Journal of Pharmacy and Pharmaceutical Sciences

Open access Perspective

Antibody Based Therapeutics is at the Center of Drug Discovery

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INTRODUCTION

In humans 5 classes of Abs (interchangeable with immunoglobulins or Igs). IgG, IgA, IgD, IgE, IgM are secreted as glycoproteins by activated B cells. All human Igs have a basic monomeric 'H2L2' structure consisting of two heavy (H) chains and two light (L) chains. Each H chain is paired with an L chain. The H chains define the class of Igs (represented by the Greek letters γ, α, δ, ε, μ), while the L chains consist of either κ or λ isoforms. Each Ig has two defined regions. Antigen-binding region (Fab) in the top half and crystallizable fragment (Fc) in the bottom half. The Fc region is composed entirely of H chains, whereas the Fab region is composed of both H and L chain domains. Mouse-derived antibodies elicited unwanted immune responses in humans. Reduced effector function in humans also limited Ab potency in mice. In the last 2-3 decades, various technologies (display technology, humanization, and transgenic mice) have enabled the generation of antibody drugs more suitable for the human immune system. Antibody (Ab)-based therapeutics is therefore at the center of drug discovery, with antibodies being the fastest growing class of drugs.

DESCRIPTION

Antibody production in the body begins with the expression of IgM and IgD on the surface of naive B cells in response to antigenic stimulation. High-affinity IgG is generated through a process of hyper mutation and class switching. Human IgG is further divided into IgG1, IgG2, IgG3, and IgG4 isotypes. The Fab domain is composed of two variable domains and two constant domains, with the two variable domains forming a variable fragment (Fv). The Fv provides the Ab's antigenic specificity and the constant domains provide the structural framework. Each Fv contains three hyper variable loops known as complementarity determining regions (CDRs). In theory, it is the hyper variability of the CDRs that allows Abs to recognize an unlimited number of antigens.

The smallest antigen-binding fragment that retains the entire antigen-binding site is the Fv fragment, which consists only of the variable (V) region. A soluble and flexible amino acid peptide linker is used to connect the V region with an scFv (single chain fragment variable) fragment to stabilize the molecule, or a constant (C) domain is added to the V region to form a Fab fragment (fragment, antigen binding). scFv and Fab are common fragments that are readily produced in prokaryotic hosts. Expression of recombinant monoclonal antibodies is an established production technique based on cloning a synthetic DNA sequence of the antibody of interest into an expression vector. These plasmid vectors are then transiently or stably introduced into expression hosts to produce recombinant antibodies.

CONCLUSION

Antibodies have been excellent tools in laboratory research for many years. MAbs were developed about 25 years ago and have extended the scope of antibodies to *ex vivo* diagnosis of a wide range of diseases. Scientists are increasingly exploiting their high specificity and selective binding capacity by using them in immunotherapy. The advent of hybridoma technology has made MAbs endlessly available. A large number of MAbs generated using this technique have helped identify and analyze tumor-associated antigens from several different human melanomas, carcinomas, lymphomas, and leukemias. The available literature to date reports over 100 unique MAbs against human cancers. MAbs are produced using hybridoma technology. This method provides an unlimited supply of homogeneous antibodies with the desired specificity.

ACKNOWLEDGEMENT

The author is grateful to the journal editor and the anonymous reviewers for their helpful comments and suggestions.

CONFLICT OF INTEREST

The author declared no potential conflicts of interest for the research, authorship, and/or publication of this article.

Received:	O3-October-2022	**Manuscript No:**	IPIPR-22-14542
Editor assigned:	05-October-2022	**PreQC No:**	IPIPR-22-14542 (PQ)
Reviewed:	19-October-2022	**QC No:**	IPIPR-22-14542
Revised:	24-October-2022	**Manuscript No:**	IPIPR-22-14542 (R)
Published:	31-October-2022	**DOI:**	10.21767/IPIPR.22.6.23

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Citation Salvator C (2022) Antibody Based Therapeutics is at the Center of Drug Discovery. J Pharm Pharm Res.6:23.