Piezoelectric cellular stimulation: An innovative approach for brain cancer therapy

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The generation of small electric charges upon the application of mechanical stimuli to piezoelectric nanomaterials is a unique phenomenon in the context of remote stimulation of cells and tissues. Electrical cues are known to foster specific biological responses, and piezoelectric nanomaterials own the ability to act as real "nanotransducers", thus allowing obtaining "wireless" and remote electric stimulation thanks to non-invasive excitation through mechanical sources [1].
Cancer cells are known to be sensitive to electric stimuli, and in the past years we demonstrated as piezoelectric nanoparticles activated by ultrasounds (US) can be exploited for the non-invasive and remote delivery of electric cues, enabling cell cycle arrest and apoptosis [2-3].
More recently, we proposed the exploitation of nutlin-loaded poly(vinylidene fluoride-co-trifluoroethylene) -P(VDF-TrFE)- nanoparticles stimulated with US for the treatment of glioma cells (Figure 1) [4]. Moreover, we showed that the angiogenic behavior of human cerebral microvascular endothelial cells can be inhibited by using the same approach. The anti-angiogenic effect, derived from the use of chemotherapy and chronic piezoelectric stimulation, leads to disruption of tubular vessel formation, decreased cell migration and invasion, and inhibition of angiogenic growth factors in the presence of migratory cues released by the tumor cells [5].
In a further work, we focused our attention on glioma-associated microglia (GAM), representing the largest population of "supporting" cells of the tumor microenvironment, which express the anti-inflammatory M2 phenotype, thus promoting an immunosuppressing environment that helps tumor growth. We proposed a targeted anti-glioma immunotherapy, based on pro-inflammatory modulation of the GAM phenotype through controlled and localized electrical impulses mediated by US-stimulated piezoelectric nanoparticles [6].
Concluding, the combination of chemotherapy drug delivery with chronic piezoelectric stimulation resulted in activation of cell apoptosis and anti-proliferation pathways, induction of cell necrosis, inhibition of cancer migration, reduction of cell invasiveness in drug-resistant glioblastoma multiforme cells, and even immune actions. Obtained results pave the way for the use of innovative multifunctional nanomaterials in less invasive and more focused anticancer treatments, able to reduce drug resistance in glioblastoma and trigger microglia activity against cancer cells.

References

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