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Integration of Biochemistry and Molecular Biology as a System Curriculum in Chinese Medical Undergraduates

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Abstract: The teaching and evaluation of biochemistry and molecular biology are generally performed as two independent curricula at the universities in China. However, the knowledge of these two courses is very closely linked. At Ningbo University, we have undertaken a program to integrate of BMB as a system curriculum. The efforts have included theory teaching and experimental teaching in the manner of combination of form and content. In this study, classical references reading, small group discussion and student research and training program were also employed. We evaluated, the student learning ability and the lecturer teaching effect via question and answer and survey. The data showed increases in student performance on BMB-related integrative problems and more interest in learning BMB curriculum and doing relevant research work. Furthermore, the total time of teaching BMB was shortened by comparing with that of two independent courses. The faculty perceived an increased awareness of the across of multi-disciplinary among the students in their courses.

Key words: Biochemistry, molecular biology, integrative teaching, classical reference reading, BMB-related, multi-disciplinary

INTRODUCTION

Since, the molecular structure of nucleic acids was discovered by Watson and Crick in 1953, the molecular biology has rapidly developed in the past five decades. More and more novel concepts and disciplines teem in this fleetly changing field (Papavassiliou, 1999; Jamieson, 2001). In China, the molecular biology was set as an independent curriculum in the undergraduate medical education in early 1990s. At that time, there was not a unified textbook or material for molecular biology teaching. The universities or institutions offered unevenly the contents and the requirements of this course were usually not the same. This subject was employed as an elective or compulsory course in Chinese medical schools. However, more and more educationists and scientists have to be conscious of such a fact that the knowledge of molecular biology is very closely linked to that of biochemistry. Hence the teaching mode that Biochemistry and Molecular Biology (BMB) were taught separately for the medical undergraduates was not adapted to the requirements for the modern medicine education (Smith and Hundert, 1999; Gamulin, 2003; Trelstad, 2004).

As the developments in BMB emerged, medical students were encouraged imminently to solve an integrative question which covers BMB especially a clinical medicine-related basic BMB problem (Sykiotis and Papavassiliou, 2005; Anderson *et al*., 2008). On condition that BMB were introduced separately to the students at the same semester, the departments of BMB in medical colleges were often hard-pressed to cover the vast topics within one term. On the one hand, the same knowledge between BMB may be mentioned repeatedly in these two courses on the other hand, little opportunity and time were left for the students to question or present their opinions to the concepts they have learned during lectures. As a result, the faculty complained that they have to spend much more time in the two separate courses. Moreover, the students found it difficult to relate a clinical condition with its basic BMB principles during their clinical training.

In the past, as a change, different methods such as topic-based discussion and oral presentations have been carried out during the BMB teaching in Ningbo University. The students were asked to explain a physiological phenomenon or a disease with its BMB principles through an oral presentation in the classroom. We found that oral presentation was an effective revision exercise for medical undergraduates. In the meantime, we found it was difficult to apply a biochemical principle

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or molecular biological one to explain some physiological phenomena or complicated diseases. With the development of molecular biology, we have entered the era of molecular medicine. Not only biochemical principles but also molecular biological ones are employed in the explanation of pathogenesis and clinical therapeutic bases for diseases.

Here we describe the experience of combined biochemistry with molecular biology as a system curriculum in medical undergraduates. The students were asked to read the classical research papers to do small group discussion to participate student research and training program and to solve the integrative questions during their lectures. The assessment of this teaching reform suggests achieving the goals of integrating biochemical and molecular biological points and increasing student ability to address BMB-related integrative questions. Faculties have also noted that students are better prepared to solve BMB-based clinical problems in their research.

MATERIALS AND METHODS

Integration of biochemistry and molecular biology as a system curriculum: We constructed this system curriculum for BMB on the different topics such as the structures and functions of protein, nucleic acid and enzyme, the metabolisms of carbohydrate, lipid, nucleotide and amino acid, DNA, RNA and protein biosynthesizes, gene expression and regulation, genomics and proteomics, recombinant DNA technology and genetic engineering. The students were asked to learn all of these topics for BMB as a system course in the 3rd semester. In addition, basic biochemical and molecular methodologies including protein preparation, SDS-polyacrylamide gel electrophoresis, gene isolation, recombinant DNA technology and genetic engineering are introduced.

Classical references reading: We selected seven classical research papers for reading on different topics. These references included the amino-acid sequence in the glycyl chain of insulin, the molecular structure of nucleic acids, the genetic regulatory mechanisms in the synthesis of proteins, the potent and specific genetic interference by double-stranded RNA and the chemical synthesis of crystalline bovine insulin, etc.

