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Popular Article

Therapeutic use of Monoclonal Antibodies in Cancer

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Introduction

A tumour is developed when a single cell multiplies quickly and uncontrollably to cause cancer. The DNA repair mechanisms that typically maintain faithful replication of DNA sequence during cell division may start to fail as the tumour cells and new mutations start to accumulate, making the prognosis worse (Strome *et al*., 2007). Cancer is still one of the leading causes of death in the developed world, and despite decades of diligent and innovative research work by scientists and clinicians, a cancer diagnosis is still far too frequently accompanied by a weakening and poisonous course of treatment. Two major issues have to be addressed if anticancer medication development is to be successful.

First, any medication that binds to a cancer cell is likely to also bind to and enter the host because many cancer cells are self-derived and do not "look" all that different from healthy cells. The idea is to identify a molecule on a cancer cell's surface that is either not expressed in normal cells or is expressed at a much lower level than it is in cancer cells, and then to develop a medication that will bind to the cancer cell preferentially (Clynes, 2006).

Second, any untargeted treatment that impacts the metabolism or growth of a cancer cell will also harm normal dividing cells since cancer cells and normally dividing cells employ the same metabolic pathways to create ATP. However, the majority of the initial generation of anticancer medications concentrate on preventing cancer cell division. All of the body's cells are exposed to drugs like daunorubicin, cis-platin, and others that obstruct cell division. The patient's wellness will

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be jeopardised by both the tumour they are carrying and the treatment they receive because these treatments also target cells that divide routinely as part of their daily functions (Sharkey *et al*., 2006).

The immune system, digestive tract, skin, and hair follicle cells all divide more often than other cells, like those in the liver, kidney, and brain, and are therefore more susceptible to these medications. This is why traditional chemotherapy causes immune system impairment, gastric problems, and hair loss. Scientists saw the creation of monoclonal antibodies as a chance to particularly target tumour cells while sparing the nearby healthy cells any harm due to their amazing ability to target a single 6- to 8-amino-acid length of a protein (Strome *et al*., 2007).

The development of mAbs that specifically target cancer cells for death while sparing their healthy neighbours is known as immunotherapy. Monoclonal antibodies are now a tool in the therapeutic toolbox and have had some degree of effectiveness. The following is a list of several modern reagents and an explanation of how they work.

1. **Competitive binding to cell surface receptors and preventing their activation**

When an antibody binds to molecules on a cell's surface, it may prevent interactions that are important for the cell to proliferate. For instance, many tumour cells become reliant on the binding of particular growth factors like epidermal growth factor (EGF) for their proliferation. Many of the mAbs currently being used in clinical settings, including erbitux, bind to the EGF receptor (EGFR) and disrupt its normal operation. A very effective medication that targets the Her-2 EGFR on cells with advanced breast cancer is Herceptin. To deliver a growth signal to the nucleus, all EGFRs must dimerize when they bind to EGF. Herceptin disrupts the EGFR signal by interfering with this dimerization reaction (Saltz *et al.*, 2008).

2. **Interference with the generation of new blood vessels**

Bevacizumab (Avastin), one of a different class of medications, inhibits the function of vascular endothelial growth factor (VEGF). VEGF interacts with blood vessel-based VEGF receptors (VEGFR1 and VEGFR2). Binding promotes the growth of new blood vessels that can be exploited to feed the developing tumour cells. Avastin binds to VEGF and stops it from communicating with its receptors, which suppresses the creation of new blood vessels and inhibits tumour development (Rivera et al., 2008).

3. **Direct binding to receptors with induction of apoptosis**

Some mAbs, like rituximab (Rituxan), have the potential to kill the cells they are meant to target by attaching to the surface of the cell and simulating the binding of organic ligands. When rituximab binds to follicular B lymphoma cells, it interferes with cell cycle control and triggers

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apoptosis (Rosenberg *et al*., 2016).

4. Induction of ADCC (antibody-dependent cell-mediated cytotoxicity)

The induction of ADCC happens when specific isotypes of antibodies bind to a cell's surface. Human IgG1 or IgG3 subclass antibodies may coat tumour cells, and natural killer (NK) cells and other immune cells' FcϒRIII molecules will bind to the Fc sections of these antibodies. The tumour cell becomes the target of released perforin and granzymes once it has been linked to the NK cell, which causes the affected cell to undergo apoptosis. Additionally, macrophages will be stimulated to phagocytose the antibody-cell complex and/or produce hazardous compounds when they recognize the Fc region of antibody clusters of the IgG1 isotype that are linked to a cell surface (Galon *et al*., 2006).

5. Induction of complement fixation

A group of serum proteins known as the complement cascade can attach (fix) to the surface of a cell as a result of IgG3 and IgG1 antibody binding (Iannello and Ahmad, 2005).

6. Delivery of toxins

Very early in the development of mAbs as clinical tools, scientists began modifying mAbs with toxins such as radioactive isotopes and cytotoxic reagents. Any object that the conjugated antibody binds can get short-range lethal radiation doses from the isotopes ^{90}Y and ^{131}I. Modified bacterial toxins like Pseudomonas exotoxin A, which has been conjugated to a mAb directed towards the CD22 molecule and has shown promise in the treatment of chemo resistant hairy cell leukemia, are among the other toxins that have been investigated in the lab and/or used in the clinic. Acute lymphoblastic leukemia and pediatric leukemia are being treated using ricin, a different bacterial toxin that has also been successfully conjugated with antibodies against CD22 and CD19 (Bailly *et al*., 2020).

The biological effectiveness of the antibodies used in cancer treatment is now being improved through in vitro modification of the tested antibodies, followed by selection utilizing phage display technology to increase the affinity and selectivity of binding to tumour cells. Others are combining mAbs with more traditional chemotherapeutic techniques, or combining numerous antibodies with various specificities to the same cell in a single treatment. One of the most dynamic and fascinating research fields at the nexus of the lab and the clinic is immunotherapeutic. Every day, new concepts are developed, and new reagents are probably to follow.

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