World Hellenic Biomedical News

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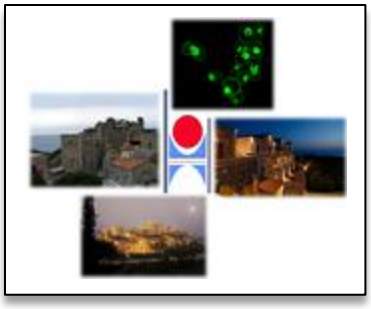

1st Summer School of the WHBA in Medical & Biosciences Research and Management

In collaboration with the UPenn's Roy & Diana Vagelos Program in Life Sciences Management

Combining cancer vaccines and T lymphocyte modulation
Short Review Article
by the group of
Emmanuel Katsanis, MD

University of Arizona, USA

WHBA & Hellenic Cardiological Society Joint Symposium

Sponsored by the American Heart Association

Orlando, FL - USA

"Meet with Hellenes Investigators from around the World"

Eleftherios Diamandis, MD, PhD
Professor of Clinical Biochemisty, University of Toronto, Ontario, Canada

Hellenic Biomedical activities around the World

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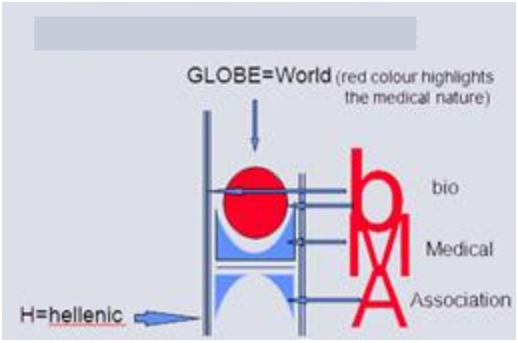
"Meet with Hellenes Investigators from Around the World" Eleftherios Diamandis – University of Toronto ,Canada



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World Hellenic Biomedical News

Konstantinos Drosatos, MSc, PhD
President of the World Hellenic Biomedical Association (2012-2014)

With the beginning of my term as the president of the executive board of the World Hellenic Biomedical Association for 2012-2014, I am taking the opportunity to wish everyone a Healthy and Productive New Year. The New Year that emerges during an earthshaking global financial turmoil can be the opportunity for the societies to invest on new developments that may arise from Medicine and Biosciences.

The World Hellenic Biomedical Association, a network of physicians and bioscientists of Greek and Cypriot origin or descent, throughout its 20-year history, has set challenging values and priorities that this board aims to meet. These are the promotion of excellence in medical practice, biomedical research and education, the facilitation of establishment of collaborations among clinical and basic researchers, as well as the enhancement of the scientific profile of Greek and Cypriot physicians and bioscientists within an international scientific mosaic. Moreover, especially under current circumstances, the World Hellenic Biomedical Association may represent a major advisory entity for Greece and Cyprus in aspects such as the reorganization of the health system, the education and the research environment.

The role of the World Hellenic Biomedical Association in these important missions will be executed via:

- The enhancement of its continuously expanding communication network, which now includes almost 3,000 physicians and bioscientists from 27 countries around the world.
- The organization of the World Hellenic Biomedical Congress, which is now reaching its 10th anniversary, as well as smaller symposia that are being held in coordination with international scientific organizations. This aims to establish a permanent participation of Hellenes physicians and biomedical researchers in scientific dialogues about current developments and future trends in Medicine and Biosciences.
- The organization of educational activities, such as the summer school that begins in 2012 and aims to contribute to the education of young people from the areas of medicine and biosciences.
- The development of the communication platform that promotes interaction among Hellenic medical and bioscientific societies around the world, in order to ignite actions that serve aims of mutual interest.
- The enhancement of the information flow regarding scientific and professional aspects, such as funding opportunities, prizes and awards, research consortia, job availabilities etc.

Hellenes carry a timeless Heritage of major contributions in the development of medicine and sciences. It is among the top priorities for the World Hellenic Biomedical Association to highlight current contribution of Hellenes to these disciplines and preserve values of excellence and innovation within the Hellenic biomedical community around the world.

10th joint Cyprus-Greek Cardiology Conference

May 4 – 5, 2012- Nicosia, Cyprus

Information & Registration: Cyprus Society of Cardiology

http://www.cycardio.org/En/Conference.html

World Hellenic Biomedical Association & Hellenic Cardiological Society International Lunch Forum

American Heart Association Scientific Sessions 2011

Orlando, FL – USA

Sunday November 13, 2011

The World Hellenic Biomedical Association and the Hellenic Cardiological Society represented Greece in the International Lunch Forum of the American Heart Association Scientific Sessions of 2011 at Orlando, FL.

