UPCONVERTING NANOCOMPLEX DELIVERY TO DISTINCT PHENOTYPES OF CANCER BY MESENCHYMAL STEM CELLS

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Colorectal cancer is the third most common cancer diagnosed and the second leading cause of cancer-related deaths worldwide. It is often diagnosed at an advanced stage when treatment options are limited and usually non-specific [1]. Selective delivery of anticancer agents to the tumour is needed to avoid the side effects of cancer treatment. Mesenchymal stem cells (MSCs) can be used for this purpose. MSCs are found in specific niches in the body and can be isolated from a wide variety of tissues. The main sources of MSCs are bone marrow or adipose tissue, but much less is known about MSCs isolated from skin or menstrual blood, which is what our research focuses on. Nowadays, MSCs are being widely studied as a tool for the delivery of anticancer agents. Due to MSCs oncotropic properties it is hoped to use MSCs as a Trojan horse for the delivery of therapeutic nanoparticles directly to the tumour [2]. The dense extracellular matrix and high intracellular hypertension in tumours make diffusion and penetration of nanoparticles and other anticancer drugs inefficient. Therefore, MSCs can be employed as vehicles, so anticancer agents can be actively delivered to the interior of the tumour tissue. To fulfil the latter purpose, it is necessary to have a good understanding of MSCs ability to migrate towards the tumour, because the type of tumour and its microenvironment may affect the migration of MSCs.

The study aimed to investigate the migration of upconverting nanocomplexes (UCNP-Ce6) uploaded MSCs towards 3 different phenotypes of colorectal cancer cells.

To ensure that the UCNP-Ce6 complex is suitable for biological applications, we evaluated the accumulation and cytotoxicity of this complex in skin and menstrual blood MSCs, and colon cancer cell lines DLD-1, HCT116, LS1034. Results of confocal microscopy showed that UCNP-Ce6 accumulates inside cells and localizes in the perinuclear region. The cytotoxicity was assessed using the lactate dehydrogenase (LDH) cytotoxicity assay. Results showed that nanoparticles are biocompatible and have no dark toxicity after 24h. The efficiency of MSCs migration and the ability to transport nanoparticles was investigated using two sources of MSCs: skin and menstrual blood. The migration of MSCs was investigated using the Transwell migration assay in 2D and 3D environments. It was found that the migration efficiency of MSCs is different and depends on the phenotype of the colon cancer cells.

Overall, our results showed that active upconverting nanocomplex transportation using MSCs could increase the delivery of nanotherapeutics to cancer cells. The demonstrated potential of MSCs as nanoparticle carriers may lead to new opportunities for the development of targeted cancer therapy.

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