Clin Exp Pharmacol 2016, 6:4(Suppl)
http://dx.doi.org/10.4172/2161-1459.C1.014

Simulation study of the mechanism of uptake of cell pentrating peptides in cancer cells

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It is somehow easy to understand why it is still so controversial the mechanisms of cellular uptake of cell-penetrating peptides. Although there is evidence that these peptides are capable of directly crossing the plasma membrane without any intermediate step, still several researchers claim that endocytosis is an intermediate step required for entry into the cells. It is well known that ionic interactions play a critical role for the binding to the plasma membrane and translocation of CPPs. A simulation of the interaction between (RG)5 and (HE)5, as well as with DOPC of the lipid bilayer was conducted in order to calculate the free binding energy. The results supported the data obtained in the *in vitro* release, cell uptake and cytotoxicity studies. The absolute value of binding energy of (RG)5 with (HE)5 was the highest, however a decrease in the pH was found to diminish this strong bond. Interestingly, the conjugation of (RG)5 to PEG-PLA copolymer increased the binding energy to DOPC. In summary, the peptides tend to interact with the cell membrane which facilitates the uptake in an energy and receptor independent manner as postulated by many researchers.

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Expression and polymorphism of MT_1 receptor in patients with gastric adenocarcinoma and its relationship with clinicopathological features

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Gastric cancer accounts 8% of the total cancer cases and 10% of total cancer deaths worldwide. The indoleamine N-acetyl-5-methoxytryptamine, better known as Melatonin, is the principal hormone produced by the pineal gland. Recently, it has been shown for some anti-cancer role for Melatonin in some malignancies as breast and colon cancer; also some protective role for Melatonin in the GI tract has been known for free radical scavenging, anti-mitogenic and apoptotic properties. According to the anti-cancer effects of Melatonin and due to the wide distribution of this neurohormone in GI tract, some proposed physiologic and pharmacologic role for this neurohormone. Following our previous study, which has shown expression of MT_2 receptor in gastric adenocarcinoma, was initially studied to determine the expression of Melatonin receptor MT_1 in tissue samples of adenocarcinoma cancer patients. For this aim, a total of 10 gastric adenocarcinoma patients and 10 normal individuals were selected and examined for MT_1 gene expression by real-time PCR also for genotyping and screening of different alleles of MT_1 in our samples, and the SSCP-PCR procedures were developed. Our results showed interestingly high expression for MT_1 receptor in cancer and marginal cancer tissues comparing with normal people. Although, our experiments have shown many relations between MT_1 receptor expressions, grade and clinicopathological figures of tumour. SSCP-PCR results have shown a variation between individuals which might be effective on their expression gene patterns. This study concluded for the first time for the expression of MT_1 receptor in gastric adenocarcinoma tissues which was in agree with our previous study but with some difference in comparisons between the kind of tissue expression and difference in polymorphisms.

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