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Effect of single-walled carbon nanotubes on the expression of proliferation and apoptosis related genes in normal human astrocytes

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One of the most perspective directions in biomedicine during the past decades is the application of nanoparticles, including single-walled carbon nanotubes (SWCNTs) due to their unique and versatile properties. SWCNTs are considered as a new effective option for drug delivery, gene therapy, and bioengineering. However, increasing worries near their chronic toxicity results in the need to study the effects of SWCNTs on the genome functional stability.

Aim. The goal of our study was to evaluate the effect of low quantities of SWCNTs on the expression of *DNAJB9* (DnaJ heat shock protein family (Hsp40), member B9), *IGFBP3* (Insulin-like growth factor binding protein 3), *IGFBP6*, *ZNF395* (Zinc finger protein 39), *HILPDA* (hypoxia inducible lipid droplet associated), as well as corresponding microRNAs, which have relation to the control of studied mRNAs: miR-27-3p, miR-19a-5p, miR-145-5p, miR-7-5p, miR-150-5p, in normal human astrocytes.

Materials and Methods. The immortalized normal human astrocytes (NHA/TS cell line) were treated 24 hours by SWCNTs (2 and 8 ng/ml of medium). The expression level of *DNAJB9, IGFBP3, IGFBP6, ZNF395*,

and *HILPDA* genes as well as microRNA miR -27-3p, miR-19a-5p, miR-145-5p, miR-7-5p, miR-150-5p in normal human astrocytes by quantitative polymerase chain reaction was studied.

Results. It was detected the substantial up-regulation of the expression level of genes encoding the endoplasmic reticulum stress responsible proteins *DNAJB9* and *IGFBP3* in normal human astrocytes treated by SWCNTs (both 2 and 8 ng/ml of medium). Moreover, a significantly stronger effect (+102 and +160%, correspondingly for 2 and 8 ng/ml of SWCNTs) compared to the control cells was observed for the *DNAJB9* gene. We have also shown that the exposure of normal human astrocytes to SWCNTs (2 and 8 ng/ml of medium) led to down-regulation of the expression level of transcription factor *ZNF395* (-44 and −45%, correspondingly). Besides, dose-dependent down-regulation of the expression was detected for *IGFBP6* and *HILPDA* genes. We have also studied the effect of SWCNTs on the level of corresponding microRNA expressions. It was shown that the expression level of almost all studied microRNAs was up-regulated by SWCNTs. The exception was the expression level of miR-19a-5p (-30 %), which related to the control of IGFBP3 mRNA.

Conclusions. The results demonstrate that single-walled carbon nanotubes significantly affect the expression of studied genes in a dose-dependent and gene specific manner possibly through endoplasmic reticulum stress introduced by these nanoparticles through transcriptional and post-transcriptional mechanisms and lead to dysregulation of functional integrity of the genome. These results confirm the requirement of more cautions in biomedical applications of nanoparticles, including carbon nanotubes.