ANGIOGENIN-MIMICKING PLGA-PEG-RhB NANOPARTICLES FOR PROSTATE CANCER TREATMENT

R. Di Leo[1], L. Chiaverini[1], E. Barresi[1], C. Giacomelli[1], G. Ferraro[2], D. La Mendola[1] and T. Marzo[1]
[1]Department of Pharmacy, University of Pisa, Via Bonanno Pisano 6, Pisa, 56126, Italy, riccardo.dileo@farm.unipi.it; [2]Department of Chemical Sciences, University of Naples Federico II, Via Cinthia 21, Naples, I-80126, Italy

Nowadays, prostate cancer (PC) represents the most common cause of mortality due to cancer in males. The clinical features observed among patients with PC are conditioned by the stage at when the diagnosis is made. This highlights the importance of regular screening and accurate diagnosis. While early and localized PC is often associated with a favorable prognosis, late or metastatic PC is usually linked to markedly poorer five-year survival rates. The treatment of advanced prostate cancer typically involves a combination of hormone therapy, chemotherapy and radiation therapy [1]. In cases of advanced disease, chemotherapy may be combined with anti-androgen therapy, and surgical or chemical castration also may be employed to inhibit cancer cell growth. Despite the urgent need for efficacious treatments, there is a deficit of approved pharmaceutical agents for the treatment of prostate cancer. The restricted number of pharmaceutical agents that have been approved by the FDA for this indication include taxanes (docetaxel, paclitaxel and cabazitaxel) [2]. These agents have been demonstrated to confer a substantial benefit when combined with cisplatin analogues. Considering the urgent necessity for novel treatment strategies, the identification of biomarkers for PC assumed increasing significance. In this context, angiogenin (Ang) has emerged as a promising candidate. Indeed, Ang is a potent pro-angiogenic protein from the pancreas-like ribonuclease superfamily, which plays a pivotal role in the progression and invasion of PC. The expression of this protein is increased when prostate epithelial cells undergo a transition from a benign to an invasive state [3]. Based on these considerations, fluorescent biocompatible PLGA-PEG-RhB nanoparticles (NPs) loaded with docetaxel, a cisplatin derivative, or a combination of both were prepared. Moreover, a second set of PLGA-PEG NPs was developed incorporating Ang-mimicking peptides and loaded with the same pharmaceutical species to facilitate the targeted delivery of drugs to PC cells. This dual approach is designed to inhibit cancer cell angiogenesis and enhance drug delivery to the tumor site. The chemico-physical properties of the NPs were evaluated using dynamic light scattering (DLS) and transmission electron microscopy (TEM). The encapsulation efficiency (EE) of each drug was determined by HPLC, exhibiting an EE range of 8-19% at a drug concentration of around10^{-5} M. By competing with Ang for cell recognition sites, the functionalized NPs may reduce or prevent the uptake of plasma-circulating Ang into PC cells, thereby inhibiting angiogenesis. This stealth delivery system has the potential to enhance the uptake and therapeutic effects of the drugs, thereby rendering the drug combinations effective even in the presence of drug resistance. Furthermore, this system allows for the tracking of drugs and enhances the tolerability of chemotherapy, while simultaneously reducing the likelihood of off-target effects. The anti-cancer activity of these two sets of NPs will be evaluated on PC3 cells.

REFERENCES

[1] A. Ponholzer, F. Steinbacher, S. Madersbacher, and P. Schramek, "Current treatment of locally advanced and metastatic prostate cancer", Wien Med Wochenschr, vol. 161, no. 15-16, pp. 377-381, 2011.
[2] J. Ansari, S. A. Hussain, A. Zarkar, J. S. Tanguay, J. Bliss, and J. Glahom, "Docetaxel chemotherapy for metastatic hormone refractory prostate cancer as first-line palliative chemotherapy and subsequent re-treatment: Birmingham experience", Oncol Rep, vol. 20, no. 4, pp. 891-896, 2008.
[3] T. M. Katona, B. L. Neubauer, P. W. Iversen, S. Zhang, L. A. Baldridge, and L. Cheng, "Elevated expression of angiogenin in prostate cancer and its precursors", Clin Cancer Res, vol. 11, no. 23, pp. 8358-8363, 2005.

The Italian Ministry of University (MUR) is acknowledged for funding the project PRIN 2022- "Biocompatible nanostructures for the chemotherapy treatment of prostate cancer" (2022ALJRPL).