogenic acid regulated extracellular signal-regulated kinase 1/2 (ERK1/2) and transforming growth factor-beta (TGF-β) pathways via miR-21a-5p, leading to reduced inflammation. Moreover, high caffeine consumption (2–3 cups/day of coffee or ≥5 cups/day of tea) showed a protective effect particularly against estrogen receptor-negative breast cancer cases. Another meta-analysis reported that caffeinated coffee intake was associated with a lower risk of non-melanoma skin cancer, an effect not observed with decaffeinated coffee or tea, suggesting that the protective role may be attributable to caffeine itself. In a high-galactose diet–induced cataract model in rats, caffeine suppressed microRNA expression, thereby preventing gene silencing and exerting an epigenetic protective effect. Another study found that Pseudomonas aeruginosa infection suppressed immune activation through miR-301b upregulation, whereas caffeine decreased this microRNA, regulating inflammation at the epigenetic level. In ethanol-induced cerebellar models, elevated miRNA expression was suppressed by caffeine, demonstrating a neuroprotective effect. A cohort study revealed that maternal intake of sugary caffeinated beverages increased DNA hypermethylation rates in cord blood, showing similarity to leukemia-related methylation patterns in specific genomic regions. Prenatal caffeine exposure in female rats altered histone modifications through the GR–C/EBPα–SIRT1 pathway, increased hepatic lipid accumulation, and enhanced susceptibility to non-alcoholic fatty liver disease via epigenetic programming. Another study showed that prenatal caffeine exposure reduced histone H3 lysine 9 (H3K9) acetylation, suppressed Krüppel-like factor 4 (KLF4) gene expression, and adversely affected podocyte development in male offspring. Caffeine intake during pregnancy has also been associated with spontaneous abortion, intrauterine growth restriction, low birth weight, small head circumference, macrosomia, childhood obesity, and cognitive developmental impairments. **Conclusion:** Considering the available studies, human evidence supporting the association between these effects and epigenetic mechanisms remains limited, with most current findings derived from experimental research. According to the European Food Safety Authority (EFSA), the safe level of caffeine consumption is set at 400 mg/day for adults, 200 mg/day for pregnant and lactating women, and an upper intake level of 3 mg/kg/day for children and adolescents. The literature indicates that the effects of caffeine may vary depending on dose, individual genetic differences, and physiological conditions, acting through diverse epigenetic mechanisms. Evaluating these factors, increasing human data, and establishing links between epigenetic markers and clinical outcomes are essential for future research. In conclusion, caffeine is a potent bioactive compound capable of modulating epigenetic mechanisms and, depending on exposure level and physiological state, may exert both protective and adverse biological effects.

Keywords: Caffeine, coffe, epigenetics, chronic diseases, pregnancy.

