Application of Problem-based Learning on Monoclonal Antibody Preparation

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Abstract: Problem driven teaching method is a teaching method based on constructivism theory, which is student-centered, problem driven and practical ability to solve problems as the main goal, breaking the traditional mode of instilling knowledge. Constructivism theory holds that knowledge is constructed by cognitive subject through the interaction of new and old experience. This paper mainly discusses the application of problem driven teaching method in the teaching of monoclonal antibody preparation. Problem driven teaching method can promote students' thinking and expand their thinking. Driven by problems, it can mobilize students' initiative, cultivate students' thinking and innovative spirit, and train students' ability to analyze and solve problems.

1. Introduction

The problem driven teaching method takes solving problems as the main line, students as the center, problems as the driving force, and cultivating learners' problem awareness, critical thinking skills and practical ability to solve problems as the main goal [1]. Students construct knowledge according to their own knowledge background and re recognize and understand the information. The design of problems should be enlightening, guiding and exploratory. Through the in-depth exploration of problems, students' thinking mode should be changed, new knowledge and old knowledge should be integrated to construct new knowledge [2]. Based on students' existing knowledge and experience, teachers create a problem system in line with students' experience to help students construct knowledge.

Monoclonal antibody preparation is an important learning content in biotechnology and pharmacy. It is the research hotspot of disease diagnosis and targeted therapy in precision medicine [3, 4]. This paper will explore the application of problem driven teaching method in the teaching of monoclonal antibody preparation, combine knowledge points with problems, guide students to study and analyze independently, master relevant key and difficult points, and cultivate students' ability to analyze and solve problems.

2. Analysis of driving problems based on key and difficult points

According to the principle of driving teaching method, the corresponding problems should be designed based on the key and difficult points in the teaching of monoclonal antibody preparation. The knowledge goal of monoclonal antibody is to master the concept, preparation process and principle of monoclonal antibody; The ability goal is to use the required knowledge of cells to analyze the theoretical basis of monoclonal antibody preparation and screening; The emotional goal is to learn scientists' innovative spirit and scientific methods, improve students' innovative consciousness and cultivate the ability to explore knowledge. Key points: understand the process and principle of monoclonal antibody preparation, including: (1). obtain B cells that can produce antibodies (2). B cells producing monoclonal antibodies fuse with tumor cells (3). Screening cells that can produce monoclonal antibodies and infinite passage. The difficulty is the principle of screening fusion cells producing monoclonal antibodies.

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3. Design and implementation of driving problem chain

The setting of questions is the key to the problem driven teaching method. The goal and logic of raising questions will have a certain impact on the teaching effect of the problem driven teaching method. The following will describe the design of problem driven Teaching in the course of "monoclonal antibody preparation".

3.1 Cases

Problem driven teaching requires students to learn from practical problems. In teaching, by introducing the practical application scenario of monoclonal antibodies, students are prompted to think, summarize the role of monoclonal antibodies, stimulate students' enthusiasm for further learning how to obtain monoclonal antibodies, so as to introduce the key points of the course. Firstly, we introduce the cases of acute rejection after transplantation. According to the learned immune knowledge and life experience, the students can quickly infer that the body has an immune response. Introduced in 1986, OKT3, the world's first monoclonal antibody drug, was approved by FDA and applied to the acute rejection after organ transplantation. Then we introduced the clinical application of the chimeric monoclonal antibody rituximab and the monoclonal antibody infliximab of tumor necrosis factor A. students summarized the role of monoclonal antibody drugs in combination with case analysis, which has great application prospects in tumor, autoimmune diseases and inflammation.

3.2 Concept introduction and related knowledge paving

After the introduction of the course, the concepts of antibody and monoclonal antibody are directly given to clarify the key points that students will learn, especially to help them think about a series of subsequent problems. Students think according to problems, actively construct new knowledge through the combination of new knowledge and original knowledge, and strengthen their understanding of concepts. Monoclonal antibodies are secreted by B cell clones that recognize antigen epitopes and target immunoglobulins of an antigen determinant. Through the introduction of the concept, students can know that monoclonal antibody is produced by B cells. Pave the way for the thinking of the following problems.

