*Biomedical Research and Therapy* **2014, 1(2):32-34**
ISSN 2198-4093
www.bmrat.org

10.7603/s40730-014-0006-5

**EDITORIAL**

# Biological therapy: a new age of cancer treatment

**Ngoc Kim Phan**

Laboratory of Stem Cell Research and Application, University of Science, Vietnam National University, Ho Chi Minh City, Vietnam.
*Corresponding author: pkngoc@hcmus.edu.vn

**Received**: 15 February 2014 / **Published online**: 22 March 2014


Cancer is an important reason causing death in many countries. So cancer studies become as interesting research field. Many research groups approached cancer treatment with some different strategies. To date, there are four main strategies used in preclinical and clinical treatment included surgery, chemotherapy, radiation therapy, and biological therapy. In some indications, doctors combined them to make combinatorial therapies. In recent years, biological therapies have become a promising therapy, especially in invasive cancer. Biological agents formed the targeting therapies that in principle only cancer cells effected by drugs. Biological therapies as monoclonal antibodies, immune cells based immunotherapies showed that the treatment efficiency in some cancers, in recent years. Biomedical Research and Therapy is developed basing on the progress in research and application of biology, biotechnology in disease treatment that included cancer. So that, in this year, *Biomedical Research and Therapy* will have a special issue with the theme "*Biological therapy for cancer treatment*". We will invite some of the leaders in this field to review this issue. We expect that this issue will be of great interest for developing the novel approaches and innovations for cancer treatment.

Cancer is known as malignant neoplasia related to uncontrolled cell proliferation. This proliferation forms malignant tumor that can invade nearby parts of the body. To date, there are over 200 different kinds of cancers that can affect the human body. Cancer is a leading cause of death worldwide, accounting for 8.2 million deaths in 2012. Hence, cancer research, especially cancer treatment studies, are prior programs in a lot of countries.

At the present, cancer is treated by some different methods included surgery, chemical treatment, radiation therapy or combinatorial therapy. Although these therapies also gave promising results in patients, they faced with relapse and invasion. Some hypothesis considered that almost present therapies have not attacked the cancerous target cells. In fact, cancer stem cells that drive tumor growth are considered as targets of cancer treatment therapies (Tu et al., 2009; Yang et al., 2014). Biological therapy is the advanced method that can target the cancer stem cells (Duggal et al., 2013).

By definition, biological therapy is the use of living organisms, substances derived from living organisms to treat disease. Some popular biological therapies used in cancer treatment included monoclonal antibodies (Glassman and Balthasar, 2014), cytokine therapies, vaccine therapies (Aranda et al., 2013), adoptive T-cell therapies, dendritic cell based therapies (Qian et al., 2014), oncolytic virus therapies (Bell and McFadden, 2014), gene therapies (Brenner et al., 2013), DNA oligonucleotide therapies, and RNA oligonucleotide therapies (Cho-Chung, 2005). Several biological therapies were approved by U.S FDA and other countries in cancer treatment.

More than half of biological therapy based on body's immune system and other is based on cell signaling. So immune system holds an essential role in these biological therapies and decides the success of treatment. In generally it is believed that the immune system can detect and destroy the foreign cells or abnormal cells to prevent the tumor formation. However, the immune system is tolerated by cancerous cells, cancer cells can rapidly growth to form tumors that the immune system cannot recognize them. To destroy the cancerous cells, these biological therapies restore or increase the immune system activity to attack cancer cells.

Monoclonal antibodies (Mabs) are efficient agents in cancer treatment. Different to polyclonal antibody, Mab can specifically bind to antigen expressed by cancer cells or cancer stem cells. Mabs were firstly produced by Kohler and Milstein in 1975 (Kohler and Milstein, 1975). This technology related to hybridoma cells that are fusion cells from myeloma cells (cancerous B cell) and antibody producing cells. The first effect of Mabs is triggering the immune system to destroy the cancer cells. There are some commercial Mabs of

this type included rituximab, alemtuzumab (Frankfurt et al., 2014). These Mabs will bind on cancerous cell surface. Another Mab is bind to immune cell surface to stimulate the immune system such as ipilimumab in melanoma treatment (Della Vittoria Scarpati et al., 2014). Some Mabs act with different mechanisms as binding to VEGF that interfere to development of blood vessel (bevacizumab) (Becouarn et al., 2014) while cetuximab, panitumumab and trastuzumab that bind to EGFR prevent the signaling of EGF to promote the cancer cell growth (Johnston et al., 2006). Besides some Mabs are developed as immunotoxins that attach to cell-killing substances such as a plant or bacterial toxin, a chemotherapy drug or radioactive molecules (Y-ibritumomab tiuxetan, I-tositumomab, ado-trastuzumab emtansine) (Baron et al., 2014; Cheung et al., 2009; Hohloch et al., 2011).

