

Сборник научных трудов Павлодар, Республика Казахстан В научный сборник вошли научные работы, посвященные широкому кругу современных проблем науки и образования, вопросов образовательных технологий

## ИННОВАЦИОННОЕ РАЗВИТИЕ НАУКИ И ОБРАЗОВАНИЯ 2022

Главный редактор

Роза Муслимовна Жамиева

#### Редакционная коллегия

## 1. Абильдина Салтанат Куатовна

Заведующая кафедрой педагогики и методики начального обучения, доктор педагогических наук, профессор ККСОН

## 2. Ильясова Гульжазира Актуреевна

Заведующая кафедрой гражданского и трудового права, кандидат юридических наук, Профессор (Full Professor)

## 3. Досова Бибигуль Арал бае вна

доцент кафедры всемирной истории и международных отношений, кандидат исторических наук

## Д.Сабыржан Али Сабыржанович

доцент кафедры аудита, кандидат экономических наук, ассоциированный профессор.

## 5. Тлеужанова Гульназ Кошкимбаевна

декан факультета иностранных языков, Кандидат педагогических наук Ассоциированный профессор

## 6. Сейтжанов Олжас Темирбекович

зам начальника КА МВД РК им. Б. Бейсенова, к.ю.н, доцент полковник полиции

## 7. Аренова Лейла Климентьевна

к.ю.н. доцент кафедры уголовного права, процесса и криминалистики

Издательство не несет ответственности за материалы, опубликованные в сборнике. Все материалы поданы в авторской редакции и отображают персональную позицию участника конференци

Контактная информация организационного комитета конференции: Официальный сайт: conferences.kz

https://doi.org/10.5281/zenodo.7353873

### **OCTOBER 2022**

Павлодар, Казахстан 2022

# Experimental substantiation of the use of hypoxia-inducible factor (HIF-1 $\alpha$ ) for the development of toxic hepatitis.

Kurbonova Z.Ch., Sayfutdinova Z.A., Muhammadiev X.G., Xashimova G.T.

**Annotation.** This article provides an experimental justification for the use of hypoxia-inducible factor (HIF-1 $\alpha$ ) on the development and course of toxic hepatitis based on heliothrin intoxication. Acute heliothrin intoxication was reproduced by a single subcutaneous injection of a sublethal dose of heliothrin, prepared at the rate of 40 mg per 100 g of body weight, to rats. During the reproduction of experimental toxic hepatitis by the administration of heliothrin, it was found that the content of HIF-1 was on average equal to  $0.101667\pm0.0022$  ng/l. In blood plasma, mean HIF-1 levels were  $0.2136\pm0.0066$  ng/l.

**Key words**: hypoxia-inducible factor; heliotrin intoxication; experimental toxic hepatitis; aryl hydrocarbon receptor transolator.

**Relevance.** Hypoxia-inducible factor (HIF)-1 is a dimeric protein complex that plays an important role in the body's response to low oxygen concentrations or hypoxia [3, 6]. HIF-1 is one of the main genes involved in the homeostatic process, which can increase vascularization in hypoxic areas such as localized ischemia and tumors [1, 4]. It is a transcription factor for dozens of target genes; HIF-1 is also important for immunological responses and is an important physiological regulator of homeostasis, vascularization, and anaerobic metabolism [2, 5, 7]. However, the pathophysiological mechanisms of the influence of HIF-1 $\alpha$  on the development of toxic hepatitis have not yet been disclosed, which was the relevance of this study.

**Purpose of the study.** To determine the significance of the hypoxia-inducible factor (HIF- $1\alpha$ ) on the development and course of experimental toxic hepatitis.

**Materials and research methods.** To achieve this goal, a model of toxic hepatitis was reproduced using the example of heliotrin intoxication.

Acute heliothrin intoxication was reproduced by a single subcutaneous injection of a sublethal dose of heliothrin, prepared at the rate of 40 mg per 100 g of body weight, to rats. Toxic hepatitis was reproduced by subcutaneous administration of heliothrin

(25 mg/100 g). The material for the study is venous blood. The content of HIF-1 in the blood was determined by enzyme immunoassay. Animals were divided into equal groups:

Group I - before reproduction of heliotrin intoxication (intact)

Group II (control) - with heliotrin intoxication,

Group III (control, comparisons) - with heliotrin intoxication after the introduction of the reference drug "Infezol 40", within 5 days 24 hours after the last injection; Group IV (main, experimental) - animals with heliotrin intoxication after the introduction of a new amino acid blood substitute, within 5 days, 24 hours after the last injection. Statistical processing was carried out using the Student-Fisher test, the nonparametric Mann-Winney test, the Kraskes-Wallis test

Research results. During the reproduction of experimental toxic hepatitis by the administration of heliothrin, it was found that the content of HIF-1 was on average equal to  $0.101667\pm0.0022$  ng/l. In blood plasma, mean HIF-1 levels were  $0.2136\pm0.0066$  ng/l. Such indicators are explained by the effect of heliothrin on the liver and, above all, on hepatocytes, in which mitochondria are deficient in oxygen. Thus, HIF-1 acts as an early biomarker of tissue oxygen deprivation, and since it induces angiogenesis, upregulation of this gene in experimental animals with ischemia may promote vascular proliferation required for oxygenation. On the contrary, since HIF-1 promotes the survival and proliferation of cancer cells due to its angiogenic properties, inhibition could potentially prevent the spread of cancer. With the growing understanding of the HIF-1 pathway, inhibition and stimulation of its transcriptional activity by small molecules is currently an attractive target.

