Chapter 2
Therapeutic Approaches to Employ Monoclonal Antibody for Cancer Treatment

Salonee Martins
National Institute of Virology (ICMR), India

Purva Salvi
National Institute of Virology (ICMR), India

Sai Tejaswi Lavuri
Chalmeda Anand Rao College of Medical Sciences, KNR University of Health Sciences, India

Manjita Srivastava
National Institute of Virology (ICMR), India

Shalini Sakthivel
Department of Bio-Medical Science, Bharathidasan University, India

Muneesh Kumar Barman
Laboratory for HIV Research, National Centre for Cell Sciences, Pune, India

Kailash Chand
National Centre for Cell Sciences, Pune, India

Meenakshi Singh
Transplant Immunology and Immunogenetics Lab (HLA), ACTREC, Tata Memorial Centre, India

Subash C. Sonkar
https://orcid.org/0000-0001-7929-3464
Multidisciplinary Research Unit, Department of Biochemistry, New Delhi, India

Prudhvilal Bhukya
https://orcid.org/0000-0001-5657-9996
National Institute of Virology (ICMR), Pune, India

ABSTRACT

With the evolution of the tissue system and division of function among differentiated cells/tissues, the property of controlled cell growth also evolved in animals. It is when this very control is lost that cancers develop. The immune system's ability to distinguish between self and non-self is central to impeding cancer progression. However, cancer cells in time can develop multiple ways of escaping immune control. Even today, cancer remains a disease of baffling complexity on account of its diverse origin

DOI: 10.4018/978-1-7998-6530-8.ch002

and pathogenesis. Classical methods like surgery, radiation, and chemotherapy have failed to make the cut as idyllic therapy, especially considering the encumbering side-effects and high failure rate. Alternative therapeutic strategies that exploit the immune system itself have proved promising. One of these is monoclonal antibody therapy. In this chapter, the relationship between the immune system and cancer and various forms of immunotherapy are discussed in detail.

CANCER: AN OVERVIEW

'Cancer' is a generic term for a large group of diseases typified by the unrestrained growth and spread of abnormal cells. This is the result of a multistage process involving the transformation of normal cells. A failure to contain the progression from a pre-cancerous lesion to a malignant tumour and its subsequent spread throughout the body can prove fatal. As of 2018, an estimated 9.6 million deaths were attributed to it, making it the second leading cause of death at the global level. Around 70% of these deaths occur in low- and middle-income countries; the reason being a lack of timely and quality diagnosis and treatment. [WHO, 2018]

Onset of cancer may be initiated by inherited or acquired genetic mutations, such as translocation, chromosomal gain/loss, or changes in glycosylation; or epigenetic alterations like DNA methylation. They occur in oncogenes and tumour suppressor genes, recognized as promoters and inhibitors of cell growth, respectively [Pinho & Reis, 2015; Sharma et al.; 2010; Akhavan-Niaki & Samadani, 2013]. Besides, many risk factors have also been identified, which may contribute to the occurrence and growth of cancer. These may be changeable or avoidable e.g. dietary and behavioural factors, infectious diseases; or are unchangeable-like immune deficiencies. [American Cancer Society]

Certain terminologies must be considered while dealing with the field of oncology. A mass of anomalous cell growth is called a 'tumour'. It is can be either 'benign' if localized at the site of origin (primary site), or 'malignant'. cancerous, with ability to migrate and invade other locations of the body (secondary site) [Lodish et al., 2000]. The latter is the result of 'metastases', and is the main cause of deaths linked to cancer [Chambers & Werb, 2015].

Metastases is a multi-step cascade whereby the cancer cells from lone solid tumours acquire distinct characteristics over time; thus, enabling their escape from the primary site, followed by dissemination through the circulation and finally, colonization of distant organs. [Chambers & Werb; 2015, Lambert et al., 2017; Gonzalez et al., 2018]. Metastases remains a significant hindrance in the treatment and complete cure of cancer [Weigelt et al., 2005]. The process is summarized as follows:

First, is the invasion of the local tissue at the primary tumour site by the metastatic cancer cells. These cells secrete enzymes like matrix metalloproteinases that degrade extracellular matrix proteins, allowing them to detach from the primary site. This is followed by intravasation into blood or lymph vessels. Here, only the cancer cells that survive migrate through the blood circulation or lymphatic flow using signalling mechanisms and reach distant secondary sites. The adaptation and proliferation of these cells requires sufficient supply of nutrients and oxygen, along with waste removal. This is afforded by the induction of angiogenesis, which is regulated by a wide variety of cytokines, interleukins and growth factors [Hanahan & Weinberg, 2011; van Zijl et al., 2011; Pantel & Brakenhoff, 2004; Reymond et al., 2013; Rundhaug J. E., 2003; Nishida et al., 2006; Blanpain C., 2013].