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# CONCENTRATION OF SOLUBLE FORM OF B-CELL MATURATION ANTIGEN (SBCMA) IN THE SERUM OF PATIENTS WITH MULTIPLE MYELOMA

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## 1. Introduction

B cell maturation antigen (BCMA) is present on mature B lymphocytes and normal plasma cells. However, significantly increased expression is found on cancer plasma cells. In recent years, this molecule has become a new target for immunotherapy in the group of patients with multiple myeloma (MM). The BCMA antigen may also exist as a soluble BCMA molecule (sBCMA), which is released into the circulation via  $\gamma$ -secretase from the cell surface.

## 2. Aim of the study

The aim of the conducted research was to assess the concentration of sBCMA in the blood serum of MM patients and to analyze the relationship between the level of the molecule and selected biochemical and hematological parameters and the type of monoclonal protein. The prognostic value of the sBCMA level was also analyzed and the usefulness of molecule determinations during treatment was assessed.

## 3. Materials and methods

The study was conducted on a group of 77 patients, of which 15 people constituted the control group, and the study group consisted of 62 patients with newly diagnosed multiple myeloma who were treated at the Department of Hematooncology and Bone Marrow Transplantation SPSK No. 1 in Lublin. The concentration of sBCMA in blood serum was determined using the enzyme-linked immunosorbent method (ELISA). Additionally, the following tests were performed: determination of biochemical and hematological parameters, electrophoretic separations and immunofixation of serum proteins, and determination of the concentration of free light chains (FLC), the results of which were presented in the form of calculated involved/uninvolved FLC ratios (i/u FLC).

## 4. Results

The concentration of sBCMA was significantly higher in the group of patients than in the group of healthy people. In the analysis of the relationship for sBCMA, statistically significant correlations with all the parameters were found. A significant, positive correlation was obtained between sBCMA concentration and the level of  $\beta_2$ -microglobulin, creatinine and monoclonal protein and i/u FLC ratio. A significant negative correlation was also found between sBCMA concentration and hemoglobin and albumin levels. Statistical analysis of the results performed in a selected group of patients after treatment with at least a very good partial response (VGPR) showed a significant decrease in sBCMA concentration. In turn, the assessment of Kaplan-Meier survival curves proved the association of high sBCMA concentration in serum with a significantly shorter overall and progression-free survival compared to patients with low sBCMA levels.

## 5. Conclusion

The presented results prove the high usefulness of sBCMA determinations, including: in assessing disease activity, monitoring treatment effectiveness and prognostic assessment of MM patients. In the future, this molecule may become a routinely measured biochemical parameter in the group of MM patients.

# ASSESSMENT OF DAMAGE MARKERS ENDOTHELIUM IN PATIENTS WITH COVID-19

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**Keywords:** COVID-19, endothelium, cardiovascular risk, SARS-CoV-2

## 1. Introduction

Coronavirus disease (COVID-19) is caused by the SARS-CoV-2 virus. Primarily, COVID-19 affects the respiratory system, leading to coughing, shortness of breath and fever. Numerous patients, who recovered from COVID-19, have reported chronic loss of taste and smell, and some have suffered from heart palpitation and chest pain. It has been found that, in many cases, COVID-19 may develop into post-COVID syndrome, which can result in cardiovascular disease.

## 2. Aim of the study

The aim of this study was to assess the prevalence of markers of vascular endothelial damage in survivors of COVID-19 and to investigate whether survivors are at risk of developing cardiovascular and embolic-thrombotic diseases due to vascular endothelial dysfunction after COVID-19.

## 3. Materials and methods

The study group consisted of 215 patients, who had been infected with SARS-CoV-2 virus and did not report any other diseases. The control group was composed of 79 people, who were not affected by the virus. All subjects

were objectively healthy people between 18 and 65 years old, who did not use permanent medication. In addition, all patients qualified for blood donation and were blood donors registered in Regional Blood Center in Warsaw. Concentrations of hs-CRP and NT-proBNP were measured on a Dimension EXL analyser, by turbidymetric immunoassay and by chemiluminescence, while concentrations of VCAM-1 and sE-selectin were measured by ELISA.

