

1 Abstract

2 **MiR-378a-3p as a Potential Marker of Xenon Abuse Detection**
3 **in Blood Plasma during Doping Control[†]**4 Irina Pronina ^{1,2,*}, Elena Mochalova ² and Pavel Postnikov ²5 ¹ Institute of General Pathology and Pathophysiology, Moscow, Russia; zolly_sten@mail.ru (I.P.)6 ² National Antidoping Laboratory, Moscow State University, Moscow, Russia; mochalova@dopingtest.ru
7 (E.M.); postnikov@dopingtest.ru (P.P.)8 * Correspondence: zolly_sten@mail.ru; Tel.: +7-985-766-83-819 [†] Presented at the 9th International Electronic Conference on Medicinal Chemistry, 1-30 November 2023.

10 **Abstract:** The inert gas xenon (Xe) is used in medicine as a safe and high-quality anesthetic during
11 complex surgical interventions, as well as an antipsychotic agent. Sports medicine publications have
12 described the properties of xenon in the recovery processes after prolonged physical training when
13 used in xenon/oxygen (Xe/O₂) inhalations. Since 2014, xenon is in the World Anti-Doping Agency
14 Prohibited List, in accordance with article S2 “Peptide hormones, growth factors, similar substances
15 and mimetics” 1.2 “Hypoxia-inducible factor (HIF) activators”. MicroRNAs involved in the regula-
16 tion of the HIF-signaling can be the markers to indirect determination of the abuse of HIF-activators.
17 The aim of our work was to identify potential marker microRNAs, the alteration in expression of
18 which could reveal the abuse of Xe in cases where the direct determination of this substance be-
19 comes practically impossible, for example, after the expiration of Xe excretion from the body. Clin-
20 ical blood test were carried out on analyser SysmexXN-1000 (Germany). Isolation of miRNAs from
21 blood plasma samples was performed using the PAXgene Blood miRNA Kit (Qiagen, USA). RT-
22 qPCR was performed using miRCURY LNA SYBR Green PCR Kits and panels for studying the
23 expression profiles of mature microRNAs of miRCURY LNA miRNA Focus PCR Panel (Qiagen,
24 USA). Reference genes are included in the used panel. Statistical processing of the results was car-
25 ried out using Bio-Rad CFX Maestro 3.0 software (USA). After five daily Xe/O₂ (25:75 v/v) inhal-
26 ations for 30 minutes, the activation of erythropoiesis, including an increase in the number of eryth-
27 rocytes, an increase in hemoglobin concentration, etc., was determined. Simultaneously, the altera-
tions in the expression profile of microRNAs circulating in blood plasma were observed. We found
that the expression of hsa-miR-378a-3p in the blood plasma of volunteers after Xe/O₂ inhalation
increases approximately 70 times (p<0.05) and is not detrmined at all in some volunteers before the
inhalations. Thus, hsa-miR-378a-3p can be recomended as a potential candidate for the role of a
marker of abuse of Xe in doping control.

Citation: Pronina, I.; Mochalova, E. 28

Postnikov, P. Title. *Med. Sci. Forum* 29
2023, 2, x. 30<https://doi.org/10.3390/xxxxx> 31Academic Editor: Firstname Last- 32
name

Published: date 33

34
Publisher’s Note: MDPI stays neu-
tral with regard to jurisdictional
claims in published maps and insti-
tutional affiliations. 3536
Copyright: © 2023 by the author, 37
Submitted for possible open access 38
publication under the terms and 39
conditions of the Creative Common 40
Attribution (CC BY) licens 41
(<https://creativecommons.org/licenses/by/4.0/>).**Keywords:** hypoxia; xenon; microRNA; doping control.36 **Supplementary Materials:** Pronina_poster**Author Contributions:** Conceptualization, methodology, I.P. and P.P.; software, I.P.; formal analy-
sis, E.M.; investigation, I.P.; resources, E.M.; data curation, P.P.; writing—original draft preparation,
I.P.; writing—review and editing, I.P.; visualization, I.P.; supervision, P.P.; project administration,
E.M.; funding acquisition, E.M. All authors have read and agreed to the published version of the
manuscript.

1 **Funding:** This research received no external funding.

2 **Institutional Review Board Statement:** All subjects gave their informed consent for inclusion before
3 they participated in the study. The study was conducted in accordance with the Declaration of Hel-
4 sinki, and the permission for medical xenon (Xemed®) for clinical trials was approved by the Ethics
5 Committee of the Ministry of Health of the Russian Federation (Ext. No. 55292 dated August 27,
6 2019, extract from protocol No. 197).

7 **Informed Consent Statement:** Informed consent was obtained from all subjects involved in the
8 study.

9 **Data Availability Statement:** Data available on reasonable request from the corresponding author.

10 **Conflicts of Interest:** The authors declare no conflict of interest.

11