Small group discussion: At the end of this course, the students were encouraged to prepare different objective type questions on the following integrative topics which cover knowledge of BMB or classical references. Then they presented their questions in turn and discussed the answers in the group discussion. Finally they were required to make a speech about their answers or findings on some topics.

Student Research and Training Program (SRTP): The Student Research Training Programs (SRTPs) were designed as some research projects which covered the knowledge of biochemistry, cell and molecular biology. Students who joined in it were required to finish them independently.

Firstly, faculties instructed them to read main references about the research topics and design the experimental procedure of some program. Then they did all the experiments and discussed the results with their mentors. Finally, they were encouraged to publish their research work in a peer-reviewed journal.

Assessment of learning and teaching effectiveness: Student ability to answer BMB-related questions was assessed using a ten-question multiple choice test.

Content questions used to assess the BMB-related integrative problem: You clone a human gene which encodes Cyclin Dependent Kinase 2 (CDK2) and want to express it in *E. coli*. To do this you would NOT to…

- Amplify *cdk2* gene from human genomic DNA
- Isolate total RNA from some human tissue and amplify *cdk2* gene from total RNA by RT-PCR
- Subclone *cdk2* gene into a appropriate vector and transfect the recombinant plasmid into *E. coli* cells
- Express CDK2 protein in *E. coli* cells under appropriate conditions
- Purify protein from *E. coli* cells and make them to form native conformation

To determine the quality of a food protein, the easiest evidence is:

- The content of nitrogen
- The content of total amino acids
- The category of total amino acids
- The category and content of human essential amino acids each of above

All of the following are true about prokaryotic and eukaryotic DNA replication except:

- Replication is semi-conservative in both systems
- Replication is continuous on one strand and discontinuous on the other in both systems
- RNA primers are used on the discontinuous strand in both systems
- The size of Okazaki fragments in the prokaryotic system is the same as in the eukaryotic system
- The rate of replication in prokaryotes is faster than in eukaryotes

Which of the following general statements about eukaryotic transcription is incorrect:

- RNA pol II is most sensitive to aminitin
- RNA pol I transcribes nuclear DNA into rRNA precursors
- RNA pol III transcribes mRNA precursors
- The function of polyA at the 3' end may be to increase mRNA half-life
- None of the above

Which of the following is a characteristic of a eukaryotic enhancer element?

- It occurs in the promoter sequence
- It is often used in translation regulation
- Its sequence can still function if its orientation is reversed
- It is always within the coding portion of the gene
- None of the above

Which of the following can inhibit both prokaryotic and eukaryotic translation?

- Penicillin
- Diphtheria toxin
- Ricin
- Cycloheximide
- Interferon

Which of the following is a possible base sequence for the DNA strand segment which is transcribed to give the mRNA for the tripeptide Ile-Cys-Phe? (Use the following codons: Ile, AUC; Cys, UGC and Phe, UUU):

- 5'-TAGACGAAA-3'
- 5'-AAAGCAGAT-3'
- 5'-AUCUGCUUU-3'
- 5'-AAAGCAGAU-3'
- None of the above

Which of the following components of the rough endoplasmic reticulum is composed of 6 polypeptides and a 300 nucleotide RNA molecule:

- The signal peptidase
- The signal sequence
- The docking protein
- The signal recognition particle
- None of the above

Dihydrofolate Reductase (DHFR) is required for synthesis of Tetrahydrofolate (THF), tetrahydrofolate is required for synthesis of 5, 10-methylene THF and N10-formyl THF. Methotrexate is an inhibitor of Dihydrofolate Reductase (DHFR). In mammalian cells treated with methotrexate, de novo synthesis of which compound below will NOT be inhibited:

- Guanosine triphosphate
- Deoxythymidine monophosphate
- Inosine monophosphate
- Cytidine triphosphate
- Adenosine monophosphate

Which of the following statements about eukaryotic DNA structure is incorrect:

- C_0t analyses demonstrate that eukaryotic DNA has highly repetitive, middle repetitive and unique DNA sequences
- Alu sequences are clustered near the centromere
- rRNA genes are examples of middle repetitive DNA
- Both intron and exon sequences are found within protein coding genes
- None of the above

The first two questions asked students to solve some BMB-specific questions such as how to clone and express a eukaryotic gene in a prokaryotic organism which covers the knowledge of both traditional protein expression and modern molecular cloning. The following eight questions dealt with some key BMB concepts such as eukaryotic DNA structure and transcription.