This was the first among several activities that have been scheduled aiming to enhance the scientific profile of Greek physicians and bioscientists within international scientific audiences.

The WHBA and the HCS plan to organize the International Lunch Forum of the 2012 Scientific Sessions of the American Heart Association at Los Angeles.

Panelists

Suzanne Oparil, University of Alabama at Birmingham, USA

Nikolaos G. Frangogiannis, Albert Einstein College of Medicine, USA

Michael Doumas, Aristotle University of Thessaloniki, Greece

George D. Dangas, Mount Sinai School of Medicine - New York, USA

Vasilios Papademetriou, Georgetown University, Washington DC, USA

George D. Dangas
Professor - Mount Sinai School of Medicine - New York, USA
Chairman of the Advisory Board of the World Hellenic Biomedical Association
Opening talk

Leonidas V. Athanasopoulos
Brigham & Women's Hospital, Boston, USA
Predictors of Reverse Remodeling Failure and Survival Following Mitral Valve Repair

Konstantinos Toutouzas
University of Athens Medical School, Greece
Increased Thermal Heterogeneity in Carotid Arteries as a Surrogate Marker for Coronary Artery Disease. First Clinical Application of Microwave Radiometry

Evangelos D. Michelakis
University of Alberta - Canada
Metabolism, Angiogenesis and Emerging Concepts on the Regulation of Right Ventricular Hypertrophy and Failure

Costas Tsioufis
University of Athens Medical School - Greece
Current Perspectives on Hypertension: Target Organ Damage Progression and Therapeutic Challenges

World Hellenic Biomedical Association Group

Middle East and North Africa

Middle East and its entire region (MENA, Middle East and North Africa) host a considerable number of Greeks and Cypriots physicians and bioscientists. Most of them and especially the bioscientists, work in governmental institutions (eg the King Faisal University Hospital in Riyad, Saudi Arabia, the Shafallah Medical Genetics Center in Doha, Qatar) or private organizations (eg the American Hospital in Dubai, UAE). Additionally, a lot of the physicians in countries like Egypt, Lebanon, Jordan, where the Greek community was well-established historically, practice medicine in their private clinics.

Since the number of the Greeks and Cypriots physicians and bioscientists in Middle-East, started being increased significantly the last year, there was a need and common request from the scientists of this region to get organized in a group. Ideally and in order to have a substantial presence, this group should be a part (branch) of an international association, such as the World Hellenic Biomedical Association (WHBA). In this effort, we found complete support by the President of WHBA, Dr Konstantinos Drosatos.

The role of this group would be mainly to create a scientific network among the Greeks and Cypriots physicians and bioscientists in Middle East, which will help to get to know each other, inform about scientific projects and positions all over the world, exchange knowledge and promote possible collaborations among their institutions, but also with other institutions outside Middle-East.

Vasiliki Chini, PhD, vasiliki.chini@gmail.com
Senior Research Scientist,Shafallah Medical Genetics Center,Doha – Qatar

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Supervisor, Cytopathology Section, Clinical Lecturer, Laboratory Sciences; College of Applied Medical Sciences, KSAUHS
Program Education Coordinator, Post-Baccalaureate Certification Program
Dept of Pathology and Laboratory Medicine (MBC 1122), King Abdulaziz Medical City - Central Region, PO Box 22490, Riyadh, 11426, Kingdom of Saudi Arabia

Expansion of the WHBA communication network in Australia

Through a continuous effort to expand the WHBA frontiers, Mr. Kostas Biliouris and Dr. George Syros, in coordination with Professor Steven Boyages from the University of Sydney Medical School, have been communicating with physicians and bioscientists of Hellenic Heritage in Australia. More than 60 individuals agreed to be enlisted in the WHBA directory and are receiving the current newsletter for the first time. Focus was not only on Professors and established scientists with an expertise spanning through various specialties, but also on young investigators and PhD candidates. Several professionals from the Universities of Sydney, Victoria, Melbourne, Adelaide, Monash, Deakin, Flinder, Griffith, La Trobe, RMIT and New South Wale wholeheartedly embraced the effort to unite Greek scientists around the world. It is promising that these new members will further attract more Greek scientists and promote their co-operation in the fields of Biosciences and Health Sciences.

