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Strategies to Enhance the Drug Distribution: A Comprehensive Review

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ABSTRACT: A heterogeneous mixture of cells with varying amounts of nutrients and oxygen composes the microenvironment inside tumors. Oxygen content variations result in survival or compensatory processes within tumors that may benefit a phenotype that is more malignant or lethal. Rapidly proliferating cells are richly nourished and positioned near blood vessels preferentially. Chemotherapy may target and destroy cells adjacent to the vasculature, while cells residing farther away are often not exposed to sufficient quantities of medication and may survive and repopulate after treatment. In order to devise more effective therapies, the dynamics of the tumor microenvironment can be manipulated. In this report, we identify important features of the microenvironment of the tumor and address techniques that can enhance the delivery and action of drugs. Within an extracellular matrix (ECM) protected by an irregular vascular network, solid tumors comprise a heterogeneous mix of tumor cells and non-malignant cells. Tumor blood vessels are often further apart than normal tissues and differ in blood flow, resulting in inadequate nutrient distribution and impaired clearance of tumor metabolic breakdown products.

KEYWORDS: Biological, Blood, Cells, Oxygen, Vessels.

INTRODUCTION

Nano materials have sizes ranging from about one nanometer to several hundred nanometers, equivalent to several biological macromolecules such as enzymes, antibodies, and DNA plasmids. Materials in this size range exhibit interesting physical properties, distinct from both molecular and bulk sizes, offering new possibilities for biomedical research and applications in numerous fields, including biology and medicine[1]. The emerging field of nano biotechnology bridges the physical sciences with the biological sciences through chemical methods in the development of novel tools and platforms for understanding biological systems and disease diagnosis and treatment. Hypoxia is a hallmark of many various types of tumors. As shown in Figure 1, the convoluted vasculature of tumors can lead to inadequate oxygen supply through blood vessels[2].

This form of hypoxia is known as minimal hypoxia, chronic or diffusion. Due to intermittent blood flow, acute hypoxia may also occur in solid tumors. Because of the restricted diffusion of oxygen, cells that reside far away from functional blood vessels can become hypoxic: the distance from blood vessels to hypoxic regions depends on the rate of oxygen consumption by the tumor cells, but usually cells that reside at a distance greater than 70μm from functional blood vessels obtain insufficient oxygen levels[3]. Hypoxic cells may be viable, but typically proliferate slowly, probably because of their decreased output of ATP; but recent laboratory work has shown that hypoxic cells can reoxygenate and proliferate, presumably because of a better supply of nutrients and oxygen, as chemotherapy causes the death of cells close to blood vessels[4].

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Via the vasculature, anticancer drugs need to enter target tumor cells. Drug penetration into tumor cells is based on convection and/or diffusion. Convection relies on pressure gradients, and since the pressure inside the blood vessels of the tumor and the interstitium of the tumor are also very high, there is possibly limited movement of drugs through this process from the vasculature to the tumor[5]. Diffusion includes the transfer of drugs from areas where they are concentrated (within the vasculature) to less concentrated regions along a concentration gradient, i.e. (the tumor interstitium)[6].

