Second External Evaluation

Graduate Program in Cellular and Genetic Etiology, Diagnosis, and Treatment of Human Disease

University of Crete-Medical School, Heraklion, Crete

May 30, 2011

Committee Report

A. Introduction

This was the second external evaluation of the Graduate Program in "The Molecular Basis of Human Disease", officially known as the post-graduate program in "Cellular and Genetic Etiology, Diagnosis and Treatment of Human Disease". The goal of this program continues to be to train M.D. physicians in the fundamentals of biomedical research, so that they may become leaders in academic medicine; and to train B.Sc. biologists, biochemists, and other basic scientists in the medical sciences, so that they can apply their skills to problems of human disease in their subsequent careers in biomedical research. The program is described on the internet at http://www.molmedgp.med.uoc.gr/.

D. Boumpas, Professor of Internal Medicine, Program Director, charged the External Review Committee with undertaking a critical review of the program organization, courses, infrastructure, research opportunities, faculty, students, and outcomes. An update on the program was provided by the Associate Director, D. Kardassis, Professor of Biochemistry, and is the source of information on the program itemized below. Following an initial meeting with the Coordinating Committee, the

External Evaluation Committee met with students in the program, had a question and answer session with the Coordinating Committee, met *in camera*, and then had another session with the Coordinating Committee to provide preliminary feedback.

B. History

The program began in the academic year 2003-2004. Key innovations of the program include:

- *The program combines clinical expertise with basic science in order to investigate the molecular basis and the pathogenesis of human diseases.*
- *The program prepares its students to fill positions in Greek universities and research institutions and to compete for national and international funding*
- *The students of the program have the opportunity to select among 40 top research laboratories in Greece*
- *The program allows its graduate students to do research in selected laboratories abroad*
- *The program continues to train the students through a M.Sc. and a Ph.D. cycle. As mandated by the Ministry of Education the Ph.D. is awarded by the Department of Medicine*
- *The program is evaluated periodically by an External Evaluation Committee*

In 2008, the coursework for the program was modified, eliminating the survey course on molecular basis of disease and replacing it with a series of disease-oriented courses. All courses were made required, not elective.

C. Prior Review

The first external review was in March 2006. Some of the major findings and recommendations, and actions in response to those recommendations included:

- *An inadequate number of computers: the students now all have their own laptops, and there is wireless internet access, as recommended in the prior review.*
- *Inadequate access to journals on-line: this has not been addressed due to lack of funds.*
- *Improve infrastructure: there have been no major infrastructure improvements, due to lack of funds. It is hoped that the pending Regpot grant by the EU will address this.*
- *Recruit additional faculty: this has been carried out.*
- *Improve faculty and peer-to-peer mentoring: individualized mentoring is provided by the Coordinating Committee including in particular V. Zannis. Peer mentoring has not been implemented.*
- *Improve coordination of courses: this has been carried out with the curricular changes described above.*
- *Scholarships: this is not possible given the program resources, although the students can compete for individual grants and scholarships through external agencies.*
- *Balance M.D. and B.Sc. candidates: this is a continuing priority and has been successful.*

D. Facilities

The laboratories and classrooms are sited in the recently constructed buildings of the Medical School of the University of Crete in Heraklion. These facilities are spacious and modern and have all the necessary technological facilities for the performance of molecular and cellular biomedical research, including access to DNA sequencing, flow cytometry, confocal microscopy, cell culture equipment, polymerase chain reactors, *etc*. The first round of funding for the program provided support for needed equipment items. There have been no recent additions.

Recommendations: It is hoped that the Regpot grant by the EU will support new genetics and stem cell cores that will provide access for the graduate students to new state of the art research capabilities.

E. Program Faculty and Administration

The program faculty includes ~50 faculty from the University of Crete Medical School, from the Departments of Basic Sciences, Lab Sciences and Internal Medicine, and from other Departments of the University (Biology, Materials Science). In addition there are ~25 faculty from outside of the University of Crete. These faculty come from IMBB-FoRTH, Heraklion; School of Medicine, University of Athens;Alexander Fleming Institute, Athens;Bioacademy Institute, Athens; Boston University School of Medicine, Boston; Harvard Medical School, Boston;
Mount Sinai Medical Center, NY; NCI, NIH, Frederick, Maryland; NIH, Bethesda, USA; Tufts Univ., Medical School, Boston, USA; University of Cologne, Cologne; University of Geneva, Geneva; University of Texas, MD Anderson Cancer Center, Houston; University of Texas, Southwestern Medical Center, Dallas; Washington University, St. Louis.

