Acta Scientific Biotechnology

Volume 3 Issue 5 October 2022

Short Communication

Antibody Engineering

Rajeshwar Reddy Kasarla[1]*, Rahul Reddy Kasarla[2] and Sruthi Reddy Thummala[3]

[1]Professor and Head, Department of Microbiology, Universal College of Medical Sciences, Bhairahawa, Nepal

[2]Consultant Orthopaedic Surgeon, Medivison Super Speciality Hospital, Hyderabad, India

[3]Assistant Professor, Department of Obstetrics & Gynaecology, Gandhi Medical College, Hyderabad, India

***Corresponding Author:** Rajeshwar Reddy Kasarla, Professor and Head, Department of Microbiology, Universal College of Medical Sciences, Bhairahawa, Nepal.

Received: September 26, 2022

Published: September 28, 2022

Introduction

The discovery of hybridoma technology by Kohler & Milstein for the production of monoclonal antibodies (1975) revolutionized Medicine and biological sciences by enabling the use of highly specific monoclonal antibodies in basic research, diagnostic applications, and therapeutic molecules. Antibody engineering is a new area of biotechnology which combines molecular biology and recombinant protein production [1].

Chimeric antibodies and humanization

Antibody engineering started with chimerization in 1984. Chimeric antibodies are produced by combining the variable domain of an antibody from an animal like mouse with the constant domain of an antibody from human being. The discovery techniques developed in 1990s and onwards for the production of humanized antibodies include transgenic mice, phage display, and B cell sequencing [2].

Phage display

A gene coding for a protein is introduced into a phage coat protein gene, allowing a direct link between the DNA sequence and protein [3].

Antibody fragments

Following the advent of antibody engineering techniques, researchers started looking at generation and production of recombinant antibody fragments for a cleaner and easier production process [4]. Three main fragments were developed that became the building blocks of many alternative formats: i. Recombinant Fab, ii. Single chain variable fragment (ScFv), iii. There are two types of single domain antibodies (sdAb) or nanobodies. V-NAR from cartilaginous fishes such as sharks and VhH from camelid species [5].

Enhancing half-life

In certain situations, one of the key advantage of IgG as therapeutic is the long serum half-life. Serum half-life is dependent on protein size, glycolysation, receptor mediated clearance, and FcRn mediated recycling. A number of mutations have been reported for enhanced half-life and could lead to reduced frequency of dosing [6].

Bispecific antibodies

They can simultaneously bind to two different antigens at the same time. Bispecific antibodies are used in the treatment of cancer [7]. Catumaxomab, the first bispecific, was approved for use in Europe in 2009 for malignant ascites, but later withdrawn in 2017.

Other FDA approved drugs include Blinatumomab for lymphoblastic leukemia, Emicizumab for hemophilia, Amivantamab for non-small-cell lung cancer, and Faricimab for macular degeneration and diabetic macular edema [8].

Heavy chain heterodimerization

In this technique, CH3-CH3 interface responsible for heavy chain pairing [9]. Quadroma and knobs-into-holes technologies are available.

Antibody drug conjugates (ADCs)

Antibody–drug conjugates (ADC) combine monoclonal antibodies specific to surface antigens present on particular tumor cells with highly potent anti-cancer agents linked via a chemical linker. The monoclonal antibody binds to specific proteins or receptors found on cancer cells. The linked drug enters these cancer cells and kills them without harming other cells, and used for the treatment of cancer [10].

Fc fusion proteins

Non-antibody proteins suffer from short serum half-life, in the range of a few minutes to hours. Fusion proteins are proteins created through the joining of two or more genes which originally coded for separate proteins. Translation of this fusion gene results in a single polypeptide with functional properties derived from each of the original proteins [6].

Immunokines

Antibody-cytokine fusions (immunokines) are being developed with the antibody targeting tumor associated antigens. Cytokines can act as modulators of the immune system, some such as IFN-alpha and IL-2 are approved therapies [11].

Conclusion

Antibody engineering is an emerging branch of biotechnology which combines molecular biology and recombinant protein production and has wide range of applications in medicine for the production of therapeutic drugs and molecules.

Bibliography

1. Saeed AFUH., *et al*. "Antibody engineering for pursuing a healthier future". *Frontiers in Microbiology* 8 (2017): 495.
2. Jennifer Maynard and George Georgiou. "Antibody engineering". *Annual Review of Biomedical Engineering* 2 (2000): 339-376.
3. Ledsgaard L., *et al*. "Basics of antibody phage display technology". *Toxins (Basel)* 10.6 (2018): 236.
4. Asaadi Y., *et al*. "A comprehensive comparison between camelid nanobodies and single chain variable fragments". *Biomarker Research* 9 (2021): 87.
5. Wesolowski J., *et al*. "Single domain antibodies: promising experimental and therapeutic tools in infection and immunity". *Medical Microbiology and Immunology* 198.3 (2009): 157-174.
6. Saunders KO. "Conceptual Approaches to modulating antibody effector functions and circulation half-life". *Frontiers in Immunology* 10 (2019): 1296.
7. Karen J Vincent and Mauro Zurini. "Current strategies in antibody engineering: Fc engineering and pH-dependent antigen binding, bispecific antibodies and antibody drug conjugates". *Biotechnology Journal* 7.12 (2012).
8. Sliwkowski MX and Mellman I. "Antibody therapeutics in cancer". *Science* 341 (2013): 1192-1198.
9. Schaefer W., *et al*. "Heavy and light chain pairing of bivalent quadroma and knobs-into-holes antibodies analyzed by UHR-ESI-QTOF mass spectrometry". *MAbs* 8.1 (2016): 49-55.
10. Beck A., *et al*. "Strategies and challenges for the next generation of antibody-drug conjugates". *Nature Reviews Drug Discovery* 16 (2017): 315.
11. Patrick Chames and Daniel Baty. "Antibody engineering and its applications in tumor targeting and intracellular immunization". *FEMS Microbiology Letters* 189 (2000): 1-8.