EBioMedicine 30 (2018) 7–8

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Commentary

A Nanomedicine Approach to Manage Cancer – Imaging Pancreatic Cancer Using Targeted Iron Oxide Nanoparticles

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Pancreatic cancer is one of the most lethal diseases, partially due to late diagnosis. Usually, once the disease is diagnosed, surgical resection is regarded as the only potentially curative treatment and chemotherapy, with an oral fluoropyrimidine derivative, is given after surgery (Kamisawa et al., 2016). One of the most promising routes being studied in the past years to manage the disease is using a nanomedicine approach. This approach allows for the combination of different imaging methods for multimodality imaging using a single nano-system (Israel et al., 2015; Rosenberger et al., 2015), as well as carry small molecules, chemotherapy agents, nucleic acids, peptides, and antibodies, potentially being functionalized further to carry treatment enabling moieties (Bae et al., 2011; Zhou et al., 2015). Amongst these potential carriers, iron oxide nanoparticles pose great potential as they can be used as a contrast agent for magnetic resonance imaging (MRI), which is a non-invasive imaging methodology widely used in the clinics today. Other potential uses include MPI (magnetic particle imaging, preclinical), magnetic targeting, and magnetic hyperthermia (Lee et al., 2015). Many nanoparticles, including superparamagnetic iron oxide nanoparticles (SPIONs), aimed at imaging or delivery to a tumor site, uses the "leakiness" of formed blood vessels near the tumor in order to deliver these small nanoparticles and their load (EPR or "enhanced permeability and a retention" effect) to the tumor (Maeda et al., 2009). However, active targeting may increase the nanoparticles uptake in the tumor, making either imaging or potential treatment much more efficient. Peptides, antibodies, and small molecules can all be used as ligands for nanomaterials in order to actively target an overexpressed feature of the cancer, most commonly a receptor, improving the agent as well as reducing any undesired "off target" effects. In addition to targeting, polymer coating such as poly ethylene glycol (PEG) species are also commonly used to help improve the pharmacokinetics of a designed nanomaterial. These surface polymers postpone the SPIONs uptake by the immune system macrophages, which may cause an increased uptake in the liver and spleen, and simultaneously reduce the uptake in the tumor. Another common possibility is to encapsulate the SPIONs in an organic matrix, which may increase the size of the nano-system. The nano-system characteristics, such as hydrodynamic diameter (the size of the nanoparticle or aggregate within a liquid, also provides information about colloidal stability), nanoparticle size (measured by microscopic methods), and surface potential are also important, since larger particles, for example, may have lower penetration to a solid tumor tissue. Therefore, functionalizing crystalline SPIONs with a polymer, without encapsulating them, and conjugate a targeting moiety (especially a large one, such as an antibody) and additional functionalities, while preserving the nano-system characteristics within parameters suitable for *in vivo* use (and future clinical use), is a challenge. Amongst the studied targets for pancreatic cancer, we can find for example galactin-1 which was reported to be upregulated in pancreatic cancer cells but is not expressed in adjacent normal tissues (Rosenberger et al., 2015), integrin $\alpha v\beta 6$, which is overexpressed in pancreatic cancer but is negligibly expressed in normal tissues (Gao et al., 2015), and also the highly expressed plectin-1 (Bausch et al., 2011). In a recent work done by Chen et al., published in *EBioMedicine*, an iron oxide platform, was successfully functionalized with an anti-plectin-1 monoclonal antibody, as well as PEG and a NIR (near infra-red) fluorescent dye as an additional imaging method to MRI (Chen et al., 2018). The authors managed to keep the nanoparticle characteristics within parameters for *in vivo* use aimed at tumor imaging and demonstrated high uptake in the tumor, along with good MRI and NIR imaging capabilities. The plectin-1 targeted nano system and a non-targeted control were fully characterized, and the data also includes stability and pharmacokinetics measurements. This nano system has the potential to be improved even further, by replacing the NIR dye with a PET (positron emission tomography) enabling radionucleotide, which will make this tumor detection nano-system even more effective. In conclusion, I would like to congratulate the authors for fabricating an iron oxide based nano-system that can target and image pancreatic cancer effectively. Hopefully, this type of nanomedicine approach, may help facilitate fast diagnosis and therapy for hard to manage diseases such as pancreatic cancer.

Disclosure

I declare no competing interests.

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DOI of original article: https://doi.org/10.1016/j.ebiom.2018.03.008
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https://doi.org/10.1016/j.ebiom.2018.03.011

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