

Non-thermal atmospheric pressure plasma as an efficient tool to activate the proliferation of human mesoderm-derived stem cells through epigenetic modifications

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Non-thermal atmospheric pressure plasma (NTAPP) is a partially ionized gas containing charged particles and radicals at atmospheric pressure [1]. Many researches have recently reported the beneficial effects of NTAPP including wound healing [2, 3], the activation of immune response [4, 5] and the regeneration of tissues [6, 7]. Here, our study showed that NTAPP activates the proliferation of various mesoderm-derived adult stem cells including adipose tissue-derived stem cells (ASCs), bone marrow-derived stem cells (BM-MSCs) and hematopoietic stem cells (HSCs) by 1.5 to 2-fold, when we exposed cells to NTAPP generated in a helium-based dielectric barrier discharge (DBD) device for 50 s each time every h for total of 10 times, compared with unexposed cells. NTAPP exposure highly augmented the expression of well-known pluripotent genes of stemness such as Oct4, Sox2 and Nanog in ASCs and BM-MSCs compared to that in unexposed control cells, suggesting that NTAPP activated the proliferation of various adult stem cells while maintaining the stem cell properties. To understand the molecular mechanism of these physiological effects of NTAPP, we examined the whole genome expression profiles of ASCs whose proliferation is highly activated by NTAPP using the whole RNA sequencing (RNA-seq) analysis. NTAPP upregulated the expression of genes for cytokines and growth factors, and downregulated the genes in apoptotic pathways. When ASCs were treated with NTAPP in the presence of a nitric oxide (NO) scavenger, the expression of various cytokines and growth factors decreased, demonstrating that NO is the main factor for the enhanced cytokine and growth factor expression induced by NTAPP. In addition, increased histone deacetyl transferase 1 (HDAC1) and decreased acetylated histone 3 were detected in NTAPP-exposed ASCs. Consistently, ASCs pre-treated with inhibitors for HDAC, DNA methylation or histone methylation decreased the expression of cytokines and growth factors after NTAPP exposure. Collectively, these results demonstrate that NTAPP activates the expression of cytokines and growth factors through epigenetic modifications to activate the proliferation. Our results strongly suggest how NTAPP acts as an efficient tool for tissue regeneration and wound healing.

References

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