The American College of Cardiology, World Hellenic Biomedical Association, Hellenic Cardiological Society and Cyprus Society of Cardiology Symposium

"Mediterranean Diet and its Protective effect on Cardiovascular Disease"

March 26, 2012
3:45 – 5:15pm
McCormick Conference Center - Room S105
Chicago, IL - USA

Co – Chairs

George Dangas, MD, PhD, FACC
Professor of Medicine at the Mount Sinai School of Medicine
Director of Cardiovascular Innovation at the Zena and Michael A. Weiner Cardiovascular Institute

George Parharidis, MD, FACC
Professor, AHEPA, University Hospital, Thessaloniki, Greece

Speakers

3:45- 4:00 ***"The role of sodium and potassium in CV health"***
George L. Bakris, MD
Professor of Medicine, University of Chicago School of Medicine
Director Hypertension Center Diabetes Institute

4:00 – 4:15 **"Effects of diet, exercise and weight loss on inflammation"**
Christie M. Ballantyne MD
Professor of Medicine, Baylor College of Medicine
Chief, Cardiovascular Research Section, Division of Atherosclerosis and Vascular Medicine
Director, The Maria and Alando J. Ballantyne, M.D., Atherosclerosis Clinical Research Laboratory
Director, Center for Cardiovascular Disease Prevention, Methodist DeBakey Heart Center
Co-director, Lipid Metabolism and Atherosclerosis Clinic, The Methodist Hospital

4:15 – 4:30 **"The role of Cardiovascular Imaging in Coronary heart Disease"**
Petros Nihoyannopoulos MD, FRCP, FACC, FESC
Professor of Cardiology, Imperial College London

4:30 – 4:45 ***"An Overview of the Cypriot contribution to the Diet"***
Panayiotis Avraamides MD, BSc(Hons), MB BS(Lond), FRCP(Lond), FRCP(Edin), MRCPI, FESC, FSCAI, FACC
Director, Department of Cardiology, Limassol General Hospital
President, Cyprus Society of Cardiology
President, Cyprus Working Group on Interventional Cardiology

4:45 – 5:00 **"Cardiovascular mortality in Greece"**
Vlassis Pyrgakis, MD
Past President of the Hellenic Cardiological Society

5:00 – 5:15 **Open discussion**

World Hellenic Biomedical Association

1st Summer School in

Medical & Biosciences

Research & Management

1st part: May 20-26, 2012 – Itilo Manis, Peloponnese, Greece

2nd part: May 26-30, 2012 – Athens, Greece

In collaboration with the Roy & Diana Vagelos Life Sciences Management program of the University of Pennsylvania, Philadelphia - USA

The World Hellenic Biomedical Association is organizing the 1st Summer School in Medical & Biosciences Research and Management, which will take place in **Greece on May 20-30, 2012** for undergraduate and graduate students of **universities in Greece and abroad**.

The aim of this educational activity is to expose prominent **graduate and undergraduate students of medical and biosciences background** to knowledge given by top-notch experts from the most advanced medical and biosciences research centers in the United States, Canada, the United Kingdom, Switzerland and Greece, as well as from the Pharmaceutical and Biotechnology industry.

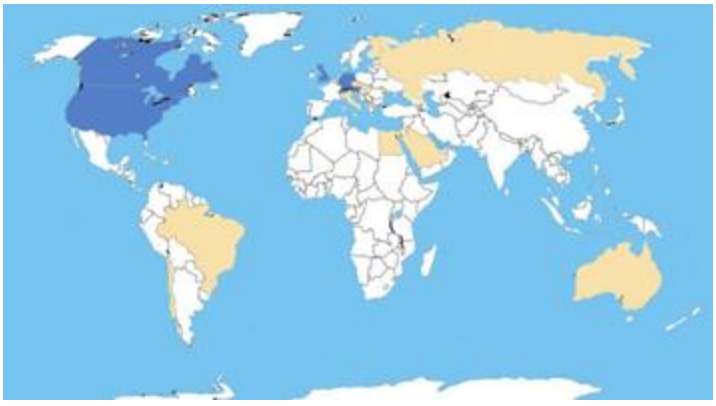
The program is divided in two parts. The 1st part will take place in the beautiful scenery of Itilo in Mani, Peloponnese from May 20 to May 26, 2012. For this part 10 instructors and 2 plenary speakers of worldwide reputation will present the most recent breakthroughs and current trends in several topics of basic and clinical medical research. During the 2nd part that will take place in Athens on May 26-30 the students will attend lectures in Merck Group about drug development and successful placement of a new drug in the market. Moreover, the schedule includes visits of the students to the Biomedical Research Foundation of the Academy of Athens, while visits to the Standing Committee on Cultural and Educational Affairs of the Parliament of Greece and the Ministry of Education, Lifelong Learning and Religious Affairs are being planned.

