2016-01-06

Cancer Nanotheranostics: What Have We Learned So Far?

Joao Conde
Massachusetts Institute of Technology, jdconde@mit.edu

Furong Tian
Dublin Institute of Technology, furong.tian@dit.ie

Jesus M. de la Fuente
Shangai Jiao Tong University

Pedro V. Baptista
Universidade Nova de Lisboa

Recommended Citation

Frontiers in Chemistry. 2015; 3: 71. PMCID: PMC4701939

Cancer Nanotheranostics: What have we learned so far?

João Conde[1,2,]*, Furong Tian[3], Jesus M. de la Fuente[4,5], Pedro V. Baptista[6]

[1] Massachusetts Institute of Technology, Institute for Medical Engineering and Science, Harvard-MIT Division for Health Sciences and Technology, Cambridge, Massachusetts, USA.

[2] School of Engineering and Materials Science, Queen Mary University of London, London, UK.

[3] School of Food Science and Environmental Health, College of Sciences and Health, Dublin Institute of Technology, Dublin, Ireland.

[4] Department of Bio-Nano Science and Engineering, Key Laboratory for Thin Film and Microfabrication of Ministry of Education, Institute of Micro/Nano Science and Technology, Shanghai Jiao Tong University, Shanghai, P.R. China.

[5] Instituto de Nanociencia de Aragón, Universidad de Zaragoza, Zaragoza, Spain.

[6] UCIBIO, Departamento de Ciências da Vida, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa. Campus da Caparica, Caparica, Portugal.

* Corresponding author: João Conde, jdconde@mit.edu or conde.bio@gmail.com

Keywords: Oncology; Cancer; Nanotechnology; Nanotheranostics; Nanomaterials: Nanoparticles

After a quarter of century of rapid technological advances, research has revealed the complexity of cancer, a disease intimately related to the dynamic transformation of the genome. However, the full understanding of the molecular onset of this disease is still far from achieved and the search for mechanisms of treatment will follow closely.

It is here that Nanotechnology enters the fray offering a wealth of tools to diagnose and treat cancer. Today, Nanotechnology is a burgeoning field that is helping to address critical global problems from cancer treatment to climate change. In fact, Nanotechnology is everywhere and is everyday practice [1], offering numerous tools to diagnose and treat cancer, such as new imaging agents, multifunctional devices capable of overcome biological barriers to deliver therapeutic agents directly to cells and tissues involved in cancer growth and metastasis, and devices capable of predicting molecular changes to prevent action against precancerous cells [2].

Nanomaterials-based delivery systems in Theranostics (Diagnostics & Therapy) provide better penetration of therapeutic and diagnostic substances within the body at a reduced risk in comparison to conventional therapies. At the present time, there is a growing need to enhance the capability of theranostics procedures where innovative multifunctional nanocarriers for cancer theranostics may allow the development of diagnostics systems such as colorimetric and immunoassays, and in therapy approaches through gene therapy, drug delivery and tumor targeting systems in cancer [3].

Some of the thousands and thousands of published nanosystems so far will most likely revolutionize our understanding of biological mechanisms and push forward the clinical practice through their integration in future diagnostics platforms. Nevertheless, despite the significant efforts towards the use of nanomaterials in biologically relevant research, more *in vivo* studies are needed to assess the applicability of these materials as delivery agents. In fact, only a few went through feasible clinical trials. Nanomaterials have to serve as the norm rather than an exception in the future conventional cancer treatments. Future *in vivo* work will need to carefully consider the correct choice of chemical modifications to incorporate into the multifunctional nanocarriers to avoid activation off-target, side effects and toxicity.

It is imperious to learn how advances in nanosystem's capabilities are being used to identify new diagnostic and therapy apparatuses driving the development of personalized and precision medicine in cancer therapy and diagnostics; learn how incorporating cancer research and nanotechnology can help patient life quality; identify how to decipher nanotheranostics data into a real clinical strategy; and last but not least, learn what methods are showing fertile results in turning promising clinical data into treatment realities [3].