There were no statistically significant differences between the recovered group and the healthy subjects in hs-CRP, NT-proBNP and VCAM-1 concentrations. The concentration of soluble E-selectin was higher in convalescents than in non-affected by COVID-19. The difference was statistically significant ( $p=0.0135$ ). There was no correlation between the parameters studied.

## 4. Conclusions

On the basis of E-selectin results it can be concluded, that vascular endothelial damage can occur in COVID-19 survivors. Individuals without chronic diseases who have undergone SARS-CoV-2 infection do not show an increased risk of developing cardiovascular and embolic-thrombotic diseases.

## FROM REST TO MOTION.

### UNDERSTANDING LIPID PROFILES IN THE CONTEXT OF SLEEP AND ACTIVITY

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#### 1. Introduction

Maintaining a healthy lifestyle and adhering to recommended sleep patterns and physical activity are paramount in preserving optimal physiological parameters, particularly within the cardiovascular system. The reduction of risk factors has long been established as the cornerstone in preventing and managing coronary heart disease (CHD). The prolonged presence of elevated levels of triglyceride-rich particles in the bloodstream can lead to disruptions in the functionality of LDL and HDL. These factors have both been linked to impairments in endothelial function, and they play a direct or indirect role in the development of atherosclerosis. Notably, small, dense LDL particles and residual triglyceride-rich remnants have the capacity to enhance the accumulation of cholesterol esters within the walls of blood vessels.

#### 2. Materials and methods

Cholesterol, HDL and triglyceride concentration was determined using the ACCENT-200 kit on a CORMAY ACCENT200. LDL concentration was calculated based on the FRIEDEWALD formula. Statistica software was used for statistical calculations. Material was collected from 200 patients after obtaining informed consent and a questionnaire form including questions about health status, sleeping problems, physical activity and others.

#### 3. Results

The study encompassed a cohort of 200 individuals, evenly distributed into two groups based on the presence or absence of sleep problems and their engagement in physical exercise. The primary objective was to investigate the potential impact of these lifestyle factors on lipid profile parameters, specifically cholesterol, HDL, LDL, and triglycerides. The analysis revealed that across all demographic categories, including gender, the presence or absence of sleep problems, and physical activity levels, there were no statistically significant differences observed in lipid profile parameters. All the results obtained were similar within each of the specified groups.

#### 4. Conclusions

Physical activity and sleep quality will not significantly affect lipid profile levels. Nevertheless, proper sleep hygiene and physical exercise, combined with a healthy diet, can effectively reduce the amount of cholesterol and decrease the chances of cardiovascular disease, as well as atherosclerosis. It's essential to note that the absence of an association in this specific sample does not rule out the possibility of such associations in different populations or under different conditions.

# EFFECT OF N21 SUPPLEMENT ON NEURAL DIFFERENTIATION CAPACITY AND NEUROPROTECTIVE POTENTIAL OF DFAT CELLS

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**Keywords:** DFAT cells, N21 supplement, neural differentiation, neuroprotection, cell therapy in neurology

## 1. Introduction

The use of Mesenchymal Stem/Stromal Cells (MSCs) in regenerative medicine has been widely studied over the last decades. MSC's therapeutic potential has been seen in two crucial mechanisms: paracrine activity and ability to repopulate at the site of injury. The multipotency also remains a major feature of MSC's, but it was shown that under specific environmental conditions or supplement addition they can differentiate into different germ layers, like ectoderm, or tissues, for example neural tissue. Recently, other unique MSC's subpopulations has been found in the adipose tissue. One of them is dedifferentiated fat cells (DFAT), that has been discovered to represent more clonogenic and pluripotent-like cells.

## 2. Aim of the study

In this study we investigated the effect of the N21 supplement on the neural differentiation capacity of DFAT cells and their neuroprotective and secretory potential after the contact with damaged nerve tissue.