Hotel expenses will be covered for 24 students that will be selected by the scientific board of the summer school, which consists of Prof. George P. Chrousos (chairman), Prof. Dimitrios Boumpas, Prof. Diomedes Logothetis and Prof. Emmanouil Dermitzakis.

The summer school has become available to students of the University of Pennsylvania, Philadelphia – USA through the Roy & Diana Vagelos Life Sciences Management program. This important development has been secured thanks to the support by Dr. P. Roy Vagelos, distinguished physician and biomedical scientist of Greek descent and member of the advisory board of the World Hellenic Biomedical Association.

The financial support of the summer school is provided by Lakonian international organizations, as well as by individual "Omogeneis" Lakones, indicating clearly the eagerness of Lakones that live abroad to support the economy and education of Greece and particularly their homeland. Special thanks should be extended to Mr. Stavros Vougiouklakis, who coordinates the fundraising efforts.

Applications by students in medicine and biosciences from approximately 10 countries have been received for participation in the summer school. The selected students will be announced at the end of February.



Instructors of the 1st WHBA Summer School in Medical & Biosciences Research & Management

George P. Chrousos,
Professor and Chairman, First Dept of Pediatrics UNESCO Chair on Adolescent Health Care & Chief of Endocrinology, Metabolism and Diabetes - University of Athens Medical School, Greece

Argiris Efstratiadis,
Scientific Director, Biomedical Research Foundation, Academy of Athens
Higgins Professor Emeritus of Genetics and Development, Columbia University,New York, USA

Eleftherios Diamandis
Professor of Clinical Biochemisty, University of Toronto, Ontario, Canada

Dimitrios T. Boumpas
Professor of Medicine, University of Crete and Professor-elect, University of Athens, Greece

Diomedes Logothetis
Professor & Department Head, Physiology and Biophysics
Virginia Commonwealth University, Richmond, USA

Spyros Kollias
Professor, Institute of Neuroradiology, University Hospital of Zurich, Switzerland

Dimitris Kardassis
Professor of Biochemistry, Faculty of Medicine, University of Crete, Greece

Sakis Mantalaris
Professor in Biosystems Engineering, Imperial College, London, UK

Emmanouil Dermitzakis
Professor of Genetics, University of Geneva Medical School, Switzerland

Dimitris Iliopoulos
Assistant Professor of Pathology, Department of Cancer Immunology & AIDS Harvard Medical School, Boston, USA

Despina Sanoudou
Assistant Professor of Pharmacology, Medical School, University of Athens, Greece

Sophie Mavrogeni
Consultant cardiologist in Onassis Cardiac Surgery Center,
Athens, Greece

Dimitris Sakellariou
Medical Advisor, Merck Group BU CardioMetabolicCare & General Medicine – Cardiometabolic diseases

Michalis Arvanitis
Medical Director at Merck Group Hellas - Oncology

Combining cancer vaccines and T lymphocyte modulation

Emmanuel Katsanis, M.D. and Nicolas Larmonier, Ph.D.

Department of Pediatrics, Steele Children's Research Center, University of Arizona, Tucson, AZ

INTRODUCTION

With the increasing role of immunotherapy in cancer treatment, tumor vaccines have generated interest because of their specificity and their minor side effects. The demonstration that the immunogenicity of tumor cell lysate or necrotic tumor cell is associated with members of the chaperone protein family has led to the development of tumor-derived chaperone-based vaccines(1). The immunostimulatory potential of chaperone proteins stems from their function as carriers of tumor-derived antigenic peptides and from their adjuvant properties(1,2).