Although all studies described here provide a baseline level of data in support of the effectiveness and safety of nanomaterials, we wonder what have we learned so far?

Current trends in biomedicine have been focused towards the use of new materials capable to address particular and individual characteristics in strategies for molecular precision therapies. In this endeavor, nanoparticles have allowed a tremendous leap forward in combining diagnostics and therapy in a single system and doing so at the nanoscale. Nanotheranostics have enabled the integration of targeting, imaging and therapeutics in a single platform, with proven applicability on the management of heterogeneous diseases.

Despite the plethora of proposed systems, only but a few products are currently included clinical trials and much remains to be done to allow effective clinical translation of these promising nanotheranostics platforms.

Several nanoconjugates have been proposed, varying in material, size and shape; some bringing current therapeutic approaches to the nanometer scale while others enact disruptive properties only possible by combination of different molecules and chemistries at the nanoscale [4]. For example, achieving controlled cellular responses of nanoparticles is critical for the successful development and translation of NP-based drug delivery systems. *Conde* et al [4] and *Hong* et al [5] reported a complete survey on the most important factors for careful design of nanoparticles and the demand for precise control over the physicochemical and biological properties of NPs.

Liu et al [6] discuss the potential of star shaped nanoparticles in novel imaging approaches and strategies combining therapy and imaging in cancer. In fact, the potential of application of nanoconjugates in enhanced imaging strategies and platforms is discussed by *Alcantara* et al [7] with particular emphasis in current trends in molecular imaging for optimized management of breast cancer.

Theranostics of brain diseases such as brain cancer, is a daunting challenge due to the unique environment of central nervous system [8]. Yet passing the blood-brain barrier (BBB) is particularly difficult. The proper design of such engineered 'nanocarriers' becomes very important in translocating the impermeable membranes of the brain to facilitate drug delivery. At the same time, it is also required to retain the drug stability and ensure that early degradation of drugs from the nanocarriers does not take place. In fact, *Mahmoudi* and *Hadjipanayis* [9] reported a great opinion piece about the application of magnetic nanoparticles (MNPS) for the treatment of brain tumors and how MNPs will likely assume a larger role in brain cancer treatment in combination with other adjuvant therapies.

Talking about other adjuvant therapies, radiation and gene therapy have also gained momentum in the last years when using nanomaterials for cancer therapy. *Cooper* et al. [10] reported how radiation therapy is one of the most commonly used treatments for cancer and which directions to follow for the future based on current state of nanoparticle-assisted radiation therapy.

Regarding gene therapy, Moreno et al. [11] reported a critical overview of using therapeutic antisense oligonucleotides against cancer and how difficult has been to get to the clinic. This is in fact not only a problem with gene therapy but a universal issue as whilst many pre-clinical data has been generated, a lack of understanding still exists on how to efficiently tackle all the different challenges presented for cancer targeting in a clinical setting.

Perhaps another interesting avenue in cancer nanotheranostics is the interfering effect of the immune system in the efficacy of proposed platforms. In fact, a clear perspective on the interaction between immune response and immune modulators is still missing from the general picture of nanotheranostics, not only in what concerns the organisms response to the systemic delivery of nanoconjugates that may hamper efficacy, but also the use of the immune response and nanoconjugates interaction with immune system as means to achieve higher and more directed/targeted therapy to the cancer site. As such, the effect and response of diverse properties of nanodiagnostics platforms in the organisms have been discussed by *Clift* et al [12], where nanoconjugates are discussed in terms of the immune response triggered after systemic delivery; whereas *Conniot* et al [13] and *Pearson* et al [14] have demonstrated how nanotheranostics may use and profit from the specific and unspecific immune response to enhance efficacy. Actually, cancer immunotherapy is nowadays consider a hot topic and a huge breakthrough in modern Science [15].

