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Editorial

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Nanotechnology for Circulating Tumor Biomarker Analysis

Giuseppe Toffoli[1]*, Matteo Castronovo[1] and Flavio Rizzolio[1]

Circulating biomarkers are essential for cancer diagnosis and progression monitoring. Nowadays, it is commonly accepted and widely highlighted the need to discover tumour markers to enable early diagnosis, prognosis as well as giving insight into pathogenesis and identifying potentially new treatments. In early stage disease, the application of adjuvant chemo- or radio- therapy after surgery depends on the risk of early tumor recurrence and in advanced stage diseases, the choice between aggressive and mild therapies depends on the stratification of patient risk [1]. Once again, prognostic information relative to cancer patients is expected to allow the definition of effective and personalized treatment strategies.

In the last two decades, different examples of innovative biomarkers or technologies have been suggested as most promising tools in cancer management, thus opening the door to novel approaches to the clinical practice [2]. Considering the large timeline gap between the early development of malignant lesions and the appearance of full-blown primary or metastatic cancer, different opportunities are under investigations. Serological signatures, circulating tumor cells, autoantibodies, proangiogenetic factors, epigenetic markers and miRNAs have, among others, been explored to detect cancer at early stages and tumor progression, in addition to the circulating biomarkers currently used in clinical practice (i.e. PSA, CEA).

However, the routine application of circulating biomarkers to tumors still remains restricted to a few cases and their predictive and prognostic value is controversial. Innovative strategies are required to increase the clinical utility of biomarkers and their discovery and validation seem incomplete as an approach. A novel generation of analytical tools is necessary to respond to the timely need of early diagnosis and reliable prognosis aiming at effectively treating cancer patients (http://nano.cancer.gov/learn/impact/). The application of nanotechnologies to the management of cancer is one of the most important strategies to extend the current limits of and refine the molecular diagnostics approaches. In the last few years, several strategies have been adopted and nanoparticles, among the others, are very promising. Nanoparticles can be conjugated with monoclonal antibodies and specifically target the tumors. For examples, targeted-gold nanoparticles or nanorods can be detected with SPR scattering imaging or SPR absorption spectroscopy (heating phenomena) or fluorescence imaging. Magnetic nanoparticles can be utilized in "sandwich" assays over an array of different antibodies to detect biomarker proteins on a range of concentrations three folds bigger than any existing method and its accuracy is mostly independent on the type of body fluid to analyze [3]. In addition, nanoparticle can be integrated into newly-developed, innovative, nanotechnology-based, sensitive devices, with minimal sample volume requirements and low costs, and ease of use in facilitating rapid diagnosis and timely treatment adjustments at points-of-care testing (POCT) sites [4].

Over the last five years, several funding opportunity announcements, issued by the National Cancer Institute (NCI) and the National Institutes of Health (NIH) in the USA, have supported pre-clinical optimization and testing of cancer-relevant nanotechnology applications to develop new, or to improve existing applications for therapeutics and/or in vivo diagnostics, clearly directed toward the development of ultimate commercial products [3]. Up until now however, very few nanotechnology-based applications have been translated into commercial products, thus demonstrating that the nanotechnology innovation for cancer treatment is still at its early stage.

Recent progresses of nanotechnology have put biomarkers analysis and discovery back under the spotlight. A recent research article of C. Mirkin and co-workers has demonstrated that a nanoparticle-based bio-barcode assay, 300 times more sensitive than commercial immunoassay, redefines "undetectable" PSA and biochemical recurrence after radical prostatectomy [5]. Although, the clinical utility of this supersensitive approach on PSA protein remains an open question, the authors hypothesize that an increase in the frequency of sample collection, especially in the year after treatment, would allow an earlier detection of a PSA profile consistent with disease recurrence, thus identifying those patients who may benefit most from early detection.

Nanotechnology can help evaluate the risk during therapeutic treatment, towards a potential improvement and personalization of the drug dosage in cancer patients. This approach is commonly called therapeutic drug monitoring (TDM). Many patients manifest toxic side effects after drug treatment, nevertheless at present TDM is very limited in clinical practice due to the analytical complexity of currently available technologies. POCT-dedicated devices could represent a novel and effective strategy that may allow carrying out TDM in real-time to increase drug efficacy at the bedside [6].

The availability of POCT-dedicated devices for cancer patients, to sensitively measure in real-time the concentrations of circulating biomarkers, currently used in the clinical practice, or to perform TDM, would allow to complete diagnostic tests avoiding traditional centralized laboratories, thus improving the quality and the effectiveness of the process, and leading to an increase of higher compliance (benefiting patients), with a corresponding decrease of costs (benefiting the Health Care System).

To adapt such devices to the clinical practice, a multidisciplinary approach, which combines the effort of experimental physicists, chemists, biologists and clinicians is required to accelerate the transfer of knowledge from the laboratory to hospitals.

The application of nanotechnology in clinical oncology is very promising although still challenging. This is mostly due to the diversity of clinical approaches, and, in minor extent to technological issues.

***Corresponding author:** Dr. Giuseppe Toffoli, Director of Experimental and Clinical Pharmacology Unit, Via Franco Gallini, 2- 33081, Aviano, Pordenone, Italy, Tel: +39 0434 659 612; Fax: +39 0434 569 799; E-mail: gtoffoli@cro.it

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Nanotechnology, in conclusion, is likely to significantly improve the clinical application of circulating biomarker analysis, and, also facilitate the discovery of novel biomarkers for the early diagnostics and the personalized treatment of cancer patients.

Many challenges still remain to be resolved prior to widespread use of nanodevices in clinical oncology. These regard not only the technologies issues and the validation of the technology approaches, but also the different clinical approaches that will be required by using innovative devices for biomarkers assay.

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Author Affiliations

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[1]*Centro di Riferimento Oncologico - CRO - National Cancer Institute, Experimental and Clinical Pharmacology Unit, Via Franco Gallini, 2- 33081, Aviano, Pordenone, Italy*