Chaperone-rich, cell lysate (CRCL) anticancer vaccine: Murine models

Our laboratory has developed an original anticancer vaccine termed chaperone-rich, cell lysate (CRCL)(3). CRCL is generated by free-solution isoelectric-focusing of total tumor lysates resulting in the enrichment of chaperone proteins rather than a purification of them. CRCL contains HSP90 and HSP70 family members, the endoplasmic reticulum chaperones GRP94/gp96 and calreticulin. Each of these chaperones is individually capable of generating specific immune responses against their tumors of origin(4-9). CRCL vaccines have a more pronounced immunologic effect per unit of protein than any of the individual chaperone protein vaccines. Moreover, CRCL vaccines elicit specific protective and durable immunity in different murine models and compare favorably to other conventional vaccine strategies such as irradiated whole tumor cells, tumor cell lysates or peptides. (3,6,10-17). The effectiveness of CRCL across murine tumor types that differ in genetic strain, histological origin, tumorigenicity, and metastatic potential supports its broad clinical application. In all the tumor models we have studied, such as 12B1 leukemia, A20 and BDL-2 lymphoma, B16 melanoma, neuro-2a neuroblastoma, Sa1 fibrosarcoma, and 4T1 and TUBO mammary carcinoma, CRCL stimulated measurable anti-tumor immune responses.

The efficacy of peptide-based vaccines has been widely studied. Limitations of this strategy include the emergence of tumor escape variants following single peptide vaccination and the lack of DC activation by peptides. For example a chromosomal translocation resulting in the BCR-ABL fusion gene is the primary mutation that leads to malignant leukemic transformation in chronic myelogenous leukemia; however, secondary mutations often occur. Therefore, BCR-ABL+ leukemic cells can easily develop escape mechanisms following vaccination with a single BCR-ABL peptide. CRCL may circumvent the problems associated with single peptide vaccines by providing an extensive antigen repertoire. Indeed, we demonstrated that vaccination with DC loaded with CRCL led to significantly higher survival rates in mice with BCR-ABL positive leukemia compared to vaccination with DC loaded with single BCR-ABL peptide(14,16). (Figure 1)

Necrotic tumor cell death immunogenicity is associated with the release of so-called “danger signals” such as High Mobility Box-1 (HMGB1), uric acid, calreticulin, and heat shock proteins (HSPs) (18). Tumors genetically modified to express HSPs, are associated with a decreased expression of the immunosuppressive cytokine IL-10 in the microenvironment(19). CRCL, which contains at least a 20-fold enrichment of major HSPs, provides a high concentration of local danger signals. CRCL not only provides and channels tumor antigens to dendritic cells (DC) but by virtue of its adjuvant effects, this vaccine also triggers DC activation(3,6,11). DC co-stimulatory molecules fundamental for T-cell activation such as CD40, CD80/86 and CD70 are upregulated by CRCL(13). When incubated with DC, unfractionated tumor lysate did not change DC phenotype or enhance their immunostimulatory function as was the case with CRCL prepared from the same tumor tissues. Interestingly, further supporting the efficacy of CRCL, we have demonstrated that DC loaded with tumor-derived CRCL resist regulatory T-cell and TGF-β-mediated suppression(20,21).

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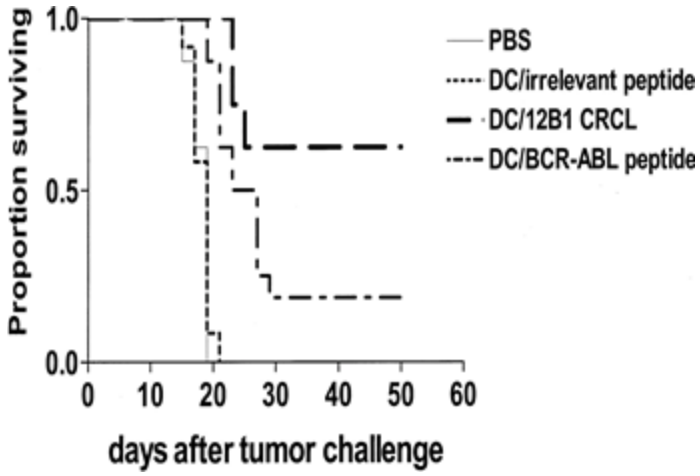

Figure 1. Immunization of mice with 12B1-derived CRCL-loaded DCs provides superior therapeutic effects. BALB/c mice were injected with 3 x 10^3 12B1 cells subcutaneously in the right groin on day 0. On day 2, mice were immunized with 5 x 10^6 DCs that had been loaded with 12B1-derived CRCL or indicated peptides. Survival of mice was monitored and displayed in the Kaplan-Meier plot (n = 8-16 mice per group). PBS versus DC/CRCL, P < .05; PBS versus DC/BCR-ABL peptide, P < .05; DC/irrelevant peptide versus DC/CRCL, P < .05; DC/irrelevant peptide versus DC/BCR-ABL peptide, P < .05; DC/CRCL versus DC/BCR-ABL, P < .05.

