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[PP-01]
One Molecule with Two Faces: Cellular Response of Dinuclear Pd(II) Complex on Breast Cancer Cell Lines

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ABSTRACT

Objective: Breast cancer is one of the leading cancer types in terms of morbidity and mortality globally. Although cisplatin has a strong anti-tumor effect, studies show that it is extremely toxic, causing nephrotoxicity and ototoxicity. To resolve these concerns, multinuclear metal complexes are synthesized. The synthesis of these complexes is crucial due to their high dna binding affinity and cytotoxic effect.

Material and Method: The cytotoxic effects of dinuclear Pd (II) complex on breast cancer cell lines(MCF-7, MDA-MB-231) and healthy breast cell line(MCF-10F) were investigated. SRB and ATP viability tests were performed to determine the effect of the Pd(II) complex on cell viability. The presence of apoptosis in breast cancer cells was demonstrated by various staining methods, flow cytometry and immunoblotting. Colony formation, invasion, and migration assays were performed to evaluate the effect of the complex on metastasis.

Results: The anti-cancer effect of the Pd (II) complex on MCF-7 was detected at low doses, while the cytotoxic effect on MCF-10F was significantly less. As a result of flow cytometry experiments, increased caspase3/7 levels and positive annexinV staining were reported in both cell lines. The presence of apoptosis was elucidated regardless of p53 expression in MCF-7 and MDA-MB-231 due to increased TNFR1 and TRADD expression with caspase8 cleavage and increased Bcl-2 inactivation with loss of mitochondiral membrane potential.

Conclusion: The Dinuclear Pd (II) complex, which is acknowledged to induce both extrinsic and intrinsic apoptosis, may be used as a promising treatment option on breast cancer, it was concluded that further in vivo experiments should be performed.

Keywords: breast cancer, apoptosis, palladium

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[PP-02]
NGS test: Novel ABCC8 K1411N Mutation Linked with Diabetes

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ABSTRACT

Objective: ATP-binding cassette transporter sub-family C member 8 (ABCC8) is involved in the formation of the sulfonylurea receptor-1 protein, a subunit of ATP-sensitive potassium channels found in the membranes of pancreatic beta cells. Gene mutations encoding the ABCC8 protein have been associated with neonatal diabetes, monogenic diabetes (MODY12), gestational diabetes, type 2 diabetes (T2DM), and obesity. Present study aimed to investigate the associations between genetic variations in ABCC8 gene, risk of T2DM and clinical phenotype using next generation sequencing (NGS) method in healthy and T2DM case groups of Turkish individuals.

Material and Method: The study groups consisted of 42 patients diagnosed with T2DM and 79 healthy individuals. Mutations in the ABCC8 gene were investigated by NGS, and statistical analysis was performed by SPSS (version 20.0) software.

Results: Body mass index, waist circumference, fasting blood glucose, hemoglobin A1c, triglyceride and C-reactive protein values were higher in case group compared to healthy group, while high-density lipoprotein cholesterol and estimated glomerular filtration rate values were lower in case group compared to healthy group. The novel K1411N (c.A4233C), which was detected in present study, was found statistically associated with risk of T2DM for the first time in the literature. Also, the K1411 rare G allele was associated with low C-peptide and increased BMI levels, in case group and control group respectively ($p<0.05$). The frequency of identified ABCC8 gene A1369S (rs757110 C>A, c.G4105T) mutation was similar in case and control groups. However, age of onset for T2DM in case group ($p<0.05$) and reduced BMI levels in control group ($p<0.01$) were found statistically associated with A1369S rare A allele. Additionally, A1369S homozygote AA genotype was statistically associated with reduced BMI and waist circumference in case group ($p<0.05$).

Conclusion: In the present study, the effects of novel K1411N and known A1369S mutations of the ABCC8 gene on risk of T2DM and obesity have been observed.

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Keywords: type 2 diabetes mellitus, ABCC8, gene, mutation, next-gene sequencing

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[PP-03]
Biyoinformatik ve Proteomik Yaklaşımlar ile CXCL12 ve Hastalık İlişkisi

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ABSTRACT

Objective: CC chemokine genes 17q11.2-12 and C-X-C chemokine genes are also located at 4q13 locus. Stromal cell-derived factor 1 is a chemokine protein encoded by the CXCL12 gene on chromosome 10 in humans. It is ubiquitously expressed in many tissues and cell types. CXCL12 has a CXCR4 receptor-ligand relationship. This gene plays an important role in multiple myeloma (MM) disease and other diseases.

Material and Method: GSEA/MSigDB was used for gene sets, UniProt for protein structure and function, STRING for other associated functional genes and protein domains, HMDB for metabolite associations, gmpdb for proteomic data analysis, Blood eQTL/BIOS /mQTLdb and GWAS for associated diseases.

Results: As a result of proteomic studies, it was seen that CXCL12 binds to the atypical chemokine receptor ACKR3, which activates the beta-binding pathway and acts as a receptor. On the other hand, it has been observed that integrins can bind to the allosteric region (site 2) and activate ITGAV:ITGB3, ITGA4:ITGB1 and ITGA5:ITGB1 integrins independently of CXCR4. CXCL12 has 523 related gene sets. There are 10 functional proteins (CXCR4, ACKR3, HMGB1, CCR4, CCR5, CXCR3, SDC4, CCR3, CCL11, PTPRC) (Homology score: 0.9). CXCR4 has a common metabolite protein linkage with its antagonist, Plerixafor. Analysis of the gene set co-expressed in the GSEA/MSigDB tool found associated diseases such as allergic disease, arthritis, autoimmune disease of the musculoskeletal system, osteoarthritis (FDR<5E-06). GWAS was also associated with respiratory system disease, bowel disease, combined immunodeficiency, multiple sclerosis, and hepatitis (P<8E-06). In addition, the GWAS databases also yielded significant results for B-lymphoblastic leukemia/lymphoma (P<7E-40).

Conclusion: CXCL12 is associated with many diseases, especially MM. This study is a preliminary feasibility study before working in a laboratory environment.

Keywords: hematology, gene, protein, bioinformatics, pathway