## 3. Materials and methods

The study utilized cells isolated from adipose tissue obtained during liposuction. DFAT cells were obtained by conducting culture using the ceiling method. The differentiation potential of DFAT cells towards a neural lineage was assessed in culture with the addition of the N21 supplement. The ability for neuroprotection was examined through co-culturing cells with damaged neural tissue.

## 4. Results

We discovered that both N21 supplementation and the presence of damaged tissue increased neural gene expression in DFAT cells, however, neither phenotype nor high expression of markers of mature neurons was obtained. The proliferation potential decreased with further differentiation of cells. N21-preconditioned cells demonstrated increased neuroprotective factors secretion during the acute phase of tissue injury, and the secretion profile varied depending on the day of the co-culture. Both undifferentiated and N21-supplemented cultured cells presented similar neuroprotective potential.

## 5. Conclusion

In conclusion, our results indicate the bilateral nature of the DFAT cells-neural tissue interactions. The high neuroprotective potential and neural differentiation abilities of N21- supplement preconditioned DFAT cells give hope for their use in the treatment of neurological diseases.

# AUTOIMMUNE HEMOLYTIC ANEMIA OF UNKNOWN ETIOLOGY IN A 46-YEAR-OLD PATIENT

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**Keywords:** autoimmune hemolytic anemia, complement, IgG class antibodies, hemolysis

## 1. Introduction

In the course of autoimmune hemolytic anemia (NAIH), autoantibodies and components of the complement system present on the surface of erythrocytes are responsible for the extravascular destruction of red blood cells. The temperature range at which autoantibodies are active is the basis for dividing NAIH into warm, cold and mixed types. In patients with NAIH of the warm type, antibodies of the IgG class are detected in most cases. Causes of NAIH include bacterial and viral infections, immune errors, lymphoproliferative diseases and systemic connective tissue diseases.

## 2. Case presentation

A 46-year-old patient, diagnosed in 2014 with NAIH with the presence of warm-type antibodies, with a history of severe pneumonia of *Pneumocystis jiroveci* etiology and abscesses of the left cerebral hemisphere, was admitted to the Department of Hematology to clarify the causes of increasing anemia with present biochemical markers of hemolysis. In August 2017, a peripheral blood lymphocyte phenotype study was performed, which showed CD3+/CD4+ T-cell deficiency. Due to a loaded history, HIV infection was suspected; however, both the screening and confirmation test were negative. During hospitalization, increasing anemia was observed with increasing indicators of hemolysis (increase in reticulocyte count, increase in LDH activity, increase in bilirubin concentration). A direct antiglobulin test confirmed the presence of warm-type IgG antibodies on erythrocytes including a C3d component. In serum, a significant decrease in the concentration of the C4 component of complement was detected. Serological tests excluded an infectious origin of the disease. Treatment included glucocorticosteroid infusions and rituximab. As a result of the therapy, inhibition of decrease in hemoglobin concentration and normalization of hemolysis indicators were observed.

## 3. Conclusions

In the presented case, the cause of NAIH could not be clearly identified. IgG class antibodies present on red blood cells including C3d component and decreased serum C4 concentration indicate active involvement of the complement system in the mechanism of hemolysis. Selective CD3+/CD4+ T-lymphocyte deficiency unrelated to HIV infection, a data history typical for AIDS infections and the occurrence of autoimmunity against red blood cell antigens should prompt an in-depth diagnosis for innate or acquired immune defects.

# A TYPICAL HAEMOLYTIC UREMIC SYNDROME TREATED WITH ECULIZUMAB IN A 7-YEAR-OLD GIRL

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## 1. Introduction

aHUS is a life-threatening disease caused by uncontrolled activation of complement system, it characterized itself with a triad of symptoms: hemolytic anemia, thrombocytopenia and renal failure. Nowadays, monoclonal antibody called eculizumab has become hope for patients suffering from aHUS.