Chaperone-rich, cell lysate (CRCL) anticancer vaccine: *In vitro* human studies

One has to recognize that the transplantable animal tumor models are seldom perfect mirrors of human malignancies, where immune tolerance, advanced immunosuppression, and genetic instability impair antitumor immune responses. We have been able to translate the findings obtained in animal models to human immune cells *in vitro*(22). CRCL prepared from ovarian cancer cells activated human DC as indicated by the higher amounts of IL-12 secretion and increased immunostimulatory functions. Furthermore, specific T cell responses were generated *in vitro* by stimulation of patient peripheral blood mononuclear cells with tumor-derived CRCL. Generated CTL displayed specific IFN-γ secretion and ovarian tumor cell killing(22). Thus, the enhanced immunogenicity arising from CRCL indicates that CRCL represents an effective cancer antigen source for personalized anticancer immunotherapies. The FS-IEF technique for enriching multiple chaperones from tumor yields sufficient immunogenic material for clinical use in a multiple vaccination setting. Over 120-200 micrograms of CRCL vaccine per 100 mg of tumor tissue can be obtained, which is desirable from a clinical standpoint since enough vaccine can be generated for 6-10 immunizations.

Combination of CRCL with effector memory T cells (emTh-1)

The advantages of active immunotherapy include its relative lack of side effects, its specificity against target tumor cells, and the generation of memory responses against tumor-specific antigens. However, even if proven clinically safe, immunotherapy has only sparked moderate enthusiasm because of the relatively limited objective clinical responses that have been observed in cancer patients. This modest therapeutic success stems in part from the immunosuppressive environment created by tumors, with CD4+CD25+FoxP3+ regulatory T lymphocytes (Treg) as prominent players. Treg critically contribute to the occurrence and persistence of tumor-induced tolerance(23). An increase in the frequency of these immunosuppressive cells in cancer patients has been widely reported. Treg expansion observed during tumor progression may result from the proliferation of naturally occurring Treg (nTreg) or from the conversion of CD4+CD25-FoxP3- T cells into CD4+CD25+FoxP3+Treg (iTreg)(24,25). Treg dampen immune responses by suppressing the function of CD4+, CD8+, and natural killer (NK) cells and by inhibiting dendritic cell activation(21,26-31). Because Treg are one of the main barriers for the eradication of tumors by immune cells, their therapeutic depletion or their functional inactivation improves responses to cancer vaccines(32-37). However, the selective elimination or inactivation of Treg constitutes a major challenge because these cells share the same surface markers as activated conventional, non-suppressive T cells.

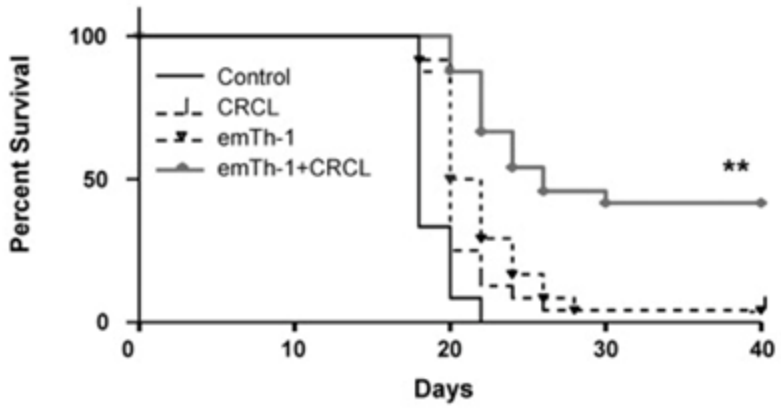

Figure 2. The combination of emTh-1 and CRCL vaccine improves the survival of mice with 12B1 leukemia. (A) Naive BALB/c mice were injected subcutaneously in the right groin with 5 × 10^3 12B1 cells on day 0. Animals (8 mice per group) were then administered via footpads on days 3, 7, and 14 with: PBS (Control), 12B1-derived CRCL (CRCL, 25 μg/mouse), emTh-1 lymphocytes (emTh-1, 1 × 10^5 cells/mouse), or a combination of CRCL plus emTh-1 (emTh-1 + CRCL). **P < .0001. Survival of mice was monitored every other day and is depicted using Kaplan-Meier analysis. NS, nonsignificant; **P < .0001.