Emergent technologies have been combined with nanoscale structures for directing to the site of interest with decreased side effects. The experience gathered thus far has shown that the next step in the effective translation of nanotheranostics into the clinics relates to the body's response to the nanoconjugates. What are the toxicity impacts of these devices and platforms? Are there enough data for the full chronic toxicity evaluation of the application of these systems? Is the immune system a friend or foe for nanotheranostics?

References

[1] J. Conde, The Golden Age in Cancer Nanobiotechnology: Quo Vadis? Frontiers in bioengineering and biotechnology 3 (2015) 142.

[2] J. Conde, G. Doria, and P. Baptista, Noble metal nanoparticles applications in cancer. J.Drug Deliv. 2012 (2012) 751075.

[3] J. Conde, F. Tian, P.V. Baptista, and J.M. de la Fuente, Multifunctional Gold Nanocarriers for Cancer Theranostics - From bench to bedside and back again? in: F. Marcos Garcia, (Ed.), Nano-Oncologicals: New Targeting And Delivery Approaches. in press with Springer International Publishing AG., 2014.

[4] J. Conde, J.T. Dias, V. Grazu, M. Moros, P.V. Baptista, and J.M. de la Fuente, Revisiting 30 years of biofunctionalization and surface chemistry of inorganic nanoparticles for nanomedicine. Front Chem. 2 (2014) 48.

[5] R.M. Pearson, V.V. Juettner, and S. Hong, Biomolecular corona on nanoparticles: a survey of recent literature and its implications in targeted drug delivery. Frontiers in chemistry 2 (2014) 108.

[6] Y. Liu, H. Yuan, A.M. Fales, J.K. Register, and T. Vo-Dinh, Multifunctional gold nanostars for molecular imaging and cancer therapy. Frontiers in chemistry 3 (2015) 51.

[7] D. Alcantara, M.P. Leal, I. Garcia-Bocanegra, and M.L. Garcia-Martin, Molecular imaging of breast cancer: present and future directions. Frontiers in chemistry 2 (2014) 112.

[8] S. Bhaskar, F. Tian, T. Stoeger, W. Kreyling, J.M. de la Fuente, V. Grazu, P. Borm, G. Estrada, V. Ntziachristos, and D. Razansky, Multifunctional Nanocarriers for diagnostics, drug delivery and targeted treatment across blood-brain barrier: perspectives on tracking and neuroimaging. Part Fibre Toxicol 7 (2010) 3.

[9] K. Mahmoudi, and C.G. Hadjipanayis, The application of magnetic nanoparticles for the treatment of brain tumors. Frontiers in chemistry 2 (2014) 109.

[10] D.R. Cooper, D. Bekah, and J.L. Nadeau, Gold nanoparticles and their alternatives for radiation therapy enhancement. Frontiers in chemistry 2 (2014) 86.

[11] P.M. Moreno, and A.P. Pego, Therapeutic antisense oligonucleotides against cancer: hurdling to the clinic. Frontiers in chemistry 2 (2014) 87.

[12] M.J. Clift, J.F. Dechezelles, B. Rothen-Rutishauser, and A. Petri-Fink, A biological perspective toward the interaction of theranostic nanoparticles with the bloodstream - what needs to be considered? Frontiers in chemistry 3 (2015) 7.
[13] J. Conniot, J.M. Silva, J.G. Fernandes, L.C. Silva, R. Gaspar, S. Brocchini, H.F. Florindo, and T.S. Barata, Cancer immunotherapy: nanodelivery approaches for immune cell targeting and tracking. Frontiers in chemistry 2 (2014) 105.
[14] C.M. Dawidczyk, L.M. Russell, and P.C. Searson, Nanomedicines for cancer therapy: state-of-the-art and limitations to pre-clinical studies that hinder future developments. Frontiers in chemistry 2 (2014) 69.
[15] J. Conde, C.E. Arnold, F. Tian, and N. Artzi, RNAi nanomaterials targeting immune cells as an anti-tumor therapy: the missing link in cancer treatment? Materials Today in press (2015).