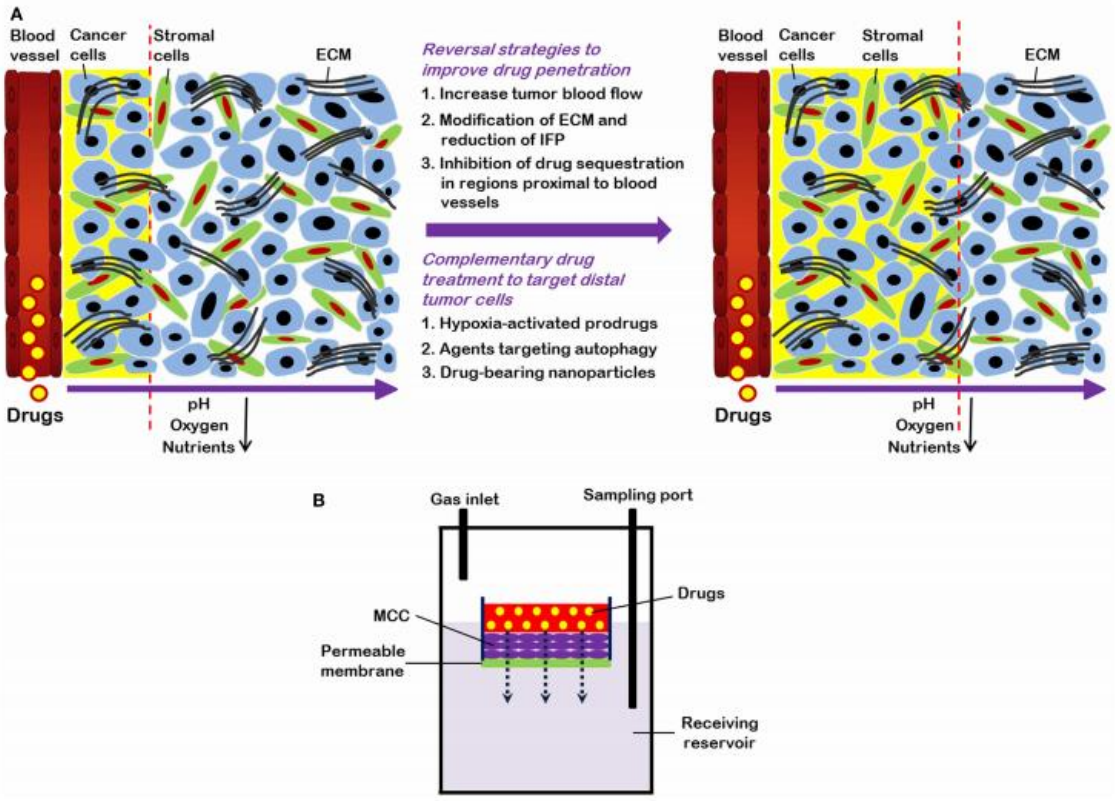

Figure 1: Illustrates plans to overcome limited drug distribution in solid tumors.

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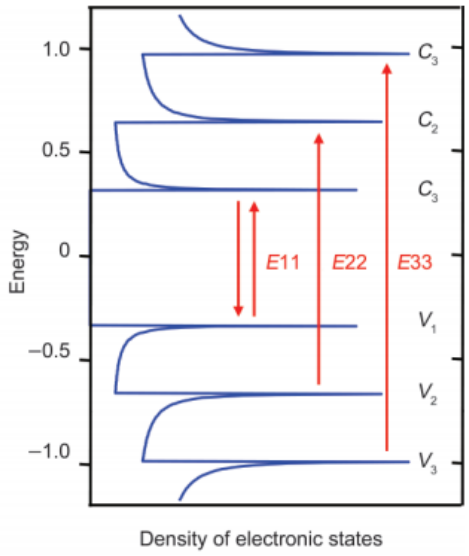

Figure 2: Depicts the UV-vis-NIR absorption spectrum of an aqueous solution of SWNTs[7]**.**

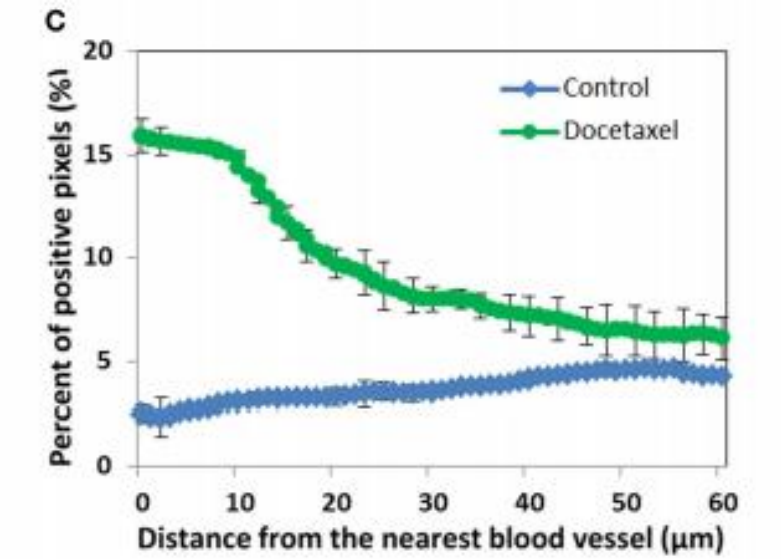

Figure 3: Depicts quantitative analysis of the distribution of γH2aX-positive cells in relation to the nearest blood vessels[8]**.**

