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Path-breaking directions of nanotechnology-based chemotherapy and molecular cancer therapy

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ABSTRACT

A fundamental question in the field of technological forecasting and foresight is how to detect likely fruitful technological trajectories in new research fields, such as nanomedicine. We confront this question by developing an approach based on trends and networks of vital variables, analyzed by bibliometrics, which endeavours to detect fruitful trajectories of nanotechnology applied to ground-breaking anti-cancer treatments. Results tend to show two main technological waves of cancer treatments by nanotechnology applications. The early technological wave in the early 2000s was embodied in some types of chemotherapy agents with a broad spectrum of application, while after 2006 the second technological wave appeared with new applications of chemotherapy agents and molecular target therapy by nanotechnology. The present study shows new directions of nanotechnology-based chemotherapy and molecular cancer therapy in new treatments for breast, lung, brain and colon cancers. A main finding of this study is the recognition that, since the late 2000s, the sharp increase of several technological trajectories of anticancer drugs applied by nanotechnology seems to be driven by high rates of mortality of some types of cancers (e.g. pancreatic and brain) in order to find more effective anticancer therapies that increase the progression-free survival of patients: the so-called technological trajectories mortality driven. The study also points out that global research leaders tend to specialize in anticancer drugs, via nanotechnology, for specific cancers (e.g. Switzerland in prostate cancer, Japan in colon cancer, China in ovarian cancer and Greece in pancreatic cancer). These ground-breaking technological trajectories are paving new directions in biomedicine and generating a revolution in clinical practice that may lead to more effective anticancer treatments in the not-too-distant future.

1. Introduction and the problem

Interdisciplinary theoretical and experimental results related to nanoscience and nanotechnology in the life sciences support the diagnosis, monitoring, prevention and treatment of diseases such as cancer, a leading cause of death in the western world (Fonseca et al., 2014). Traditional chemotherapy has low efficacy for some types of cancer and tends to generate severe adverse effects in healthy tissues (Coccia, 2014). The advent of nanotechnology in medicine is generating a vital technological change and a revolution in oncology and other fields (Islam and Miyazaki, 2010; Rafols and Meyer, 2010; Coccia, 2012b,c; Wolinsky et al., 2012; Madeira et al., 2013; Lim et al., 2010).[1] Bibliometrics is an important approach for investigating

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[1] Cf. also Genet et al., 2012; Chen et al., 2013; Tierney et al., 2013; von Raesfeld et al., 2012.

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emerging fields of nanotechnology (Arora et al., 2013). In fact, some studies, based on publications, show that the patterns of nanotechnology research are spreading among different scientific domains, generating new technological trajectories mainly in chemistry, medicine and engineering research fields (cf. Coccia, 2012b; Robinson et al., 2013). No and Park (2010), using patent citations, argue that the interaction of biotechnology and nanotechnology may provide important signals for future patterns in nano-biomedicine (cf. Sylvester and Bowman, 2011; Coccia, 2012a). Instead, Shapira and Wang (2010) show that some countries, such as the USA and China, are considered among the top nanotechnology research publishing countries. This result likely can be due to high R&D investments in vital research fields and incentives given to researchers to publish in Web of Science indexed journals (Lin and Zhang, 2007; Shapira and Wang, 2009 cf. Coccia, 2010; 2010a; 2014b; Coccia and Rolfo, 2007). However, Youtie et al. (2008) claim that publication counts do not necessarily equate to publication influence.

An interesting problem that deserves to be analysed in the field of the economics of innovation and technological foresight is how to detect the path-breaking directions of technological trajectories in oncology based on ground-breaking anticancer treatments. We confront this main issue by an approach based on trends and networks of critical variables pinpointed by bibliometrics in order to detect and analyse:

- new technological trajectories and directions of important anticancer treatments (chemotherapy agents, target therapies and chemopreventive substances) administered by new drug delivery systems based on nanotechnology;
- vital relationships between anticancer treatments based on new drug delivery systems that use nanotechnology and different cancers;
- countries that are best performers in applications of nanotechnology to treat cancers and their specialization to treat specific cancers with new drug delivery systems based on nanotechnology.