In the chapter before learning monoclonal antibodies, students have learned the course of cell culture and know the characteristics that cancerous cells can be subcultured indefinitely. On this basis, the teacher further introduces the method of cell fusion. It guarantees students to call the existing knowledge to find solutions in problem driven teaching, and further build new knowledge [5] on this basis.

In the problem driven teaching method, the difficulty and progressive logic of problems are very important. The teaching difficulty of this course is the principle of monoclonal antibody screening. This part of the problems need the knowledge of molecular biology in the second half of the course. Therefore, teachers need to help sort out the corresponding knowledge points to facilitate students to think and solve problems on this basis. The students have learned DNA replication before, and have known the principle of DNA replication. They are familiar with the corresponding professional terms, but they have not been exposed to the knowledge of DNA replication pathways required in this chapter. Therefore, the teacher needs to introduce these knowledge points. On the basis of knowing the DNA replication pathways, the students can further complete the problem thinking and active analysis. Complete the construction of screening knowledge.

4. Design of driving problem chain

4.1 Think about how to obtain antibody producing B cells

The traditional method to obtain antibodies is to activate immune cells with antigens, which are synthesized and secreted by differentiated and mature terminal B lymphocytes plasma cells. They can specifically bind to the antigens stimulated and have immune function. One plasma cell produces only one antibody. Subcutaneous injection of antigen into animals can produce antibody B

cells, but due to the diversity of antigen determinants, a single antibody B cell cannot be obtained, which needs to be isolated and purified.

4.2 Analyze why the obtained B lymphocytes cannot be continuously cultured by cell culture

B lymphocytes are short-lived cells. The cell culture method cannot make B cells subculture indefinitely, while myeloma cells have the characteristics of infinite subculture. Students can construct the methods that can be obtained according to their mastered knowledge, and combine the teacher's knowledge of cell fusion technology to fuse the myeloma cells that can be subcultured indefinitely with B cells to further construct the method of obtaining monoclonal antibodies. It is easy for students to think and participate actively, which is in line with constructivist cognitive learning theory.

4.3 How many cells are there in the culture medium after cell fusion

The design of this problem reminds students that either two cells fuse to get the target cell, and guides students to actively analyze the possible situation. Because cells are microscopic, when two kinds of cells are co cultured to promote fusion, the contact between cells is random, so there will be fusion cells that do not occur, or the fusion of the same kind of cells. Only the fusion of two kinds of cells can produce hybridoma cells producing monoclonal antibodies with infinite generation specificity.

4.4 How to screen monoclonal antibody fusion cells

Screening fusion cells is the key and difficult point. When constructing this part, we need to carefully study the knowledge foreshadowing done by the teacher, analyze the impact of culture components on cell survival in combination with the existing knowledge, and complete the screening design. In mammalian cells, there are two different pathways for DNA precursor biosynthesis, the main pathway and the supplementary pathway. A major pathway for de novo DNA synthesis from phosphoribosyl, amino acid and glutamate. This pathway can be blocked by aminopterin (a), an antagonist of folic acid. However, if the nucleotide "precursors" hypoxanthine (H) and thymine nucleotide (T) exist in the culture, the cells can also synthesize nucleotides through another remedial pathway, but the supplementary pathway requires the existence of hypoxanthine guanine phosphoribosyl transferase (HGPRT) and thymine nucleotide kinase (TK).

B lymphocytes have both synthetic pathways, but do not divide and increase in value. There is no supplementary pathway in myeloma cells. In hat medium, aminopterin (a) blocked the main pathway of DNA synthesis. Although B lymphocytes had supplementary pathway, they could not grow; Myeloma cells do not have HGPRT and TK, so they cannot grow. Therefore, only the hybridoma cells fused by the two cells can grow all the time in hat medium, select the hybridoma cells that can grow and reproduce for a long time, and use the supplementary pathway of B lymphocytes and the continuous reproduction ability of myeloma cells to produce monoclonal antibodies.

4.5 Draw a road map for the synthesis of monoclonal antibodies according to the analysis

After the previous analysis, the students have constructed the method to obtain monoclonal antibodies. According to the problem driven teaching method mode, it is necessary to summarize a certain mode and promote it [6]. Students will integrate the solutions driven by the previous problems into a complete circuit diagram as a conventional method for the preparation of monoclonal antibodies, which can be further popularized.