The courses are strengthened by selective use of visiting faculty to complement the expertise of the local faculty. Visiting external faculty in 2009-2010 included: Dr Konstantin Kandror, Prof. of Biochemistry, Boston University Medical School; Dr Stephen Farmer, Prof. of Biochemistry, Boston University Medical School; Dr Paul Pilch, Prof. of Biochemistry, Boston University Medical School; Dr Diomedes Logothetis, Professor and Dean of Graduate Studies, Department of Physiology and Biophysics, Virginia Commonwealth University; Dr Gavin Wilkinson, Professor of Medical Microbiology, Cardiff University, UK; Dr T. Liloglou, University of Liverpool, Cancer Research Center; Dr Luc Sensebe, Establissment Francais du Sang Centre-Atlantique, Groupe de Recherche sur les Cellules Souches Mesenchymaleuses (GECSofM), Tours, France.

The Program is directed by Dimitrios T. Boumpas, MD, FACP, Professor of Medicine and Director, Internal Medicine/Rheumatology, Clinical Immunology and Allergy. He is assisted by the Associate Director Dimitrios Kardassis, PhD. They function as co-directors. The program is governed by a Coordinating Committee that includes: D. Boumpas (Program Director), D. Kardassis (Assoc. Director), A. Eliopoulos, D. Georgopoulos, G. Goulielmos, A. Gravanis, D. Karagogeos, D. Mavroudis, E. Papadaki, K. Papadakis, N. Siafakas, G. Sourvinos, C. Stournaras, C. Tsatsanis, V. Zachariou, C. Savakis (Adjunct Member), and V. Zannis (Adjunct Member).

Recommendations: The review committee recommended that the Coordinating Committee consider broadening the participation of other research faculty throughout Greece, who meet appropriate criteria for mentoring students. This would provide two benefits: it would give the students more choice of laboratories for their thesis research; and it would increase the profile of the program as a national

model and resource for Greek biomedical science. In particular, inviting FP7 funded PIs to visit the program and present the research programs of their networks would expose the students to a wide range of cutting edge biomedical research in the network of Europe.

F. Course of Study

As noted above, in 2008, the program was modified to consist of 6 months of required coursework including the hands-on Graduate Lab course (30 credits), 2three month rotations (30 credits), and a year of research in the thesis laboratory (120 credits). The introductory courses include: Basic Principles of Molecular/Genetic Basis of Diseases; Basic Research Methodology; and Biostatistics, Clinical Methodology, Epidemiology. The disease-oriented courses include: Metabolic, Cardiovascular Diseases; Autoimmune/Inflammatory/Infectious Diseases; Neoplastic Diseases; Neuropsychiatric Disorders; Regenerative Medicine and Stem Cells.

The program formerly set two qualifying examinations: one a topic review between first and second year, and a second at the end of the second year that was a research proposal for the Ph.D. The research proposal will now be taken as a qualifying exam following the selection by the Coordinating Committee of the M.Sc. graduates who will continue in the Ph.D. component of their training.

After courses are completed, a first rotation is assigned to the students. In general, the M.D. students are assigned a basic laboratory, and the B.Sc. students are assigned a more clinical science laboratory, if available. The second rotation is selected by the students.

The second year is devoted to research and preparation of the M.Sc. thesis. The laboratory for this is usually one of the rotation labs. A qualifying exam that is a topic review is expected early in the second year, after courses are completed.

Recommendations: The changes in the course structure have been excellent, eliminating redundancy and improving focus. Given the size of the program and its goals, making all courses required seems wise, and the students had no problems with this. They do comment that the course work is very demanding, particularly early in the first year.

The Guide and the Coordinating Committee should clarify that the first qualifying examination is required and when it should be completed, as well as the nature of the qualifying exam for the Ph.D. that will be conferred by the Department of Medicine.

The Evaluation Committee had some concerns about the selection of rotations and thesis research labs. For some students, two rotations may not be enough to decide about the thesis laboratory. It is recommended that the Coordinating Committee consider giving students a clear option for a third rotation when needed (with the understanding that this will extend the length of the degree program). The Evaluation Committee also found that some students rotate in a single laboratory and continue their thesis there. The recommendation is that the students carry out two rotations in different areas/laboratories to expand their exposure to different aspects of biomedical research.

Student-student interactions tend to diminish in the second year of the program, as each student focuses on his/her own Masters research. A suggested remedy for this would be to institute a journal club where all program members would

participate. This would bring students of both years together and would encourage them to interact with older MSc and PhD students and investigators.

The Evaluation Committee also was concerned about the breadth of research opportunities available to the students. They suggested (as noted above) that the list of researchers from other departments and institutions be expanded, particularly in areas not emphasized by current faculty. Also, there appears to be a need to increase the pool of physician-scientists that can serve as mentors for the M.D. students in particular. New faculty would have to meet criteria set out by the Coordinating Committee and demonstrate commitment to the program and to mentoring.

