Cancer Nanomedicine at a Crossroads:

Why Our Current Nano-Strategies Fail and What Comes Next

Jesus Santamaria[1,2,3]

[1]Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza, Zaragoza 50009, Spain. [2]Department of Chemical and Environmental Engineering Universidad de Zaragoza Campus Rio Ebro, 50018 Zaragoza, Spain.[3]Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), 28029 Madrid, Spain

jesus.santamaria@unizar.es

In 1995, the first cancer nanomedicine, Doxil™ was launched, raising huge expectations that Nanomedicine could end cancer. Three decades later we are still looking at around 10 million deaths annually and this figure is expected to rise to 13 million by 2030. Obviously, cancer nanomedicine strategies have failed.

It is true that hundreds of novel nanoparticles (NPs) with exciting antitumor properties have been developed in the laboratories, but cancer nanomedicine has not achieved clinical translation, largely due to a simple fact: less than 1% of the nanoparticles injected systemically reach the tumor[1], irrespective of the nanoparticle nature or targeting method used. This causes two main problems. First, nanomedicines not reaching the tumor cause unwanted off target effects in other organs. Second, if the dose reaching the tumor is not sufficient, cancer cells survive and treatment resistances arise, leading to therapeutic failure.

In our laboratory we aim to develop solutions to the above problems by i) developing therapeutic nanoparticles able to fight cancer in a non dose-dependent manner, e.g. catalytic or hyperthermia-enabling nanoparticles. In this way, even if only a small proportion of catalyst or hyperthermia particle reaches the tumor, its therapeutic action can still go a long way, as long as the particle remains active and is activated only at the tumor; and by ii) developing ways to deliver the catalyst selectively (or at least preferentially) to the tumor. In this line, we investigate so-called Trojan Horse delivery strategies, based on extracellular vesicles as vectors able to reduce immune system recognition while keeping targeting selectivity.

In this talk we will present some recent developments of our laboratory[2-11] that create therapeutic opportunities using NPs capable of hyperthermia or of enabling catalytic therapies. Methods to load these particles in extracellular vesicles without disrupting their targeting properties will also be discussed.

References

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Abstract

Catalysis is the obvious choice when the goal is to facilitate or to inhibit certain processes in complex reaction environments. Because of this, its huge potential to modify the tumor microenvironment chemistry towards a growth inhibition scenario has been recognized for some time. However, in spite of the exciting opportunities it affords, catalysis remains a scarcely explored tool in oncology, due to the huge challenges involved in developing suitable catalysts and delivering them selectively to a growing tumor.

This scenario could be about to change, thanks to recent developments in this field. A family of catalysts capable of working within the tumor environment has now emerged, enabling a range of new therapeutic strategies based on specific reactions: depletion of molecules key for tumor growth, such as glucose or amino acids, generation of reactive oxygen species in the tumor microenvironment, and fabrication of toxic drugs via de-protection chemistry are some of the possibilities afforded. Even more importantly, different methods to deliver catalysts to the tumor with sufficient selectivity are being actively developed. When this is not possible, on-site catalyst activation methods offer an elegant alternative to confine the catalytic action to the tumor. Last but not least, novel strategies to preserve the active life of the catalyst in a hostile environment teeming with deactivating (e.g. sulfur-containing) molecules are also needed.

In this talk, some of the most recent developments from our laboratory in this field will be presented, and the challenges that must be solved for the application of catalysis in oncology will be discussed.

References

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