Kafeinin Epigenetik Etkileri

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Amaç: Kafein, kahve ve kakao çekirdeklerinde, çay yapraklarında, guarana meyvelerinde ve kola fıstığında bulunan, dünya genelinde en yaygın tüketilen biyoaktif bileşenlerden biridir. Son yıllarda kafein tüketiminin epigenetik mekanizmalarla ilişkili olarak kronik hastalıklar, nörolojik bozukluklar ve gebelik sonuçları üzerindeki etkileri dikkat çekmektedir. Bu çalışmanın amacı, kafeinin epigenetik düzeydeki etkilerini ve bu etkilerin olası sağlık sonuçlarını değerlendirmektir. **Yöntem:** Son on yılda yayınlanan deneysel, kohort, gözlemsel ve meta-analiz araştırmaların incelenmesiyle oluşturulmuştur. Kafeinin DNA metilasyonu, histon modifikasyonları ve kodlamayan RNA'lar üzerindeki etkilerine ilişkin veriler taranmıştır. İnsan ve hayvan modellerinde elde edilen epigenetik bulgular karşılaştırmalı olarak değerlendirilmiştir. **Bulgular:** Meta-analiz sonuçları incelendiğinde kahve kolorektal, kolon, endometriyal ve prostat kanserleri, kardiyovasküler hastalık, Parkinson hastalığı ve tip 2 diyabet riskinde azalma ile ilişkilendirilmiştir. Bunun yanı sıra kafein, Parkinson hastalığı ve tip 2 diyabet riskini azaltırken, gebelik dönemine ilişkin potansiyel riskleri artırabilmektedir. Yapılan bir araştırmada kolon karsinogenez modelinde kafein ve klorojenik asit uygulaması, miR-21a-5p aracılığıyla hücre dışı sinyal düzenleyici kinaz 1/2 (ERK1/2) ve dönüştürücü büyüme faktörü-beta (TGF-β) yolaklarını düzenleyerek inflamasyonu azaltmıştır. Bunun yanı sıra yüksek kafein tüketimi (2-3 fincan/gün kahve veya ≥5 fincan çay/gün) özellikle östrojen reseptörü-meme kanseri olgularına karşı koruyucu etki göstermiştir. Yürütülen bir meta-analizde, kafeinli kahve tüketiminin melanom dışı deri kanseri riskini azalttığını, bu etkinin kafeinsiz kahve ve çayda gözlenmediğini ve koruyucu etkinin kafeine bağlı olabileceği bildirilmiştir. Yüksek galaktozlu diyetle indüklenen katarakt modelindeki farelere uygulanan kafein, mikroRNA ekspresyonunu baskılayarak genin susturulmasını önlemiştir ve bu yolla epigenetik düzeyde koruyucu etki göstermiştir. Başka bir araştırmada, *Pseudomonas aeruginosa* enfeksiyonunun miR-301b bağışıklık yanıtını baskıladığı, kafeinin ise bu mikroRNA'yı azaltarak inflamasyonu epigenetik düzeyde düzenlediği saptanmıştır. Etanol ile indüklenen serebellar miRNA artışlarının, kafein aracılığıyla baskılanarak nöroprotektif etki gösterdiği bildirilmiştir. Kohort bir araştırmada, annenin şekerli kafeinli içecek tüketmesi kordon kanında hipermetilasyon oranlarını arttırmıştır ve bazı gen bölgelerinde lösemiyle ilişkili epigenetik metilasyon paternleriyle benzerlik göstermiştir. Prenatal kafein maruziyetinin dişi sıçanlarda histon modifikasyonlarını değiştirerek karaciğerde lipid birikimini arttırdığı, epigenetik programlama yoluyla alkolsüz yağlı karaciğer hastalığı duyarlılığını yükselttiği saptanmıştır. Başka bir araştırmada, prenatal kafein maruziyetinin erkek farelerde histon H3 lizin 9 (H3K9) asetilasyonunu azaltarak kruppel benzeri faktör 4 (KLF4) gen ifadesini baskıladığı ve podosit gelişimini epigenetik düzeyde olumsuz etkilediği bildirilmiştir. Gebelik döneminde kafein alımının spontan abortus, intrauterin büyüme geriliği, düşük doğum ağırlığı, küçük baş çevresi, makrozomi, çocukluk çağı obezitesi ve bilişsel gelişim bozukluklarıyla ilişkili olduğu gösterilmiştir. **Sonuç:** Yapılan çalışmalar göz önünde bulundurulduğunda bu etkilerin epigenetik mekanizmalarla ilişkisini destekleyen insan verileri sınırlı olup, mevcut kanıtlar çoğunlukla deneysel araştırmalara dayanmaktadır. Avrupa Gıda Güvenliği Otoritesi tarafından, kafeinin güvenli tüketim düzeyi yetişkinlerde 400 mg/gün, gebe ve emziren kadınlarda 200 mg/gün, çocukluk ve ergenlik döneminde üst alım düzeyi 3 mg/kg/gün olarak belirlenmiştir. Literatürdeki bulgular kafein tüketiminin doza, bireysel genetik farklılıklara ve fizyolojik duruma bağlı olarak epigenetik mekanizmalar üzerinden farklı etkiler gösterebileceğini ortaya koymaktadır. Bu etkilerin dikkate alınarak değerlendirilmesi, insan verilerinin artırılması ve epigenetik belirteçlerin klinik sonuçlarla ilişkilendirilmesi gelecekteki çalışmalar açısından önem taşımaktadır. Sonuç olarak, kafein epigenetik mekanizmaları modüle edebilen güçlü bir biyoaktif bileşen olup, fizyolojik koşullar ve maruziyet düzeyine göre hem koruyucu hem de olumsuz biyolojik etkiler oluşturabilmektedir.

Anahtar Kelimeler: Kafein, kahve, epigenetik, kronik hastalıklar, gebelik dönemi.

