



Colon Cancer Awareness Month: Focusing on Treatment Strategies

(Colon Cancer Awareness Month Guest Comment)

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The Colon Cancer Awareness Month is an annual celebration that is observed during the month of March, to increase awareness of colon cancer.

Colorectal Cancer (CRC) is a malignant tumour that arises from the inner wall of the large intestine (the colon). Being the 3rd most common cancer globally, CRC can gradually develop following an accumulation of different somatic or inherited changes within the genome and epigenome. These kind of transformations on pathological level can bring about the alteration of colonic mucosa into invasive cancer. The risk of CRC increases with increase in age, as well as in subjects who carry certain inherited genetic mutations, a personal or family history of colorectal neoplasia, or having inflammatory bowel disease (IBD). The challenge that the world is facing today is for the detection of even the most sensitive types of that which can be solved with the aid of biotechnology. In most of the cases, CRC is asymptomatic until its progression to advanced stages, the timely detection utilizing effective screening strategies, selection of relevant therapeutic approaches and efficient follow-up programs are absolutely necessary to turn down CRC associated mortalities. Biomarker recognition for CRC based on the individualized genotype and clinical information could simplify the classification of patients with certain types and stages of cancer to customize preventive and curative approaches. This editorial focuses on the various biotechnology techniques which can help in the early detection of CRC using antibody and antibody fragment.

Myriad approaches in the detection of colorectal cancer

CRC often seems to be a remediable and preventable disease due to its slow development unlike other solid malignancies. The stage of the tumour plays a crucial part at the time of diagnosis for patient survival. Therefore, timely detection of CRC through suitable screening strategies is a principle research goal that can lessen the incidence and mortality rates. As per the new

findings in the molecular basis of CRC, extremely sensitive and specific molecular markers can be appropriate in early diagnosis of CRC and an alternate to conventional CRC screening practices.¹

The targeted therapies have got lesser side-effects in comparison with the routine standard chemotherapy and are under preclinical study or clinical trials. Targeted therapeutics depend on customized medicine and they remarkably extend the 5-year disease free survival.²

The various facets through which diagnosis can get accelerated are the promising targeted therapeutic and drug delivery approaches in CRC including non-IG scaffold proteins, IG scaffold protein-based drugs, and aptamer.

Antibody and antibody fragment in CRC targeted therapy

For almost more than two decades, antibody-based therapy has been of the utmost important immunotherapeutic approach for cancer target therapy. Worldwide, around 45 antibody-based products are being used currently against colorectal cancers with 63 billion US dollars in total sales for the year 2013.³

Monoclonal antibody therapeutic effect occurs through different mechanisms such as blocking or inhibiting receptors for growth factors, suppressing tumor proliferation and apoptosis induction. Moreover, antibody-dependent cell mediated cytotoxicity or complement dependent cytotoxicity cause killing of tumor cells by recruitment of monocytes and macrophages. The vascular endothelial growth factor (VEGF) and the epidermal growth factor receptor (EGFR) signalling pathways are two important targets in colorectal cancers. Thus, they can be a point of focal interest during drug development and prime targets of antibody based treatment procedures.^{4,5}

The combination therapy consisting of monoclonal anti-body and chemotherapeutic

agents have shown a great anti-tumor effect and survival endpoints when compared to single agent therapy with a monoclonal antibody which shows only a little antitumor activity. A fusion form of Mabs along with toxins, radioisotopes or anticancer drugs for drug delivery against cancer cells has also been of interest to researchers. Furthermore, VEGF is a key pro-angiogenic factor that stimulates mitosis, angiogenesis and also controls the permeability of endothelial cells and inflammation. Currently, cetuximab, panitumumab, and bevacizumab are the three clinically-accessible Mabs that have been approved by Food and Drug Administration.^{4,5} Bevacizumab monotherapy or in combination with fluoropyrimidines has been used in patients with metastatic CRC.

Over the past few decades, genetic engineering has introduced a vast range of recombinant antibodies popularly known as bispecific antibodies. These next generation antibodies have the capability to recognize two epitopes on the same antigen.⁶ This type of antibody leads to increase in cell death in breast, colon, prostate, head-neck cancer cells. They also induce cell death in the carcinoma cells which are generally resistant to NK-mediated killing. In the last few years, targeting of different RNases to cancer cells has also been a topic of remarkable interest. Given their enzymatic and non-mutagenic behavior, immunoribonucleases (immunoribonucleases) have become one of the most upcoming therapeutic candidates. Moreover immunocytokine or diabody is another potent approach to cancer therapy that targets various cytokine to cancerous cells. Recently, a diabody has been designed by combination of murine IL4 and the antibody fragment F8, extra-domain A of fibronectin as a marker for tumor-angiogenesis. As an

immunocytokine with cytokine bioactivity and full antigen-binding activity, this structure leads to inhibition of tumor growth in the CT26 colon carcinoma.⁷

Early detection through screening and assessment of genetic and environmental risk factors can improve the chances of survival. Further exploration into novel approaches, including the targeted agents, immune-therapeutics, and new chemotherapy combinations, is required to improve the prognosis and clinical outcomes for the patients suffering from colorectal cancer.

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