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Nanoscale drug carriers for breast cancer therapy – non-toxic to human macrophages

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Abstract: In our recent work we have explored the formation of chemotherapeutic delivery vehicles constructed from four different amphiphilic linear dendritic hybrid block-copolymers. These micelles were found to form ca. 100 nm sized structures that were capable of sequestering doxorubicin. After drug loading, these constructs could deliver an efficient dose of drugs, resulting in significant decreases in cell viability. Kinetic studies indicated that the drug formulation in the polymer micelles slowed down the cell uptake compared to the non-formulated drug, but similar efficacy in viability reduction and cell apoptosis were found.

Introduction

Cancer, especially breast cancer is one of the most common causes of death in the western world. As the average life expectancy of people is increasing steadily we know that more people are going to be diagnosed with cancer over next decades.

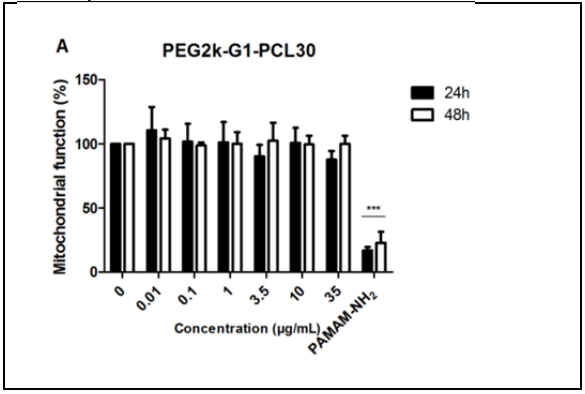
We as researchers therefore have strong interest in developing more efficient methods for treating cancer. Many cases and forms of cancer are treated with a combination of surgery and chemotherapeutics. Some chemotherapeutics are known to cause severe side effects for the patients and there is an urgent need to find new ways of administrating chemotherapeutics to reduce side-effects and achieve better treatment results for the patient.

Nanomedicine is the medical application of nanotechnology. With nanomedicines one can create systems for administrating drugs in a better way, increasing the therapeutic effect and limiting side-effects. This is done by protecting the drug inside a nanosized container that can carry it to the cancer tumor.[1]

In this work we have created nanocarriers for the most common chemotherapeutic drug, doxorubicin, and have shown that these carriers can increase the efficiency of killing breast cancer cells. The carriers are based on biodegradable, and non-toxic polymers (plastics) that are put together to nanocontainers by self-assembly.

We show that these carriers do not cause adverse effects on human macrophages (Fig 1) which are thought to be very important for the safe use of nanomedicines in cancer treatment. Macrophages are our body's trash collectors of foreign substances, such as nanoparticles, and are therefore an important part of our immune system.

Conclusion: We have created nano sized carriers of doxorubicin that are promising carriers for breast cancer therapy and show high biocompatibility in human primary macrophages that represent the first barrier to overcome *in vivo*.



Mitochondrial function of nanoparticle carriers exposed to human monocyte derived macrophages (HMDM).

Literature

1. Theresa M. Allen, Pieter R. Cullis. (2004) Drug Delivery Systems: Entering the Mainstream. Science 303:1818-1822.

Full citation:

Zhihua Wu, Xianghui Zeng, Yuning Zhang, Neus Feliu, Pontus Lundberg, Bengt Fadeel, Michael Malkoch, and Andreas M. Nyström. (2011) Linear dendritic polymeric amphiphiles as carriers of doxorubicin– in vitro evaluation of biocompatibility and drug delivery, Journal of Polymer Science Part A: Polymer Chemistry, XX:XX-XX.

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