G. Students

Data on the applying and matriculating students is in the attached appendix, provided by D. Kardassis. The number of applicants has varied, but the quality has improved over time. The program is selective and admits 6-12 students per year. The majority of the students matriculate, some select other programs or departments. The Program continues to strive to admit equal numbers of students with MD degrees and BSc degrees. Maintaining this balance is important to the character of the program. The students report that the BSc and MD students integrate well, study together, and help each other in their respective areas of expertise and training. MDs gain an increased understanding of mechanisms of disease, and BScs learn to apply science to clinically important problems.

Scholarships are lacking because of the lack of funds for the program. The lack of scholarships continues to be a major concern of the students.

Mentoring the students is somewhat informal, performed on an *ad hoc* basis by members of the Coordinating Committee and by V. Zannis on his regular visits.

The students feel that there is a lack of peer-to-peer mentoring by senior of junior students, and also a lack of career mentoring, particularly for the MDs, who may not have access and interactions with physician-scientists in their area of clinical specialization.

Now with 8 years of program history, the success of the trainees has become evident. Postgraduate students in the program have authored 79 publications to date in top journals including Immunity, Journal of Immunology, J. Exp Med, Nature Medicine, Biochemistry, Nucleic Acids Research, Neuron, Arthritis & Rheumatology, Molecular and Cellular Biology. 75% of graduates have continued on to Ph.Ds. Of program graduates, those with academic and research positions include: V. Zaxharioudaki ,Post-doc, University of Brussels; M. Nakou, Staff Scientist, Pfizer Hellas; A. Oikonomopoulos, Post-doc, Harvard Medical School; K. Tsakiri, Resident, Internal Medicine, U. of Thessaloniki; G. Bertsias, Resident, Lecturer-elect in Rheumatology/Clinical Immunology; I. Mosialou, Post-doc, Columbia University; G. Michas, Resident in Pathology, Kalamata Hospital.

Recommendations: The Review Committee was impressed with the quality of the students, their enthusiasm for the program, and their success in research productivity and careers in biomedical research. The integration of BSc and MD students works very well and is a strength of the program. It is unfortunate that scholarship opportunities are limited. The students may benefit from more formal mentoring in the areas of selecting rotations and research laboratories, and in career planning.

H. Other Program Activities.

The program has held two retreats. The first in October 2007, at Kalimera Kriti Resort in Lassithi, featured a keynote address by F. Kafatos. The second in October 2010 at the Medical School featured a keynote address by D. Logothetis. Both were apparently well-attended and successful.

The program publishes a newsletter, a graduate program guide (online and in print) and maintains a website.

Recommendations: The Evaluation Committee recommends the Graduate Program Guide and website be updated to reflect the new courses and organization of the program.

I. Conclusion

This is a unique graduate program that seeks to train physician-scientists and basic-scientists to become academic leaders for Greek medicine in the future. The training of medical school graduates is modeled on the combined MD/Ph.D. programs that exist in the US and Canada and it is unique for Greek medical schools. The External Review Committee was extremely impressed with the quality of the Program: the faculty is dedicated to its success and the students are excellent and very satisfied with the program. The revisions in the program courses were a clear improvement in the curriculum. The External Review Committee recognizes the uniqueness of this graduate program, congratulates the Coordinating Committee on its quality, and urges the Ministry of Education of Greece to recognize this as well.

If the Program continues to flourish and expand, it will be successful in serving as a source of future outstanding scientists and faculty in medicine and related basic biomedical sciences, and it will continue to further the reputation of the Medical

School of the University of Crete as a unique and outstanding research-oriented medical school. To accomplish this, the Evaluation Committee recommends expanding external faculty involvement in the program, to strive for a national presence and reputation. The program has the potential to serve as an example for other postgraduate programs in the country, improving the quality of the educational system.

To achieve such goals, the financial support of the program will need to be strengthened. Support could be provided directly from the government. Alternative sources include the Regpot EU grant for infrastructure improvement or the possibility of training funding from European Advanced Translational Research InfraStructure in Medicine (EATRIS).

A second issue facing the program in the near future is program leadership, as Dr. Boumpas will be assuming a position in Athens. The Evaluation Committee strongly recommends that the program leadership continue to be shared between an MD physician-scientist and a basic PhD biomedical scientist. The leadership and collaboration of Boumpas and Kardassis has been critical to the program's success, along with the support of the other members of the Coordinating Committee. Continued leadership by two outstanding investigators is the best model for guiding a program with the unique goals of this one. The Evaluation Committee does not favor a specific model, which could continue to be one with an MD director and PhD associate director, or a PhD director and MD associate director, or co-directors. This should be decided by the Coordinating Committee, selecting from the most committed candidates with the interest in leading the program.

