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Motivating medical students to learn basic science concepts using chronic myeloid leukemia as an integration theme

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ABSTRACT

Objective: To report on the use of chronic myeloid leukemia as a theme of basic clinical integration for first year medical students to motivate and enable in-depth understanding of the basic sciences of the future physician.

Methods: During the past thirteen years we have reviewed and updated the curriculum of the medical school of the Universidade Estadual de Campinas. The main objective of the new curriculum is to teach the students how to learn to learn. Since then, a case of chronic myeloid leukemia has been introduced to first year medical students and discussed in horizontal integration with all themes taught during a molecular and cell biology course. Cell structure and components, protein, chromosomes, gene organization, proliferation, cell cycle, apoptosis, signaling and so on are all themes approached during this course. At the end of every topic approached, the students prepare in advance the corresponding topic of clinical cases chosen randomly during the class, which are then presented by them. During the final class, a paper regarding mutations in the *abl* gene that cause resistance to tyrosine kinase inhibitors is discussed. After each class, three tests are solved in an interactive evaluation.

Results: The course has been successful since its beginning, 13 years ago. Great motivation of those who participated in the course was observed. There were less than 20% absences in the classes. At least three (and as many as nine) students every year were interested in starting research training in the field of hematology. At the end of each class, an interactive evaluation was performed and more than 70% of the answers were correct in each evaluation. Moreover, for the final evaluation, the students summarized, in a written report, the molecular and therapeutic basis of chronic myeloid leukemia, with scores ranging from 0 to 10. Considering all 13 years, a median of 78% of the class scored above 5 (min 74%–max 85%), and a median of 67% scored above 7.

Conclusion: Chronic myeloid leukemia is an excellent example of a disease that can be used for clinical basic integration as this disorder involves well known protein, cytogenetic and cell function abnormalities, has well-defined diagnostic strategies and a target oriented therapy.

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Introduction

The Faculty of Medical Sciences of the Universidade Estadual de Campinas (UNICAMP) is considered one of the best medical schools in Brazil and in Latin America. Located in São Paulo state, in Campinas, a city of one million inhabitants and center of a technological area comparable to the Silicon Valley in California, the school enrolls 110 students from at least 10 000 candidates every year from all over the country. Thus the selection process is difficult; the exams are very rigorous, and consist of approximately one week of evaluations of chemistry, physics, biology, maths, Portuguese, literature, history, geography and English.

The undergraduate medical course is nominally six years long with the first and second years being pre-clinical and years five and six are trainee intern years.

Since the creation of the medical school 45 years ago, the first year curriculum comprises biochemistry, histology, embryology and anatomy. The courses are based on lectures, laboratory classes and examinations. During the past thirteen years we have reviewed and updated the curriculum to revitalize the course. The main objective of the new curriculum was to teach the students how to learn to learn. Horizontal and vertical integration are one focus of the new curriculum as is the integration of basic and clinical courses.

In the new curriculum, the module 'The Cell' is introduced during the first eight weeks of the course. The module is given in 168 h with 75% in class studies under teacher guidance and laboratory activities, including bioinformatics, and less than 25% reserved for lectures. We would like to report the strategy used to apply the module 'The Cell' in order to maintain the principles of the new curriculum and motivate students.

The objective of this paper is to report on the use of chronic myeloid leukemia as a theme of basic clinical integration for first year medical students to motivate and enable in-depth understanding of the basic sciences of the future physician.

Method

Chronic myeloid leukemia is a disease of the hematopoietic stem cells, which acquire a reciprocal translocation between chromosomes 9 and 22 (Philadelphia chromosome). This translocation leads to a juxtaposition of the BCR gene to the ABL gene. The ABL gene is a proto-oncogene. This juxtaposition determines the activation of ABL, a tyrosine kinase involved in the intracellular signaling which culminates in increased proliferation and reduced apoptosis of the abnormal clone.[1,2]

(1) On the first day of this module, 1 h is reserved for the students to interview a patient, cured of chronic myeloid leukemia after being submitted to bone marrow transplantation.

The students have an opportunity to hear the patient, personal and family information, the complaints which culminated in going to the doctor, and the patient's feelings regarding the diagnosis and the evolution of the disorder before and after the bone marrow transplantation.

A PowerPoint presentation is then shown summarizing the epidemiology, clinical characteristics, etiologic factors of this disease and finally, a blood smear of the patient at diagnosis and of a normal person is shown and the significant differences in the numbers of white cells and platelets is discussed. This increased amount of cells is then correlated with spleen growth which the patients had mentioned as the initial symptom, during the interview.

Then, the students are given the address of the page containing the clinical case on the Internet so that they can prepare themselves for the next classes. The Internet page includes descriptions of techniques emphasizing recently acquired basic knowledge, and videos showing the separation of proteins, Western blot test, chromosome analysis by standard karyotyping and *in situ* fluorescence hybridization (FISH), polymerase chain reaction (PCR), RNA quantification by reverse transcription PCR (RT-PCR), stem cell separation and growth, and colony formation.

At the end of each basic theme, the clinical case is presented by randomly chosen students coordinated by the teacher as follows.

(2) During the presentation of the protein theme, the students discuss the basis of the western blot technique that identified an abnormal band in the patient. A picture of the Western blot results is used as an example. Only the abnormal band, present in the patient and absent in the control, is shown.

But why does the patient present this abnormal band? The answer to that question arises during the course.

The Western blot technique is also described and students watch a video showing the procedure used to make polyacrylamide gel, the application of the sample in the gel, the migration of the proteins in the gel, the verification of these proteins using Coomassie blue stain, the transference of these proteins to nitrocellulose membrane and the revelation of these proteins using a specific antibody and a secondary antibody. Both, the video (approximately 15 min long) and a brief description of the technique are available on the internet.

(3) During the classes concerning chromosomes, gene organization and transcription, the students discuss the cytogenetics of patients with the Philadelphia chromosome. The traditional cytogenetics and FISH of the patient, as well as the procedure to perform these techniques are available in the Internet site.

At this point we discuss the relationship between the abnormal band (previously showed) and this translocation. The students discuss the genes that are involved in the translocation and the relationship between these genes and the abnormal protein.

The implication of this translocation at the RNA level and the usefulness of this knowledge in the diagnosis of the translocation are also studied. RT-PCR, used to demonstrate the BCR-ABL transcript, and the importance of RT-PCR to follow up patients after bone marrow transplantation are discussed. RT-PCR products, before and after bone marrow transplantation, are shown. Finally, students are able to associate the abnormal protein to the cytogenetics and RT-PCR.

(4) During the presentation of the topic on signal transduction and the tyrosine kinase pathways, students discuss the