For evaluating the responses to this BMB curriculum program, we selected one class that includes 58 students and 4 faculties at the end of the third semester of 2009. Both students and faculties were asked to participate the survey (Table 1) after finishing learning and teaching BMB. They were asked to choose a unique response that best fits their opinions such as from strongly disagree to strongly agree. The survey was administrated in an anonymous manner to avoid unreal responses.

Table 1: Assessment of learning and teaching effects for BMB as a system curriculum

Statements (1-7 for students and 8-10 for faculties)	Responses (Mean±SD)
I think the total time for learning BMB is shortened by comparing with that of two independent courses	4.6±0.6
It is benefit for us to understand and solve a complex problem relative to BMB	4.2±0.3
The new teaching manner has introduced traditional biochemistry and modern molecular biology into clinical medical education resulting in good understanding of molecular medicine	4.1±0.4
The BMB is one of the important basic medical courses for undergraduate students who major in clinical medicine	3.9±0.7
I think BMB cannot be divided into two independent curriculums to learn in the different semesters	4.0±0.6
By participating in the BMB curriculum program, I had more interest in studying the molecular pathogenesis of diseases	4.2±0.4
Because of the BMB curriculum program, I had more opportunities to do some Student Research Training Programs (SRTP) about the molecular bases of disease development, diagnosis and treatment	4.0±0.4
The students are learning more about BMB in my courses than before	3.9±0.4
I feel that the students have a better understanding of the role of BMB in clinical medicine than before	4.3±0.5
It is a time-saving manner for teaching BMB and I am comfortable teaching BMB as an independent course in one semester	4.7±0.3

The students and faculties are required to circle responses that best fit their opinions.1): strongly disagree 2): disagree 3): neither agree nor disagree 4): agree 5): strongly agree

Statistical analysis: The data analyses were performed using SPSS 13.0 software and expressed as means±SD. A $p<0.05$ was considered as the level of significance for all the tests.

RESULTS

Improving the ability of knowledge integration via a system curriculum: We set up a new system curriculum including BMB at Ningbo University School of Medicine from 1999. In the past 10 years, the contents of BMB were introduced by different topics which covered two original courses. The repeated knowledge of these two courses was deleted in the new system curriculum. By comparing the pre-reform with post-reform, we found that not only the faculties abated their pressure on teaching two courses but also the students saved totally 20-25 class h for learning.

As both biochemistry and molecular biology are the backbone courses of clinical medicine, some physiological phenomena and clinical symptoms need to be clarified by the principles of BMB. The result showed the increasing confidence for students to solve the compositive questions in class or in clinical training (Fig. 1). In addition, the students who enrolled BMB program (post-reform) reported significantly higher confidence that those who did not receive a teaching reform (Fig. 1, $p<0.05$). In fact, the key points of these two courses were easily linked through learning an integrated program of BMB. For example, DNA as a primary role in central dogma, links RNA and protein in the regulation of gene expression. Moreover, both specific proteins and microRNAs are involved in the control of metabolism of biomacromolecules. In order to explain the pathogenesis of diseases more felicitously, the knowledge of BMB need to be integrated necessarily as a whole system curriculum.

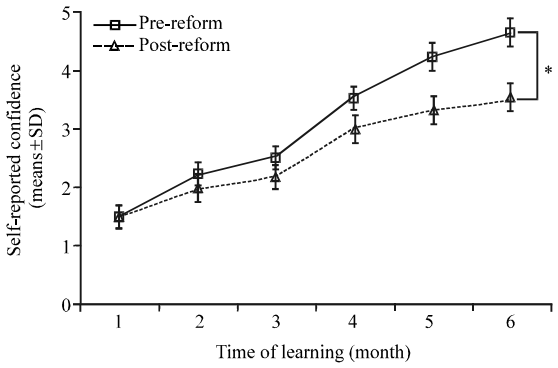

Fig. 1: Students self-reported confidence in solving compositive questions. The triangle and square lines represent pre and post-reform groups respectively. Confidence ratings were measured on a continuous scale from 1 (not at all confident) to 5 (very confident). Data are expressed as means±SD. *$p<0.05$