This study can provide important results concerning emerging and fruitful directions of ground-breaking anticancer treatments based on nanotechnology that may generate a revolution in clinical practice due to increased therapeutic efficacy and decreased toxicity of cytotoxic effects in healthy tissues.

2. Theoretical background and related works

Generally speaking, technological innovations involve "*the solution of problems*" (Dosi, 1988, p. 1125, original emphasis). The solution tends to be achieved by the technological paradigm, defined as a: "'model' and 'pattern' of solution of *selected* technological problems, based on *selected* principles derived from the natural science and on *selected* material technologies" (Dosi, 1982, p. 152, original emphasis; see also Nelson and Winter, 1982). In modern socio-economic systems, cancer is a main problem and remains a stressful condition and a leading cause of death worldwide (Fonseca et al., 2014, p. 626; Hull et al., 2014). "Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems" (US National Cancer Institute, 2014).

Science and technology are generating several patterns of technological innovation in order to find a solution to this problem for human population (Coccia, 2009, 2012d, 2013). Traditional treatments are based on chemotherapy agents that are not effective to treat and cure some types of cancer such as lung, pancreatic and ovarian cancer (Coccia, 2012a,b,c). In particular, according to Fonseca et al. (2014) actual treatments of cancer often offer limited efficacy with several secondary adverse effects as a result of severe cytotoxic effects in healthy tissues.

In general, technological paradigms are underpinned in advances of fundamental sciences, such as molecular biology, chemistry and so on. This basic scientific knowledge has to transit in applied sciences (such as engineering)[2] in order to be embodied in radical technological innovations that can generate fruitful solution to several socio-economic problems. Moreover, the technological progress is affected by *focusing devices* considered: "typical problems, opportunities, and targets that tend to focus the search process in particular directions" (Rosenberg as quoted by Dosi, 1988, p. 1127). These selective and finalized directions of innovative activities engender fruitful technological trajectories, which spur: "the activity of technological progress along the economic and technological trade-offs defined by a paradigm" (Dosi, 1988, p. 1128; cf. Sahal, 1981). Nelson (2008) seeks to clarify why certain technological paradigms support fruitful scientific and technological progress in comparison to others. Determinants include the economic and human resources,[3] aimed at strategic research and technology programmes, and to a lesser degree "effective demand" of markets (Nelson, 2008, p. 487; cf. Rosenberg, 1983). In addition, a main driver of technological trajectories is the "interest and goals" of professional "knowledge-seekers" (Clark, 1987, p. 40, original emphasis).

A main technological paradigm is the molecular biology and Linstone (2004, p. 192) stresses the importance of the molecular technology, which: "is defined by the focus on the molecular scale, with nanotechnology, biotechnology and materials science coming to the fore". The current "molecular technology era" (Linstone, 2004) is driving, more and more, new technological trajectories of path-breaking anticancer treatments. In fact, breakthroughs in nanotechnology are providing "a new dimension" to medicine by therapies integrated in nanoparticles, which are spurring new insights to ground-breaking cancer treatments (da Rocha et al., 2014). The National Cancer Institute's nanotechnology strategy started in 2004 to support multidisciplinary researchers in the applications of nanotechnology to anticancer treatments based on new drug delivery systems (Hull et al., 2014). As a matter of fact, the advent of nanotechnology is a great promise to revolutionize many fields such as oncology by advanced cancer treatments of drug delivery.[4] Correspondingly, R&D investments in biomedicine and nanomedicine have experienced an exponential growth since the early 2000s, such that: "cancer nanotherapeutics are

[2] Engineering can be considered an *intermediate scientific field* because it links basic sciences (such as physics) to practical technological applications in order to solve problems of different fields (cf. Nelson, 2008, p. 491 and p. 494).

[3] For instance, R&D intensity of countries, number of researchers in science and technology, etc. (cf. Coccia, 2008, 2011, 2012e).

[4] In this regard, several nanocarriers seem to overrule previous technologies, demonstrating increased therapeutic efficacy associated to decreased toxicity (Fonseca et al., 2014, p. 626*ff*).

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