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Cromolyn chitosan nanoparticles modulate the DNA methylation of RASSF1A and p16 tumor suppressor genes and lessen DNMT1 and METTL3 expression in MCF-7 breast cancer cell line

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D ecently, the use of nanotechnology has boosted the prevention, diagnosis and treatment of breast cancer **K**(BC) through enhancing the effectiveness of chemotherapeutic drugs and decreasing its toxicity as they can target tumour cells with high specificity. However; developing epigenetic drugs with Nano formulation for BC remains a novel therapeutic approach. Commonly is a mast cell stabilizer emerging as an anticancer drug; its encapsulation in chitosan nanoparticles (CSNPs) improves its effect and bioavailability. Howbeit, its effect on DNA and RNA methylation machineries has not been previously investigated. The possible anticancer effect of commonly CSNPs and its potential as an epigenetic drug was investigated in vitro using MCF-7 human BC cell line. Cromolyn CSNPs showed prominent anticancer effect in MCF-7 cells by reducing the cell viability percent and enhancing DNA damage in the comet assay demonstrating its apoptotic actions. Mechanistically, cromolyn CSNPs influenced potential epigenetic processes through mitigating DNA methyltransferase 1 (DNMT1) expression, reversing the hyper methylation pattern of the tumour suppressor RASSF1A and p16 genes and attenuating the expression of the RNA N6-methyladenosine writer, methyltransferase-like 3 (METTL3). Cromolyn CSNPs diminished ERK1/2 phosphorylation, a possible arm influencing DNMT1 expression. In conclusion, cromolyn CSNPs have the potential as an epigenetic drug through inhibiting ERK1/2 phosphorylation/DNMT1/DNA methylation and possibly impacting the RNA methylation machinery via mitigating METTL3 expression.

Biography

Dr. Mahmoud Ahmed Senousy Hassan: Associate Professor and Head of Biochemistry Department, Egyptian Chinese University, Cairo, Egypt, and Associate Professor of Biochemistry, Faculty of Pharmacy, Cairo University, Cairo, Egypt. I Published 22 research articles in international journals with high impact factor in biochemistry, molecular biology, genetics and epigenetics in several diseases, including cancer, <u>neurodegenerative diseases</u>, autoimmune diseases and inflammatory bowel diseases. In 2022, my h-index has been raised to 11 (Scopus) and i10 index to 12. I Reviewed 49 manuscripts for several international journals and participated in 14 thesis supervision

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