resulted in a significant decrease by 37% (Pst <0,05) in apoptotic index, and 10 days after the end of HT the figure was by 55% (Pst <0,05) lower than in control group. Conclusions. The effect of intermittent hypoxia to pancreatic endocrinocytes characterized by an increase in the number of beta-endocrinocytes that has less to do with the stimulation of proliferation, as caused by inhibition of apoptotic mechanisms.

## INLUENCE OF EXPERIMENTAL DIABETES MELLITUS AND PENTOXIFILLINE ADMINISTRATION ON THE RIG-LIKE RECEPTORS EXPRESSION IN LYMPHOID STRUCTURES OF ILEUM IN RATS

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The intestine is the largest interface between the body and the external environment. Mucosal surfaces provide portals of entry into the body not only for substances that are essential to survival, but also for many pathogens, including viruses. To protect themselves, hosts have developed many antiviral immune mechanisms to combat these attacks. We study type1 diabetes (T1D) as examples in which interactions between host and viral infections have been implicated in autoimmune diseases.The RIG-I-like receptors (RLRs) RIG-I, MDA5, and LGP2 play a major role in pathogen sensingof RNA virus infection to initiate and modulate antiviral immunity. The RLRs detect viral RNAligands or processed self RNA in the cytoplasm to triggers innate immunity and inflammation andto impart gene expression that serves to control infection. Many pathogens have been investigated, recent studies of T1D risk have focused on gastrointestinal enteroviruses,such as coxsackievirus B.Many pathogenic mechanisms are possible. In one scenario, infection of a β-cell by an enterovirus is followedby β-cell destruction — as a result of the virus itself, immune responses that kill virus-infected cells, or the 'autoimmune' sequel of such an infection. One of the most possible scenario - activated MDA5 activates the transcription factors IFN-regulatory factor3 (IRF3) and nuclear factor-κB (NF-κB), which can lead mainly to the production of pro-inflammatory cytokines and chemokines (TNFa, IL-1b, IL-18, IL-12, IL6, CXCL8), nitric oxide, co-stimulatory (CD40, CD80 и CD86) and adhesion molecules. All these factors are crucial for the recruitment and activation of effector cells and inflammatory process.Pro-inflammatory cytokines, such as TNFα play one of the most important roles in pathogenesis of T1DM. Indirect inhibitors of their production (for example, pentoxifylline, PTX) reduce risk of development of this pathology. The aim of research:To study the peculiarities of RIG-Ireceptors expression in gut-associated lymphoid tissues (GULT) of rats with experimental STZ-induced diabetes mellitus (EDM) and pentoxifilline (PTX) administration. Methods:Structure of population of RIG $^+$-cells has been studied by the analysis of serial histological sections using the method of indirect immunofluorescense with monoclonal antibodies to RIG-I of rat. Results: It has been established that diabetes development was accompanied by an increase in total density RIG$^+$-cells in the lymphoid structures of ileum by 45-50 % ($p < 0.05$) at 2$^{nd}$ week, which was reflected in the increase in population density of RIG$^+$-macrophages in 2.5 times, and also significantly increase the concentration of the RIG-protein in these cells. But this data showed a dynamics to decrease to control values by the 4th week of disease. PTX administration of diabetic animals resulted in a decrease of the total density RIG$^+$-cells by 25-30% ($p < 0.05$) at 2$^{nd}$ week of pathology, and on the 4th week of the disease this data showed dynamics to an increase.This is reflected in the reduction of population density RIG$^+$-dendritic cells by 25-90 % ($p < 0.05$) and RIG$^+$-lymphocytes by 32-37 % ( $p<0.05$) on the 14th day of pathology , and 28th day - an increase of population density RIG$^+$-macrophages 45-95 % ($p < 0.05$ ) and a decrease of this index in RIG$^+$-lymphocytes by 35-40% ( $p < 0.05$) Conclusions:The expression augmentation with RIG-Iin ileum immunopositive cells can influence the differentiation of subsets of immunopositive cells and their pro-inflammatory cytokines production, thus acting as one of triggers of diabetes development and progression.

## INTERACTIONS OF MELATONIN WITH THE LIVER MICROSOMAL CYTOCHROME P450 SYSTEM

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Melatonin, an endogenous hormone, is used as an antioxidant drug in doses quite higher than the endogenous circulating levels of this hormone. Hepatic endoplasmic reticulum contains the cytochrome P450 (CYP) system, which catalyzes one biotransformation pathway of melatonin; this organelle is also one of the main sources of reactive oxygen species in cells. The antioxidant activity of this hormone may have a biological relevance in the organelle where it is biotransformed. The aim was to conduct a literature review, which confirms the relationship of melatonin and liver detoxification system. Melatonin is critical for the regulation of circadian and seasonal changes in various aspects of physiology and neuroendocrine function. As age advances, the nocturnal production of melatonin decreases in animals of various species, including humans. There is evidence that melatonin in vitro directly scavenges OH, $H_2O_2$, singlet oxygen ($O_2^-$), and inhibits lipid peroxidation. Melatonin stimulates a number of antioxidative enzymes including SOD, glutathione peroxidase, glutathione reductase, and catalase. It has been shown that melatonin enhances intracellular glutathione levels by stimulating the rate-limiting enzyme in its synthesis, γ-glutamylcysteine synthase, which inhibits the peroxidative enzymes nitric oxide synthase and lipoxygenase. There is evidence that melatonin stabilizes microsomal membranes, thereby probably helping them resist oxidative damage. The CYP enzyme family plays a dominant role in the biotransformation of a vast number of structurally diverse drugs. Many drug interactions are a result of inhibition or induction of CYP enzymes. The expression of cytochrome P450 gene family members is regulated by the biological clock. In addition, hepatic P450 monooxygenases metabolize melatonin, the pineal hormone whose expression is controlled by the biological clock and, in turn, resets the biological clock. In vitro melatonin binds to human and rat liver microsomal cytochrome P-450 (P450) according to a type II substrate. The affinity is similar to that of aniline with a general left-shift.