Teaching BMB as system curriculum increases student ability of solving complex questions: In fact, the students who major in clinical medicine are often required to understand the pathogenesis of some disease such as identifying a molecular mechanism of pathogenesis for some disease. It's well known that the molecular basis of pathogenesis covers not only traditional biochemistry but molecular biology. The student ability to solve BMB-related complex questions was assessed using a ten-question multiple choice test. These exam questions were designed to contain both problem solving and detailed recall so that only students who could well integrate the knowledge of BMB would achieve a perfect score. The results showed that students who were in the post-reform group got a much better scores than those who were the pre-reform one (85.7±5.3 versus 76±4.7, $p<0.05$, Fig. 2). The survey result also indicated that they

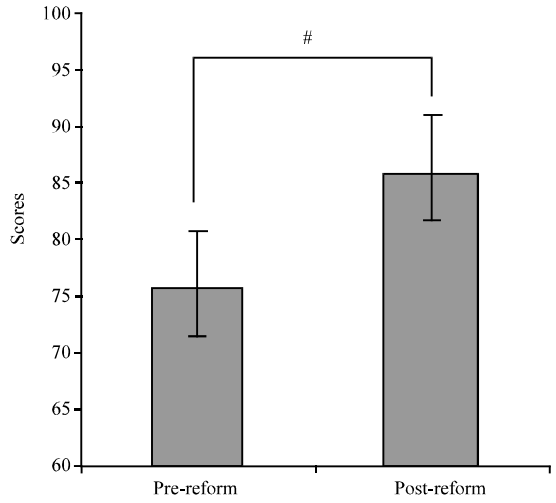

Fig. 2: The scores of assessment by using a ten-question multiple choice test (ten scores per question). The gray and black bars indicate the pre and post-reform, respectively. Data represent means±SD # $p<0.05$

have more opportunities to do some research about the molecular bases of disease development, diagnosis and treatment. In addition, their confidence in solving complex problems was also enhanced by participating in the BMB curriculum program.

Student interest in learning BMB increases with exposure: Student interest in learning BMB was greatly enhanced through classical references reading and small group discussion. In the past decades more and more Chinese students who major in clinical medicine ignored or lost their interest in basic medicine including BMB. After reading some classical references such as DNA double helix model and RNA-induced gene silence, they had more interest in gene therapy and molecular diagnosis which were based on BMB-related knowledge and skills. Furthermore, they could express freely their own opinions about BMB-related diseases in small group discussion. Even in their presentations, they were encouraged to criticize other students' results and introduce their own viewpoints. These activities enhanced their interest and confidence in learning BMB. In order to promote student interest of research, they were provided all kinds of SRTPs which they could finish by themselves. The survey data suggested that the BMB curriculum program helped students have more opportunities to participate in SRTP (Table 1, question 7). The assessment of learning effectiveness also revealed that students agreed that they had more interest in studying the molecular pathogenesis of diseases.

Better awareness and more interactions improved among faculties: Because courses with biochemistry and molecular biology content are usually taught in two different semesters by different lecturers, faculty often lack knowledge of what was taught in related courses and of the expertise of other faculty. A goal of the BMB curriculum program was to integrate the knowledge of BMB and to promote better awareness and more interaction among faculties. Faculties could organize their contents well and did not miss or repeat any key points of this course. They also had more time to interact with each other for teaching ability improvement. Faculties strongly agreed that they were comfortable teaching BMB as an independent course in a time-saving manner within one semester (Table 1, question 10).

DISCUSSION

The rapid expansion of knowledge and novel techniques in biochemistry and molecular biology has made it a difficult task to learn and teach students within the already heavy medical curriculum. In the past, as a change, many different methods were carried out to improve this situation (McClean *et al*., 2005; McGill, 2008; Pilarski *et al*., 2008) such as Problem-Based Learning (PBL) which was widely used tool for the instruction of basic medical curriculum in medical schools (Smith, 2002). Although, biochemistry and molecular biology were usually taught as two different courses in many Chinese medical schools more and more faculty were aware of the necessity that integrating them as an independent course. In the past 10 years we re-formed the teaching mode and taught BMB as a system curriculum in the same semester. Most students represented that they spent less time to gain more knowledge when they took part in the BMB curriculum reform program.

Moreover, students found that they had more interest in learning BMB through classical references reading and small group discussion. Although, the knowledge of BMB were more abstract, they were deeply impressed by the model and/or experiment mentioned in some classical references.

In this way, students were greatly enhanced the understanding of relevant concepts. In addition, their potential interest of research was aroused by some important discoveries in BMB history. After small group discussion, they could find some scientific problems and try to solve them in their own way by participating in SRTP.

CONCLUSION

The student learning ability and research interest were greatly improved by participating in BMB teaching reform program.

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