DISCUSSION

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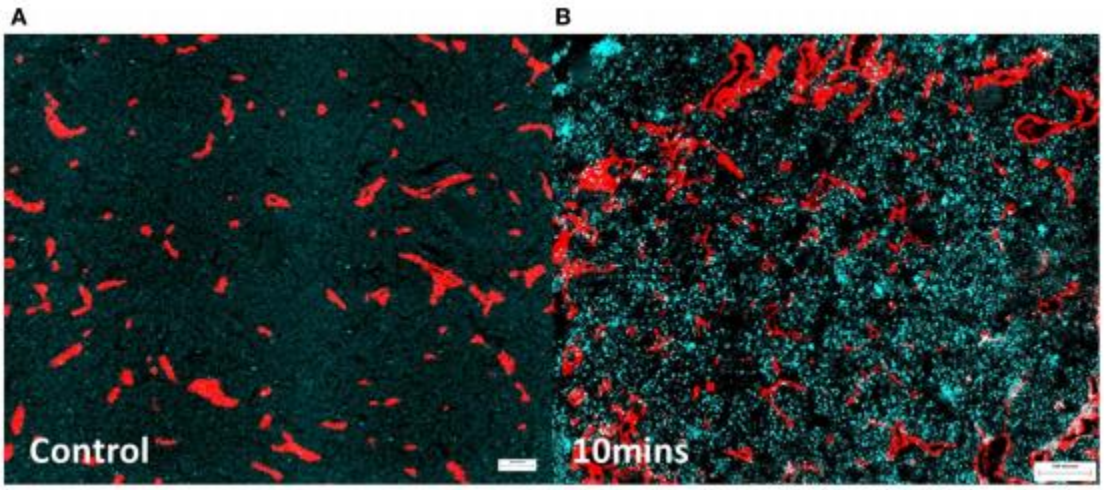

Figure 4: Illustrates changes in γH2aX (in cyan), a biomarker of drug effect, in relation to tumor blood vessels.

Bio macromolecules, including proteins, DNA, and RNA, seldom cross cell membranes on their own, unlike numerous small drug molecules that are able to diffuse through cells. In order to use these molecules for therapeutic applications, intracellular delivery is thus required[9]. For intracellular transport, proteins may be either conjugated or noncovalently absorbed into nanotubes. The hydrophobic surface of partially functionalized SWNTs (e.g. oxidized SWNTs) makes it possible to bind proteins non-specifically. Figure 4 illustrates the liquid crystalline. Figure 5 illustrates CNTs are oxidized and then conjugated with hydrophilic polymers[10]. Figure 1 illustrates plans to overcome limited drug distribution in solid tumors. Figure 2 depicts the UV-vis-NIR absorption spectrum of an aqueous solution of SWNTs. Figure 3 depicts quantitative analysis of the distribution of γH2aX-positive cells in relation to the nearest blood vessels. Figure 4 illustrates changes in γH2aX (in cyan), a biomarker of drug effect, in relation to tumor blood vessels.

CONCLUSION

A significant cause of treatment failure is limited drug distribution to tumors. The microenvironment of the tumor exerts effects that can alter the transmission to neoplastic cells of agents. New therapies that can exploit key tumor microenvironment features, such as pro-drugs triggered by hypoxia and PPIs, have the potential to result in improved clinical outcomes. We have comprehensively analysed the latest research on drug distribution for biomedical applications in this paper. To functionalize CNTs for biomedical research, various covalent and noncovalent chemicals have been created. Functionalized CNTs have been used for ultrasensitive detection of biological organisms, depending on their electric or optical properties. Surveying the literature, we demonstrate that the toxicity of CNTs in vitro and in vivo is highly dependent on the functionalization of CNTs.

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