

# Biocompatibility and Radioprotective Activity of Squid Ink-Derived Nanomelanin on Human Umbilical Cord-Derived Mesenchymal Stem Cells

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Squid ink-derived nanomelanin has recently demonstrated the radiation protective capacity on the spleen of gamma ray-irradiated mice and X-ray irradiated keratinocyte HaCaT. In this study, we aimed to evaluate the protective activity of this nanoparticle on human umbilical cord-derived mesenchymal stem cells (UCMSCs), the key players in the recovery of damaged tissue after exposure to irradiation. The results showed that nanomelanin had a high biocompatibility with low cytotoxicity, an IC<sub>50</sub> of 74,1±2,4 ug/mL, no cell senescence induction, and no effect on cell differentiation. Besides, nanomelanin nanoparticles showed a minimum effect on the migration of UCMSCs. Additionally, the expressions of functional genes involved in angiogenesis, apoptosis, antioxidant, and radiation sensitivity were not affected by nanomelanin in this cell type. X-ray radiation reduced the cell viability at the dose of 7 Gy and altered the functional gene expression in UCMSCs at 5 Gy. Interestingly, nanomelanin significantly rescued the cell viability and recovered the gene expression of UCMSCs from such irradiation. Furthermore, in vivo treatments on zebrafish embryos showed that nanomelanin was non-toxic with LC<sub>50</sub> and EC<sub>50</sub> values were 205.3 and 204.1 ug/mL. These findings suggested nanomized squid ink melanin as a radiation-protective agent on stromal cells. Keywords: Melanin, nanomelanin, radioactive protection, mesenchymal stem cells, angiogenesis