Poster Bildirisi: PB-02

Epigenetic Mechanisms of Caffeine on Athletes

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Introduction: Caffeine is one of the most widely used ergogenic aids in sports, known to enhance endurance, strength, and reaction speed. While its effects have traditionally been attributed to adenosine receptor antagonism and increased calcium release, recent studies suggest that caffeine may also influence epigenetic mechanisms that regulate gene activity without altering the genetic sequence, primarily through DNA and histone modifications. Mechanisms such as DNA methylation (the addition of methyl groups that suppress gene transcription) and histone acetylation (relaxing chromatin structure to activate genes) play a crucial role in exercise-induced skeletal muscle adaptation. **Materials and Methods**: This study reviews literature from 2023 to 2025 to evaluate whether caffeine enhances performance through such epigenetic mechanisms, focusing particularly on human data regarding chromatin remodeling and exercise-responsive gene methylation in muscle cells. Between January 2023 and October 2025, searches were conducted in PubMed, Scopus, and Web of Science using the terms: "caffeine OR coffee" AND "epigenetic* OR DNA methylation OR histone OR microRNA" AND "exercise OR athlete OR skeletal muscle." Inclusion criteria comprised studies involving physically active adults that reported epigenetic outcomes (DNA methylation, histone modification, or small RNA profiles). Mechanistic cellular and animal studies elucidating molecular pathways linking caffeine to gene regulation in muscle were also considered. **Findings:** Mechanistic Evidence (Muscle Cells): Caffeine triggers chromatin remodeling in muscle cells through a Ca^{2+}/CaMK-dependent pathway. In the study by Mukwevho et al. (2008; Figure 2), caffeine treatment reduced nuclear HDAC5 levels while increasing MEF2A binding and histone H3 acetylation at the GLUT4 promoter. These effects were abolished by the CaMK inhibitor (KN-93) or the calcium-release blocker (dantrolene), confirming a calcium- dependent mechanism. Histone acetylation relaxes chromatin, allowing transcription of glucose uptake–related genes, thereby enhancing muscle endurance. Human Exercise Data (BMC Biology, 2024): In trained men, exercise induced 10–15% hypomethylation at PGC-1α promoter regions, resulting in approximately a 3000-fold increase in mRNA levels three hours post-exercise. A negative correlation ($R = –0.63$) between methylation and gene expression was observed. The activation of the same CaMK–HDAC–MEF2 signaling pathway by caffeine in vitro supports the biological relevance of these findings. Population-Level Findings (2023–2024 EWAS): In epigenome-wide association studies involving about 15,000 participants, regular coffee consumption was associated with methylation changes in the HDAC4 and PHGDH gene regions. These results suggest that caffeine exposure, beyond its acute effects, leaves persistent epigenetic marks in humans. **Interpretation**: Figure 1 demonstrates that caffeine (CAF) reduces the amount of nuclear HDAC5 in skeletal muscle cells compared to the control group. The Western blot (C) images and corresponding bar graphs show a statistically significant decrease in the HDAC5/MEF2A ratio ($p<0.05$) following caffeine treatment. However, when caffeine was co-administered with KN93 (a CaMK inhibitor) or dantrolene (a Ca^{2+} release blocker), HDAC5 levels returned to baseline. This finding indicates that caffeine promotes the nuclear export of HDAC5 through a Ca^{2+}/CaMK-dependent pathway, supporting its role in epigenetic regulation of muscle gene expression. By removing this repressive protein (HDAC5), caffeine enables MEF2A to activate genes such as GLUT4, thereby linking caffeine intake to increased glucose metabolism and gene transcription in muscle cells. **Conclusion**: Findings from 2008 to 2025 support a coherent biological model: Cellular level: Caffeine remodels chromatin (↓HDAC5, ↑H3 acetylation, ↑MEF2A binding). Human level: Exercise decreases PGC-1α promoter methylation, enhancing metabolic gene expression. Population level: Caffeine exposure is linked to lasting methylation changes in key metabolic regulators. Thus, caffeine may enhance metabolic adaptation and recovery by reinforcing exercise-activated epigenetic pathways in already epigenetically active athletes. Although randomized controlled trials directly measuring caffeine-induced epigenetic modifications are lacking, Current evidence indicates that caffeine can activate chromatin remodeling pathways similar to those triggered by exercise. To confirm this connection, unbiased studies involving muscle biopsies and methylome analyses are required. For now, caffeine's ergogenic effects can be explained as the combination of neural stimulation and epigenetic enhancement of muscle adaptation.

Keywords: Caffeine, ergogenic, DNA Methylation, histone acetylation, sports performance.