Several reports have indicated that the adoptive transfer of allogeneic T cells may increase the efficacy of tumor immunotherapy by providing adjuvant/"danger" signals to the host immune cells(38,39). We recently reported that activated allogeneic effector/memory CD4+CD25+CD40L+CD62L- T helper-1 (emTh-1) lymphocytes when combined with CRCL tumor vaccination result in improved survival and long lasting protection in an aggressive leukemia model (Figure 2) (40). The effect of emTh-1 cells is in part based on their ability to produce large amounts of type-1 cytokines (IFN- **γ**, TNF- **α** and GM-CSF)(40,41). We found that in addition to polarizing type-1 anti-tumor immune responses, emTh-1 cells also impaired tumor-induced T regulatory cells *in vitro* and *in vivo*(40).

EmTh-1 cells inhibit the conversion of naive CD4+CD25-FoxP3- T lymphocytes into CD4+CD25+FoxP3+ Treg and skew their differentiation toward a Tbet+ GATA-3- Th-1 profile. IFN-**γ** has been identified as the primarily factor responsible for Treg impairment. Unlike conventional approaches aimed at inactivating/depleting Treg, emTh-1 cells do not hinder effector T lymphocytes, but rather promote their antitumor function. Furthermore, allogeneic emTh-1 cells were potent adjuvants capable of enhancing the *in vivo* therapeutic efficiency of a tumor-derived CRCL vaccine.

Conclusions

EmTh-1 administration is a novel approach to inhibit the suppressive activity of Treg while simultaneously promoting the function of conventional effector T cells. The combination of allogeneic emTh-1 cells with CRCL vaccine significantly increased the survival of tumor bearing mice over each approach alone and promoted durable, tumor-specific, T cell–dependent adaptive immunity. Allogeneic emTh-1 cells thus represent a powerful adjuvant capable of enhancing the therapeutic potential of the CRCL vaccine, and therefore represent a promising translational approach in cancer immunotherapy. The human equivalent of emTh-1 termed AlloStim™ is currently approved for experimental use by the FDA under an Investigational New Drug (IND) application and is being evaluated for safety and efficacy in Phase I/II clinical trials of metastatic cancer and hematological malignancies. With over 50 patients with advanced cancer treated thus far, there were no observed grade III or IV toxicities (personal communication M. Har-Noy). An IND for the CRCL vaccine to be used in combination with AlloStim™ has been submitted to the FDA and is awaiting approval.

REFERENCES

1. Blachere, N. E., and Srivastava, P. K. (1995) *Semin Cancer Biol* **6**, 349-355
2. Suto, R., and Srivastava, P. K. (1995) *Science* **269**, 1585-1588
3. Graner, M., Raymond, A., Akporiaye, E., and Katsanis, E. (2000) *Cancer Immunol Immunother* **49**, 476-484
4. Arnold, D., Faath, S., Rammensee, H., and Schild, H. (1995) *J Exp Med* **182**, 885-889
5. Basu, S., and Srivastava, P. K. (1999) *J Exp Med* **189**, 797-802

