Monoclonal antibody

A monoclonal antibody is an immunoglobulin (antibody) derived from the production of a **single clone of activated B-lymphocytes** or their effector cells (plasma cells) upon contact with a particular antigenic epitope. These antibodies are widely used today in both basic research and medicine to tag specific molecules.

Occurrence in the human body

In the human body, a response to an antigen through an antibody immune response normally produces a number of activated B-cell clones (which differentiate into plasma cells). Thus, this reaction results in the production of a mixture of different immunoglobulin molecules. This means that it is a polyclonal response[1] (http://lfp.cuni.cz/histologie/education/guides/ihc/node13.html) (from multiple antibody clones). However, **under pathological circumstances**, there may be a situation where the concentration of certain monoclonal antibodies predominates and other smaller antibody clones are suppressed due to this overproduction. It is either **chronic inflammatory stimulation** or **plasma cell tumour**, so-called **plasmacytoma (myeloma)**. However, chronic inflammatory stimulation involves antibodies derived from benign B-cell clones. In the second case, the **tumour-altered plasma cell** breaks down-regulation and begins to divide uncontrollably, but does not lose the ability to produce a particular antibody clone (depending on the antigen response). The number of altered plasma cells thus grows and thus the production of monoclonal antibodies produced by them. As a result, these immunoglobulins of myeloma origin outweigh other antibodies in the body. This knowledge has been used in modern research for the artificial production of monoclonal antibodies and their subsequent analytical, diagnostic and therapeutic use.

Procedure for the artificial production of monoclonal antibodies

Of course, it would be simplest if we were able to cultivate the desired individual clones of activated B-lymphocytes and then obtain a number of different antibodies from them. The problem, however, is that the lymphocytes themselves grow very slowly in culture and are also rapidly extinct. In contrast, the above-mentioned tumour cell plasma form (myeloma cell) has ideal properties for in vitro culture. Like any tumour cell, it divides easily and quickly and has a long lifespan. Myeloma cells are obtained in laboratory conditions by induction in experimental animals after intraperitoneal injection of mineral oil. Mineral oil acts as a carcinogen in experimental animals and some plasma cells turn into myeloma tumour cells, which can then be easily harvested and cultured. However, they do not yet produce the desired monoclonal antibodies. They still need to be fused to the desired B-cell clone. This fusion results in a hybrid cell, which is typically called a **hybridoma**. The hybridoma retains the properties of both myeloma cells and B-lymphocytes, divides rapidly, is almost immortal, and produces antibodies to the B-lymphocyte used in the fusion. Here we present a brief process for the production of hybridoma cells, provided that we have already prepared a suitable myeloma cell line, i.e. without γ enzyme (HGPRT), which catalyses purine metabolism:

1. The required B-cell clone is obtained again from an experimental animal, in which we elicited an immune response by injection of a specific antigen and thus, of course, the activation of B-cells and the subsequent production of antibodies.
2. B-lymphocytes are usually collected from the spleen or other lymphatic organs of the animal used. However, we must take into account that it is not a single clone of B-lymphocytes specific for our antigen.
3. Already outside the body (in vitro) we induce a fusion of a **line of myeloma cells without HGPRT** and extracted B-lymphocytes using propylene glycol.
4. **Hybridomas** are created. However, the solution of propylene glycol and other reactants will contain, in addition to hybridomas producing the desired monoclonal antibodies, some unfused cells (both lymphocytes and myeloma cells) and hybridomas producing other than the desired immunoglobulins. Unfused lymphocytes (in this case, more plasma cells) are very competitively weak in vitro, they do not divide and die.
5. We transfer the cell culture to a medium containing hypoxanthine (adenine derivative), aminopterin (the folic acid antagonist in the body) and thymidine (HAT-medium). Unfused myeloma cells also die as a result, because they do not contain the HGPRT enzyme and are thus unable to utilize the purine derivatives contained in the HAT nutrient medium. In contrast, hybridoma cells, due to the proportion of normal lymphocytes in the genome, contain a sequence for the HGPRT enzyme and thrive and proliferate on the HAT medium.
6. Finally, using special tests from culture, we only separate hybridomas producing only one clone of antibodies - monoclonal antibodies.

Use of monoclonal antibodies

- **For analytical purposes**: by binding monoclonal antibodies to a certain protein (here it acts as an antigen), we are able to determine its quality and quantity in the examined sample,
- **For diagnostic medical purposes**: they are able to bind specifically to antigens causing various diseases (ELISA...),
- **For therapeutic purposes in medicine**: certain cancers can be treated with tumour-specific antibodies to which we have covalently attached toxins or an emitter. This selectively kills tumour cells and minimizes damage to surrounding tissue.

Links

Related Articles

- Specific immunity
- Use of monoclonal antibodies in medicine

External Links

- Monoclonal antibodies (Wikipedia)

Monoclonal Antibody Production (https://www.youtube.com/watch?v=7ymKofaHCoY) - YouTube presentation

References

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