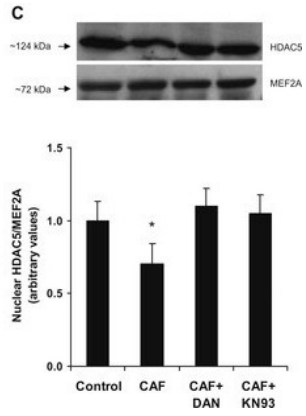

Figure 1

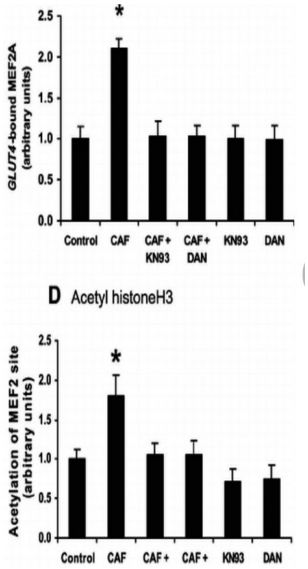

Figure 2

Kafeinin Atletler Üzerindeki Epigenetik Mekanizmaları

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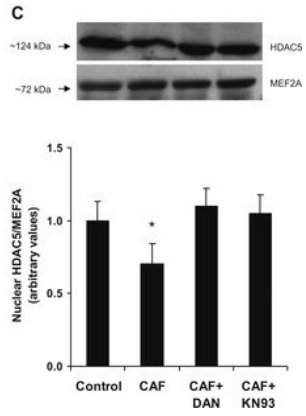
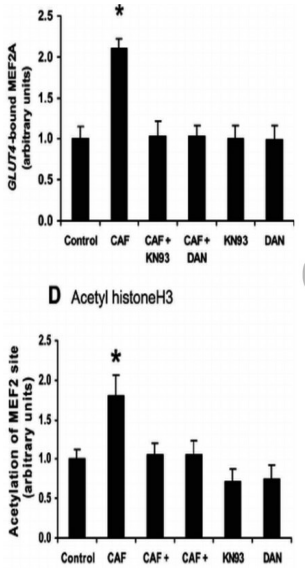
Giriş: Kafein, dayanıklılığı, kuvveti ve reaksiyon hızını artırdığı bilinen, sporda en yaygın kullanılan ergogenik desteklerden biridir. Etkileri geleneksel olarak adenozin reseptörü antagonizması ve artmış kalsiyum salınımına bağlanırken, son çalışmalar kafeinin DNA ve histon modifikasyonları yoluyla gen aktivitesini genetik diziyi değiştirmeden düzenleyen epigenetik mekanizmaları da etkileyebileceğini göstermektedir. DNA metilasyonu (gen transkripsiyonunu baskılayan metil grubu eklenmesi) ve histon asetilasyonu (kromatini gevşeterek genleri aktifleştirme) gibi mekanizmalar, egzersize bağlı kas adaptasyonunda kilit rol oynar. **Materyeller ve Metodlar:** Bu çalışma, 2023–2025 literatürünü inceleyerek kafeinin bu tür epigenetik mekanizmalar aracılığıyla performansı artırıp artırmadığını değerlendirmekte; özellikle kas hücrelerinde kromatin yeniden düzenlenmesi ve egzersize duyarlı gen metilasyonu üzerine yapılan insan verilerine odaklanmaktadır. Ocak 2023 – Ekim 2025 arasında PubMed, Scopus ve Web of Science'ta şu terimler aranmıştır: "caffeine OR coffee" VE "epigenetic* OR DNA methylation OR histone OR microRNA" VE "exercise OR athlete OR skeletal muscle." Dahil edilme kriterleri: egzersiz yapan yetişkinleri kapsayan ve epigenetik sonuçları (DNA metilasyonu, histon modifikasyonu veya küçük RNA profilleri) bildiren çalışmalardır. Mekanistik hücre ve hayvan çalışmaları da değerlendirilmiştir. **Mekanik Kanıtlar (Kas Hücreleri):** Kafein, kas hücrelerinde Ca^{2+}/CaMK-bağımlı bir yol üzerinden kromatin yeniden düzenlenmesini tetikler. Mukwevho ve ark. (2008; Figure 2) çalışmasında kafein uygulaması, çekirdekteki HDAC5 düzeylerini azaltmış, MEF2A bağlanmasını ve histon H3 asetilasyonunu GLUT4 promotör bölgesinde artırmıştır. Bu etkiler, CaMK inhibitörü (KN-93) veya kalsiyum salınım engelleyicisi (dantrolen) ile ortadan kalkmış; etkinin kalsiyum bağımlı bir mekanizma aracılığıyla gerçekleştiği doğrulanmıştır. Histon asetilasyonu, kromatini gevşeterek glukoz alımıyla ilişkili genlerin transkripsiyonuna izin verir ve kas dayanıklılığını artırır.