## 2. Case presentation

A 7-year-old girl was admitted to the Department of Nephrology due to symptoms including diarrhoea, vomiting, weakness and reluctance to eat and drink. The tests showed anaemia, thrombocytopenia, hyperbilirubinemia and hyponatremia (Table 1). A thrombotic microangiopathy (TMA) was diagnosed, and a further differential diagnosis was implemented. STEC-HUS was suspected, and a PCR test was ordered. To exclude autoimmune haemolytic anaemia (AIHA) and TTP, Coombs test and ADAMTS13 activity were ordered.

Due to poor haematological parameters, the girl received one unit of packed red blood cells (pRBC). Renal replacement therapy was started urgently, as laboratory tests indicate acute kidney injury.

Double-negative results of PCR testing for STEC allowed to exclude infection. The result of ADAMTS13 activity was 97%, and the Coombs test was negative. Hence, TTP and AIHA were excluded, and aHUS was diagnosed; thus, the girl qualified for a drug treatment program with eculizumab; on the same day, the first dose of eculizumab (600 mg) was administered without complications. For eculizumab therapy monitoring CH50 assays were performed and results <12.21 U/mL, were assessed as complete inhibition of complement activity.

Genetic test showed mutations in two copies of the CD46 gene, which predispose to aHUS occurrence. Additionally, the study showed the presence of haplotype variants in the CFH (H3) gene, a mutation in both copies of the gene. Moreover, mutation was detected in one copy of the ADAMTS13 gene.

## 3. Conclusion

This case supports the statement that eculizumab therapy is safe and efficient in paediatric patients with aHUS. In reference to an international consensus approach to the management of aHUS in children, eculizumab should be the first-line treatment, and the therapy should be initiated within 24-48 h.

# PERFORMANCE FORECASTING HEPATOTOXIC IN VARIOUS PHARMACOLOGICAL GROUPS OF DRUGS

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**Keywords:** drug-induced liver injury, hepatotoxicity, prediction, cluster analysis

## 1. Introduction

Drug-induced liver damage is a pathological condition in which as a result, hepatocyte function is impaired an adverse reaction in response to the toxic effects of drugs or their metabolites. DILI may occur as a predictable clinical event, that we can control or as an event unpredictable, which is what we most often see with many commonly used medicines, dietary supplements or preparations herbal.

## 2. Aim of the study

Predicting the hepatotoxic potential of drugs various groups of pharmacological classification, including drugs: antiarrhythmic, anticonvulsant, antituberculosis, anticancer, antiviral, antiplatelet, antifungals, antihypertensives, statins, antimetabolites, steroids anabolic, analgesic, non-steroidal anti-inflammatory drugs, immunosuppressants and single unclassified drugs. Agglomerative analysis of descriptors designated for hepatotoxicity effects of selected drugs in the study subjects classification groups.

## 3. Materials and methods

The research involved predicting the hepatotoxic effects of drugs based on the analysis of their chemical structure and toxicological risk estimation using computer software using structure-activity relationship (SAR) algorithms and quantitative structure-activity relationship (QSAR) models and artificial intelligence systems (ADMED Predictorä ver. 10.3)

## 4. Results

In this work, potential prediction was made hepatotoxic drugs in various pharmacological groups including drugs: antiarrhythmics, anticonvulsants, anti-tuberculosis, anti-cancer, anti-viral, antiplatelet, antifungal, antihypertensive, statins, antimetabolites, anabolic steroids, analgesics, non-steroidal anti-inflammatory drugs, immunosuppressants and medications not classified in the above-mentioned groups. The tests performed showed significant drug-induced changes in terms of liver parameters, including concentrations parameters: alkaline phosphatase (ALP), aminotransferase alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltranspeptidase (GGTP), dehydrogenase lactate (LDH).

## 5. Conclusions

Based on the agglomeration analysis performed it was found that drugs from different pharmacological groups different chemical structure, they may exhibit similar hepatotoxic effect. The conducted research and simulations show that Drug-induced liver damage is defined by a number of features molecular in the structure of the tested drugs. So you should presumably with the help of computer programming and machine learning algorithms, it will be possible prediction of specific toxicological effects, incl hepatotoxic effect.