DOI:

UTICAJ ŽIVOTNE SREDINE NA ZDRAVLJE – MOLEKULARNI MEHANIZMI I BOLESTI

THE INFLUENCE OF THE ENVIRONMENT ON HEALTH - MOLECULAR MECHANISMS AND DISEASES

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SAŽETAK

U poslednjih nekoliko godina problem zagađene životne sredine na ljudsko zdravlje postaje sve važniji i privlači veliko interesovanje. Naročito kada znamo da produkcija plastike neprekidno raste, trenutno 350 miliona tona po godini1. Preko 40% plastike se koristi kao pakovanje za jednokratnu upotrebu, uključujući flašice za bebe, posude za hranu i medicinske aplikacije. Stoga nije iznenađujuće što su mikro i nano plastične čestice otkrivene u kiši, vazduhu, zemljištu, snegu, soli, vodi iz česme/flaširanoj vodi, pivu, čaju, hrani kao i ljudskom mleku, placenti, folikularnoj tečnosti, krvi, mozgu1. Na žalost, uticaj plastike na ljudsko zdravlje nije u potpunosti objašnjen.

Zato smo, pored modela životinje2, upotrebili ljudske fibroblaste i indukovane pluripotentne matične ćelije (hiPSC), moderne technologije molekularne biologije uključujući RNK-sekvenciranje, DNK-metilaciju i bioinformatiku kao jedinstveni naučni alat za definisanje veze između zagađenja životne sredine i unutarćelijskog mehanizama bolesti, njegovog ishoda na rani embriološki razvoj čoveka3,4 i poreklo bolesti. I fibroblasti i hiPSC tretirani česticama nanoplastike pokazali su promene u ekspresiji ESRRB i HNF1alfa gena i genetskih mehanizama uključenih u pluripotenciju matičnih ćelija, kao i na puteve uključene u rak, inflamatorne poremećaje, glukoneogenezu, metabolizam ugljenih hidrata, urođeni imunitet i dopaminergični imunitet. Slično tome, nivoi ekspresije identifikovanih ključnih promena transkripcije i metilacije DNK (DNMT3A, ESSRB, FAM133CP, HNF1A, SEPTIN7P8 i TTC34) su značajno promenjeni i kod fibroblasta i hiPSC4 izloženi plastičnim česticama.

Ovi rezultati ilustruju moć ljudskih ćelijskih kao modela zagađenja životne sredine i omogućavaju suženje liste kandidata molekularnih biomarkera5. Na taj način, promene u naslednom materijalu mogu se u laboratoriji provocirati ili korigovati, kako bi se uzroci bolesti bolje razumeli i na vreme prepoznali6. Ovo znanje će olakšati dešifrovanje porekla ekoloških bolesti i poslužiće kao hitan apel naučnoj i političkoj zajednici da ulože više vremena i resursa za uspostavljanje pouzdanih standarda i metoda za definisanje i rešavanje posledica zagađenja plastikom po ljudsko zdravlje.

ABSTRACT

In recent years, the issue of environmental pollution and its impact on human health has become increasingly important and is attracting significant attention. This is particularly evident when we consider that plastic production is continuously rising, currently reaching 350 million tons per year. Over 40% of plastic is used as single-use packaging, including baby bottles, food containers, and medical applications. Therefore, it is not surprising that micro and nano plastic particles have been detected in rain, air, soil, snow, salt, tap water/bottled water, beer, tea, food, as well as in human milk, placenta, follicular fluid, blood, and brain. Unfortunately, the impact of plastic on human health is not fully understood.

Thus, alongside animal models, we utilized human fibroblasts and induced pluripotent stem cells (hiPSC), employing modern molecular biology technologies including RNA sequencing, DNA methylation, and bioinformatics as a unique scientific tool to define the relationship between environmental pollution and intracellular disease mechanisms, its outcomes on early embryological development in humans, and the origins of diseases. Both fibroblasts and hiPSCs treated with nano plastic particles exhibited changes in the expression of the ESRRB and HNF1alpha genes and genetic mechanisms involved in the pluripotency of stem cells, as well as pathways associated with cancer, inflammatory disorders, gluconeogenesis, carbohydrate metabolism, innate immunity, and dopaminergic immunity. Similarly, the expression levels of identified key transcriptional and DNA methylation changes (DNMT3A, ESSRB, FAM133CP, HNF1A, SEPTIN7P8, and TTC34) were significantly altered in both fibroblasts and hiPSCs exposed to plastic particles.

These results illustrate the power of human cellular models in studying environmental pollution and enable the refinement of the list of candidate molecular biomarkers. In this way, changes in genetic material can be provoked or corrected in the laboratory to better understand and timely recognize the causes of diseases. This knowledge will facilitate the deciphering of the origins of ecological diseases and serve as an urgent appeal to the scientific and political communities to invest more time and resources in establishing reliable standards and methods for defining and addressing the consequences of plastic pollution on human health.