MONOCLONAL ANTIBODIES

(Pharmacokinetics and pharmacodynamics)

M. PHARM II SEM

BY

DR. SUNISHA KULKARNI

SOS IN PHARMACEUTICAL SCIENCES

JIWAJI UNIVERSITY, GWALIOR

INTRODUCTION

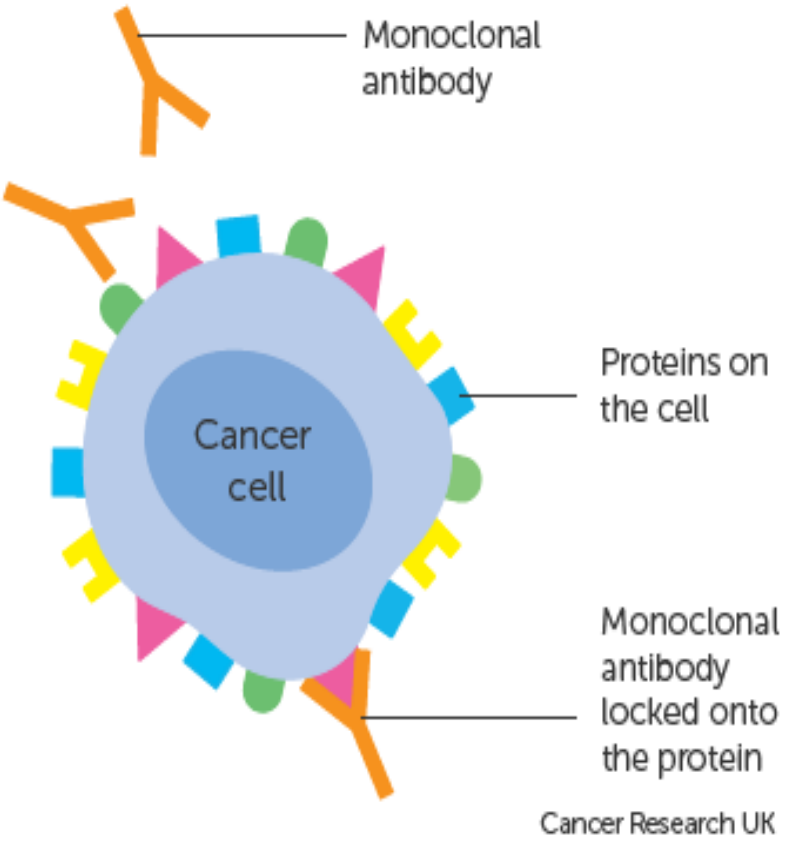
ANTIBODY - An antibody (an immunoglobulin) is a Y-shaped protein used by the immune system to identify and fight with foreign objects like bacteria and viruses. Each antibody recognizes a specific antigen unique to its target. These are produced by the B-cells of immune system in response to exposure to antigen. There are five basic kinds of antibodies. (Immunoglobulins M, G, E, D and A)

ANTIGEN — Antigens are any molecules or substances that stimulate the immune system to produce antibodies. antigens can be bacteria ,viruses or fungi that cause infection or disease. There are three basic kinds of antigens. (Exogenous, Endogenous and Autoantigens). The region of the antigen that interacts with the antibodies is called epitopes.

MONOCLONAL ANTIBBODIES

DEFINITION - Monoclonal antibodies are laboratory produced molecules engineered to serve as substitutes antibodies that can restore, enhance or mimic the immune systems attack. They are designed to bind to antigens that are in large numbers on the surface of cancer cells than healthy cells.

PURPOSE – A monoclonal antibody is made to bind to only one substance. These can be used to treat some types of cancers. They can be used alone or to carry drugs, toxins, or radioactive substances directly to cancer cells.



Human Monoclonal antibodies

Sometimes the body mistakenly identifies normal tissues as foreign bodies like bacteria, fungi and produces antibodies against the tissues. This is the cause of autoimmune conditions and the use of monoclonal antobodies to treat such conditions is called immunotherapy.

Examples of such conditions are –

- Cancer
- Rheumatoid arthritis
- Multiple sclerosis
- Ulcerative colitis
- Psoriasis
- Cardiovascular disease, etc.

Monoclonal Antibodies Drugs

Here is a list of examples of some FDA approved monoclonal antibodies drugs –

- Abciximab
- Alefacept
- Basiliximab
- Cetrolizumabpegol
- Daclizumab
- Inflectra
- Rituximab

Each drug listed above is used in treating a targeted disease for example, basiliximab treats transplant rejection while belimumab treats systemic lupus erythematosus

Pharmacokinetics

Monoclonal antibodies (mAbs) are large heterodimeric protein molecules and are composed of four polypeptide chains, two identical heavy chains and two light chains. mAbs have complex pharmacology: pharmacokinetics and pharmacodynamics depend on mAb structure and target antigens.

mAbs targeting soluble antigens often exhibit linear pharmacokinetic behavior, whereas mAbs targeting cell surface antigens exhibit non-linear behavior due to receptor-mediated clearance.

Distribution-The extent of mAb distribution relies upon rates of extravasation in tissues and distribution in the interstitial space, antibody binding to the tissue components such as cell surfaces, and clearance from the tissue, including intracellular uptake degradation.

Pharmacodynamics

PD refers to pharmacological effects elicited in the body by a drug. mAbs pharmacodynamics are often indirect, with delayed clinically relevant outcomes. So, during clinical development , studies must be carefully planned to account for complexities specific to each agent. Selection of a starting dose for human studies is difficult. Optimal dose selection should ensure uniform mAb exposure across all individuals.

Depending on the mechanism of action of the therapeutic mAb, types of PD responses include inhibition of ligand-receptor interactions by binding of mAbs to soluble targets, down modulation of target antigen by elimination of target cells. In animal or human studies, PD measrements can be directly or indirectly linked to a clinical endpoint.

Conclusion

mAb therapeutics are an important and rapidly growing class of therapeutic agents. Selecting the right mAb is very important for its clinical success and depends on early understanding of its PK/PD. Compared to small molecules, mAbs have unique characteristics that make their PK/PD quite complex. Proper understanding of its PK/PD characteristics including availability at the site of action, target occupancy and functional pharmacological activity are important in improving its clinical success.