4.6 Application expansion of monoclonal antibodies

After class assignments are given to students to think about how monoclonal antibodies called biological missiles can carry out targeted anti-cancer. Students need to carry out literature retrieval, create application scenarios, analyze how monoclonal antibodies can carry out targeted treatment in combination with radioisotopes and chemical drugs, further understand the significance of monoclonal antibodies and obtain the ability to solve problems [7].

5. Innovative thinking and scientist spirit

Under the problem driven teaching, students constructed monoclonal antibody hybridoma cells. This initial idea was put forward by British scientists Milstein and Kohler in 1975, and therefore won the Nobel Prize in 1984. In the study of antibody gene mutation, Kohler needed a cell that could not only grow in vitro, but also continuously produce a single specific antibody to a known antigenic substance, but there was no such cell at that time. Therefore, he obtained monoclonal antibody by using the cell fusion method developed at that time and completed the incredible idea at that time. It is the imagination, judgment and rich knowledge and experience of these two scientists that successfully realized this important experiment and promoted the development of the whole biomedical research. Encourage students to pay attention to the accumulation of theoretical knowledge and practice ability at the same time, so as to have sharp thinking and continuous innovation. The spirit of scientists is also an important part of cultivating students' comprehensive quality in the driving teaching method. The problem setting of this paper is also the process of basic scientific invention. Under the guidance of teachers, students are guided to complete the construction of new knowledge.

6. Analysis of teaching effect and Reflection on existing problems

Problem driven teaching method improves students' enthusiasm for active learning. Students actively explore and analyze problems, and finally put forward solutions [8]. In the student-centered constructivist teaching, combining the problems with the key and difficult points of teaching and designing the problems that meet the students' knowledge background is the key to the design. The difficulty of the problems should be greater than the level that students can complete independently, but it should also ensure that students can achieve through thinking and efforts under the guidance of teachers. It can arouse students' interest and effectively promote the construction of knowledge. In the process of students' thinking and discussion, teachers should pay attention to observing students' reactions, properly ask questions and guide students' discussion results, and help students establish solutions [9].

7. Conclusion

In this process, it produce a pleasant sense of achievement and help students improve their interest in learning. In the process of analyzing and discussing questions, students communicate more freely, especially those who do not like to answer questions at ordinary times are also very positive, and the students' response effect is better than that of teachers. Driven by problems, students connect with new knowledge and actively complete the integration of old and new knowledge, which shows that the problem driven teaching method can well improve students' interest in learning, promote students' thinking and expand their thinking. Therefore, problem driven teaching can well promote students' understanding and application of knowledge, improve their learning initiative and enthusiasm, exercise their ability to solve problems, and cultivate students' ability of thinking and innovation.

References

[1] Fu Dongmei, Research and implementation of problem driven teaching method. University Education, 2014, 2: 1-32.

[2] Fan Hongying. Application of "problem driven" teaching method in interdisciplinary curriculum teaching. Journal of Higher Education, 2015, 8: 33-34.

[3] XIAO Xiao, FENG Huijuan, GAO Chunfang. Progress in the clinical application of monoclonal antibody drugs, 2019, 34(5): 466-471.

[4] ZHAO Chen-xi, HU Zhuo-wei, CUI Bing. Recent advances in monoclonal antibody-based

therapeutics. Acta Pharmaceutica Sinica, 2017, 52 (6): 837-847.

[5] Hong Aiying, Liu Shufan. The influence of Constructivism on Autonomous Learning Theory. Journal of educational institute of Jilin province, 2014, 5: 35-36.

[6] Hu Duanping, Li Xiaogang, Yang Xianghui. Research and practice of problem driven teaching method. Studies in college mathematics, 2013, 16: 80-82.

[7] Wang Tao, Li Chenhong, Yang Xiaocui. An empirical study on problem-based learning (PBL) teaching method to promote college students' learning efficiency. University Education, 2019, 2: 11-16.

[8] Liu Yanhui, Sun Haotian. PBL Teaching and Training of Students' Clinical Thinking Ability. China Continuing Medical Education, 2020, 12(24): 18-20.

[9]Wang Xiaoliang, Yang Shaobin, Meng Chao, et al. Discussion on problem driven receptive teaching and learning model. Education Teaching Forum, 2018, 26:195-196.