As is known, the HIF-1 $\alpha$  subunit also contains two transactivation domains (TADs) that regulate HIF-1 target genes. CREB-binding protein (CBP) and p300, two HIF-1 transcription coactivators, interact with the carboxy-terminal transactivation domain (C-TAD) of HIF-1 $\alpha$ .

Both activators are required for HIF-1 transcription and therefore are targets for the regulation of HIF-1 expression; inhibition of HIF-1 $\alpha$  C-TAD interactions by proline hydroxylation suppresses HIF-1 gene expression, preventing normal transcription

and translation. HIF-1 $\beta$  contains only one such analogous region, which is not needed for the complex function of HIF-1. Recent reports indicate that HIF-1 $\beta$  is identical to a previously discovered vertebrate protein, the aryl hydrocarbon receptor nuclear translocator (ARNT).

HIF-1 is the main regulator of oxygen homeostasis in cells. As a transcription factor, it influences and regulates the expression of dozens of genes involved in maintaining homeostasis when oxygen concentration changes. One important function of HIF-1 is to promote angiogenesis; HIF-1 directs the migration of mature endothelial cells into a hypoxic environment. This is done through HIF-1 regulation of vascular endothelial growth factor (VEGF) transcription. VEGF is the main regulator of angiogenesis, which promotes the migration of endothelial cells towards the hypoxic region. During hypoxia, HIF-1 binds the regulatory region of the VEGF gene, inducing its transcription and initiating its expression. These endothelial cells eventually help form new blood vessels, supplying the area with oxygenated blood. **Conclusions.** Summarizing the above, hypoxia-inducible factor 1 (HIF- $1\alpha$ ) is an important pathogenetic link in the development of oxygen deficiency, and its deficiency at an early stage can serve as an important diagnostic biomarker of toxic hepatitis, including that caused by heliothrin, since it belongs to pyrolizidine compounds by chemical composition. alkaloids, and as you know, its precursor is cadeverdin, which is oxidized to gamma-aminobutyric aldehyde with the formation of non-innic alcohols with monobasic non-cinic acids.

## **Bibliography:**

- 1. Chen EY, Fujinaga M, Giaccia AJ. Hypoxic microenvironment within an embryo induces apoptosis and is essential for proper morphological development. Teratology. 1999; 60:215–225.
- 2. Cramer T, Yamanishi Y, Clausen BE, et al. HIF- $1\alpha$  is essential for myeloid cell-mediated inflammation. Cell. 2003; 112:645–657.
- 3. Date T, Mochizuki S, Belanger AJ, et al. Expression of constitutively stable hybrid hypoxia-inducible factor-1α protects cultured rat cardiomyocytes against simulated ischemia-reperfusion injury. Am J Physiol. 2005;288:C314–C320.
- 4. Fox SB, Braganca J, Turley H, et al. CITED4 inhibits hypoxia-activated transcription in Cancer Cells, and its cytoplasmic location in breast cancer is associated with elevated expression of tumor cell hypoxia-inducible factor 1α Cancer Res. 2004;64:6075–6081.
- 5. Genbacev O, Zhou Y, Ludlow JW, Fisher SJ. Regulation of human placental development by oxygen tension. Science. 1997; 277:1669–1672.

- 6. Hewitson KS, Schofield CJ. The HIF pathway as a therapeutic target. Drug Discov Today. 2004; 9:704–711.
- 7. Ho TK, Rajkumar V, Ponticos M, et al. Increased endogenous angiogenic response and hypoxia-inducible factor-1α in human critical limb ischemia. J Vasc Surg. 2006; 43:125–133.

# **CONTENTS**

		ΝТ.	O.	TB. /	T 7
14.4	''			<b>N</b> /	
1,1		-		I W I	

Gulixon Karimova - Organizational and legal form of entrepreneurship
GEOGRAPY Tillyakhojaeva Z. D Nosogeographic situation. Increase in the number of weather-sensitive diseases in the face of climate change
MEDICINE  Хакимов М.Ш., Асатуллаев Ж.Р., Элмуратов И.У., Жуманазаров А.У., Матризаев Т.Ж., Каримов Р.А., Муродов А.М Роль лапароскопии в выборе лечебной тактики при острой хирургической патологии органов брюшной полости
<b>Kurbonova Z.Ch., Sayfutdinova Z.A., Muhammadiev X.G., Xashimova G.T</b> Experimental substantiation of the use of hypoxia-inducible factor (HIF-1α) for the development of toxic hepatitis
PEDAGOGYSayfullayeva Nozima Baxodirovna - Maktab matematika darslarida masala- misollaryechish orqali o`quvchilarga turli kasblarga oid ma'lumotlarni singdirish
Эрназаров Алишер Эргашевич - Дарс машғулотларида мақсад ва вазифаларни аниқлашнинг ўзига хос хусусиятлари
РНІLOSOPHY Раббимова Феруза Шамсиддиновна - Воспитательное значение учения футувват в современном обществе
PSYCHOLOGY Alyona G. Ayrapetova The tendency to deviant behavior as a factor contributing to the formation of destructive religiosity
<b>TECHNOLOGY Ф.А. Абдушукуров</b> - Распознавание на основе изображения лиц