The Evaluation Committee acknowledges the excellent administrative support provided by M. Adamaki, who is invaluable to faculty and students in the program.

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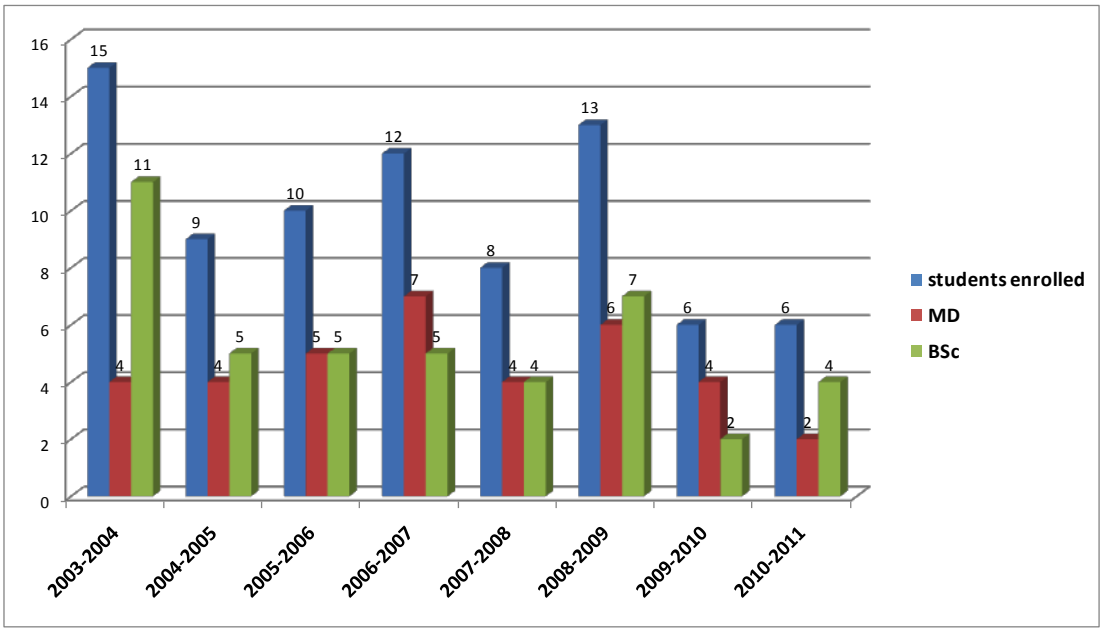
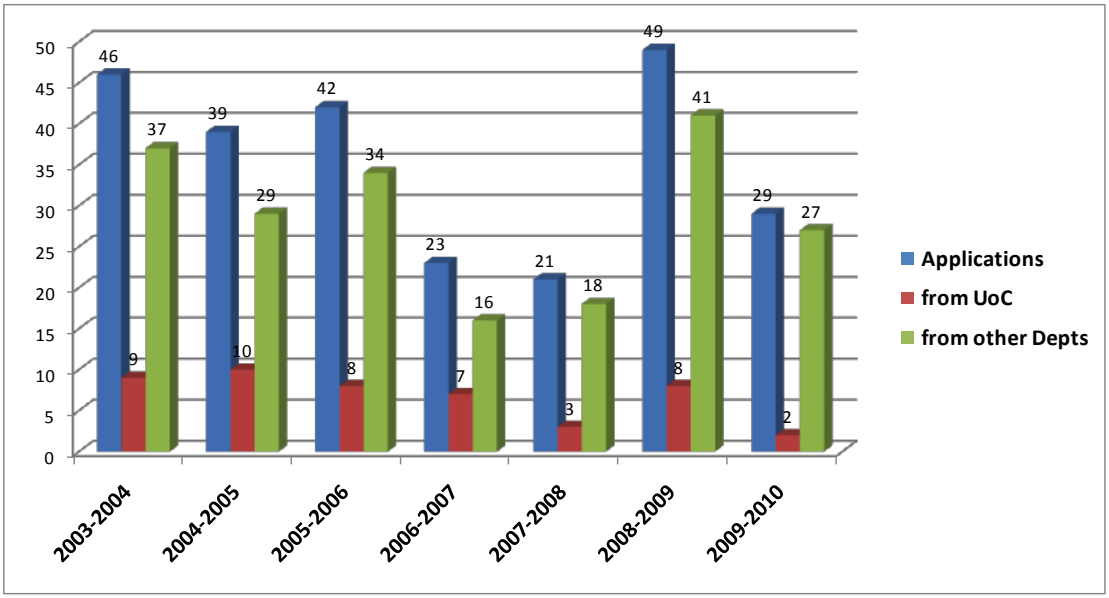
APPENDIX: STUDENT DATA

Composition of the Student Body



Applicants



Degrees Awarded to Date