İnsan Egzersiz Verileri (BMC Biology, 2024): Antrenmanlı erkeklerde yapılan egzersiz, PGC-1α geninin promotör bölgelerinde %10–15 hipometilasyon oluşturmuş, üç saat sonra mRNA düzeyinde yaklaşık 3000 kat artış sağlamıştır. Metilasyon ve gen ekspresyonu arasında negatif korelasyon ($R = –0.63$) saptanmıştır. Kafeinin aynı CaMK–HDAC–MEF2 yolunu in vitro aktive etmesi bu verilerin biyolojik önemini destekler. **Popülasyon Düzeyinde Bulgular (2023–2024 EWAS):** Yaklaşık 15 bin kişi üzerinde yapılan epigenom çapında ilişkilendirme çalışmalarında, düzenli kahve tüketimi HDAC4 ve PHGDH gen bölgelerinde metilasyon değişiklikleriyle ilişkilendirilmiştir. Bulgular, kafein maruziyetinin akut etkilerin ötesinde, insanlarda kalıcı epigenetik izler bıraktığını göstermektedir. **Yorumlama:** Görsel 1, kafeinin (CAF), kontrol grubuna kıyasla iskelet kası hücrelerinde çekirdek içi HDAC5 miktarını azalttığını göstermektedir. Western blot (C) görüntüleri ve bunlara karşılık gelen çubuk grafikler, kafein uygulamasından sonra HDAC5/MEF2A oranında istatistiksel olarak anlamlı bir azalma ($p < 0.05$) olduğunu, buna karşın KN93 (CaMK inhibitörü) veya dantrolen (Ca^{2+} salınım engelleyicisi) ile birlikte uygulandığında HDAC5 düzeylerinin eski haline döndüğünü göstermektedir.Bu durum, kafeinin Ca^{2+}/CaMK-bağımlı bir yol aracılığıyla HDAC5'in çekirdekten taşınmasını (nükleer eksport) teşvik ettiğini ortaya koymaktadır. Bu baskılayıcı proteinin (HDAC5) uzaklaştırılmasıyla kafein, MEF2A'nın GLUT4 gibi genleri aktive etmesini sağlar ve böylece kafein alımını, kas hücrelerinde artmış glukoz metabolizması ve gen transkripsiyonu ile ilişkilendirir. 2008–2025 yılları arasındaki bulgular, tutarlı bir biyolojik modeli desteklemektedir: Hücre düzeyinde: Kafein, kromatini yeniden düzenler (↓HDAC5, ↑H3 asetilasyonu, ↑MEF2A bağlanması). İnsan düzeyinde: Egzersiz, PGC-1α promotör bölgelerinin metilasyonunu azaltarak metabolik gen ekspresyonunu artırır. Popülasyon düzeyinde: Kafein maruziyeti, metabolik düzenleyicilerde kalıcı metilasyon değişimleriyle ilişkilidir. Dolayısıyla kafein, epigenetik olarak aktif atletlerin kas hücrelerinde egzersizle aktive olan yolları güçlendirerek metabolik adaptasyonu ve toparlanmayı artırma potansiyeline sahiptir. Her ne kadar kafein kaynaklı epigenetik değişimleri doğrudan ölçen rastgele kontrollü çalışmalar bulunmasa da, mevcut veriler kafeinin egzersizle tetiklenen kromatin yeniden düzenleme yollarını benzer biçimde aktive edebildiğini göstermektedir. Bu ilişkinin doğrulanması için kas biyopsileri ve metilom analizlerini içeren tarafsız çalışmalar gereklidir. Şimdilik kafeinin ergogenik etkileri, hem sinirsel uyarımın hem de epigenetik kas adaptasyonunun birleşimiyle açıklanabilir.

Anahtar Kelimeler: Kafein, ergojenik, DNA Metilasyonu, histon asetilasyonu, spor performansı.



Resim 1



Resim 2


NUTRİGENETİK EPİGENETİK
DERNEĞİ