Cytokines also are interesting in cancer treatment. They can regulate immune response, inflammation as well as hematopoiesis. There are two groups of cytokines widely used included interferon (INF) and interleukin (IL). INF-alpha is the most INF used in cancer treatment. It is known as the activator of NK cells and dendritic cells (Sutlu and Alici, 2009). Some kinds of ILs also are used in cancer treatment as IL-2, IL-12 (Amato et al., 2014)… These ILs increase the proliferation of cytotoxic T cells as well as NK cells that enhance anticancer immune response. Some other cytokines such as GCSF or GM-CSF are used as adjuvants in cancer treatment to improve the hematopoiesis after chemo or radiation therapies (Aliper et al., 2014).

Using dendritic cells as antigen presenting cells and adoptive T cells to treat cancer is novel approach that attracted by many researchers. Dendritic cells are trained to present the tumor specific antigens. In the body, these cells will present the tumor antigens to T cells, B cells or NK cells. These effectors will attack the cancerous cells by various ways. One the first DC therapy approved to treat cancer is Provenge (Dendreon) (Brower, 2010). Provenge was designed to stimulate T cells to attack the prostate cancer cells. Antigen-presenting cells are removed by leukapheresis on day 1; processed with a tumor antigen called prostatic acid phosphatase on days 2 and 3; and then fused to granulocyte–macrophage colony-stimulating factor (GM-CSF). The patients will receive an infusion on day 3 or 4, and twice more, in weeks 2 and 4.

Gene therapy is the potential approach to treat cancer. However, to date, there is not any product from this approach to be approved by FDA. In the principle, gene therapy will destroy or prevent the cancerous cell growth. At the present, there are a lot of different approaches of gene therapy in cancer treatment. Some researchers tailored two groups of genes involved tumor suppressor genes and oncogenes to inhibit the cancer cells. P53 gene therapy is the most strategy with promising results (Lane et al., 2011). This is tumor suppressor gene that it expresses to cause cell proliferation inhibition. Other strategies relate to disruption of blood vessel formation (Shibata et al., 2013), decrease of drug resistance, or introducing “suicide genes” into cancer cells (Malecki, 2012).

Oncolytic virus therapy is interested in research for some recent years. This therapy relates to usage a specific virus that can infect and lyse the target cells. By this mechanism, some oncolytic viruses were modified to infect to the cancer cells to cause them to die such as reovirus (Newcastle disease virus) and mumps virus. In another way, oncolytic viruses were used to express the specific cancer associated antigen that would be attacked by drugs (Russell et al., 2012). This is a new method in cancer treatment though there is not any product approved by US FDA, although H101, a modified form of adenovirus, was approved in China in 2006 for the treatment of patients with head and neck cancer. Several oncolytic viruses are currently being tested in clinical trials (Lu et al., 2004).

Finally, more important, almost patients want to have a vaccine to prevent the cancer. In the high effort of researchers in worldwide, some vaccines for cancers also developed and clinically tested. Most vaccines are specific antigens of cancer cells. When injected into the body, they will stimulate the immune system to produce specific antibodies that can protect patients from cancer cells. However, some vaccines to prevent some viruses causing cancers are considered as feasible cancer vaccines. In fact, cervical cancer vaccine was approved at US FDA in HPV infection prevention (Cervarix) (Szarewski, 2012).

Biological therapy opens a new age of cancer treatment. Biomedical Research and Therapy is a great forum for reporting and discussing the biological therapy for cancer treatment. We would like very much to encourage our readers to contribute their thoughts and comments on this important aspect of biological therapy.

## Abbreviations

EGF: Epidermal growth factor; EGFR: Epidermal growth factor receptor; GM-CSF: Granulocyte-macrophage colony-stimulating factor; HPV: Human papillomavirus; IL: Interleukin; INF: Interferon; Mabs: Monoclonal antibodies; NK: Natural killer cell.

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**Cite this article as:**

Phan, N. (2014). Biological therapy: a new age of cancer treatment. *Biomedical Research And Therapy, 1*(2):32-34.