6. Graner, M., Raymond, A., Romney, D., He, L., Whitesell, L., and Katsanis, E. (2000) *Clin Cancer Res* **6**, 909-915
7. Nair, S., Wearsch, P. A., Mitchell, D. A., Wassenberg, J. J., Gilboa, E., and Nicchitta, C. V. (1999) *Journal of immunology* **162**, 6426-6432
8. Udono, H., and Srivastava, P. K. (1993) *J Exp Med* **178**, 1391-1396
9. Udono, H., and Srivastava, P. K. (1994) *Journal of immunology* **152**, 5398-5403
10. Chen, X., Zeng, Y., Li, G., Larmonier, N., Graner, M. W., and Katsanis, E. (2006) *Biol Blood Marrow Transplant* **12**, 275-283
11. Graner, M. W., Zeng, Y., Feng, H., and Katsanis, E. (2003) *Cancer Immunol Immunother* **52**, 226-234
12. Kislin, K. L., Marron, M. T., Li, G., Graner, M. W., and Katsanis, E. (2007) *FASEB J* **21**, 2173-2184
13. Zeng, Y., Feng, H., Graner, M. W., and Katsanis, E. (2003) *Blood* **101**, 4485-4491
14. Zeng, Y., Graner, M. W., Feng, H., Li, G., and Katsanis, E. (2004) *Int J Cancer* **110**, 251-259
15. Zeng, Y., Graner, M. W., and Katsanis, E. (2006) *Cancer Immunol Immunother* **55**, 329-338
16. Zeng, Y., Graner, M. W., Thompson, S., Marron, M., and Katsanis, E. (2005) *Blood* **105**, 2016-2022
17. Li, G., Andreansky, S., Helguera, G., Sepassi, M., Janikashvili, N., Cantrell, J., Lacasse, C. L., Larmonier, N., Penichet, M. L., and Katsanis, E. (2008) *Mol Cancer Ther* **7**, 721-729
18. Melcher, A., Todryk, S., Hardwick, N., Ford, M., Jacobson, M., and Vile, R. G. (1998) *Nat Med* **4**, 581-587
19. Gough, M. J., Melcher, A. A., Ahmed, A., Crittenden, M. R., Riddle, D. S., Linardakis, E., Ruchatz, A. N., Emiliusen, L. M., and Vile, R. G. (2001) *Cancer research* **61**, 7240-7247
20. Cantrell, J., Larmonier, C., Janikashvili, N., Bustamante, S., Fraszczak, J., Herrell, A., Lundeen, T., C, J. L., Situ, E., Larmonier, N., and Katsanis, E. (2010) *Immunobiology* **215**, 535-544
21. Larmonier, N., Cantrell, J., Lacasse, C., Li, G., Janikashvili, N., Situ, E., Sepassi, M., Andreansky, S., and Katsanis, E. (2008) *J Leukoc Biol* **83**, 1049-1059
22. Li, G., Zeng, Y., Chen, X., Larmonier, N., Sepassi, M., Graner, M. W., Andreansky, S., Brewer, M. A., and Katsanis, E. (2007) *Clin Exp Immunol* **148**, 136-145
23. Sakaguchi, S. (2000) *Cell* **101**, 455-458
24. Curiel, T. J., Coukos, G., Zou, L., Alvarez, X., Cheng, P., Mottram, P., Evdemon-Hogan, M., Conejo-Garcia, J. R., Zhang, L., Burow, M., Zhu, Y., Wei, S., Kryczek, I., Daniel, B., Gordon, A., Myers, L., Lackner, A., Disis, M. L., Knutson, K. L., Chen, L., and Zou, W. (2004) *Nat Med* **10**, 942-949
25. Valzasina, B., Piconese, S., Guiducci, C., and Colombo, M. P. (2006) *Cancer research* **66**, 4488-4495
26. Antony, P. A., Piccirillo, C. A., Akpinarli, A., Finkelstein, S. E., Speiss, P. J., Surman, D. R., Palmer, D. C., Chan, C. C., Klebanoff, C. A., Overwijk, W. W., Rosenberg, S. A., and Restifo, N. P. (2005) *Journal of immunology* **174**, 2591-2601
27. Larmonier, N., Marron, M., Zeng, Y., Cantrell, J., Romanoski, A., Sepassi, M., Thompson, S., Chen, X., Andreansky, S., and Katsanis, E. (2007) *Cancer Immunol Immunother* **56**, 48-59
28. Misra, N., Bayry, J., Lacroix-Desmazes, S., Kazatchkine, M. D., and Kaveri, S. V. (2004) *Journal of immunology* **172**, 4676-4680
29. Nishikawa, H., Jager, E., Ritter, G., Old, L. J., and Gnjatic, S. (2005) *Blood* **106**, 1008-1011
30. Somasundaram, R., Jacob, L., Swoboda, R., Caputo, L., Song, H., Basak, S., Monos, D., Peritt, D., Marincola, F., Cai, D., Birebent, B., Bloome, E., Kim, J., Berencsi, K., Mastrangelo, M., and Herlyn, D. (2002) *Cancer research* **62**, 5267-5272
31. Sutmuller, R. P., van Duivenvoorde, L. M., van Elsas, A., Schumacher, T. N., Wildenberg, M. E., Allison, J. P., Toes, R. E., Offringa, R., and Melief, C. J. (2001) *J Exp Med* **194**, 823-832
32. Ghiringhelli, F., Larmonier, N., Schmitt, E., Parcellier, A., Cathelin, D., Garrido, C., Chauffert, B., Solary, E., Bonnotte, B., and Martin, F. (2004) *Eur J Immunol* **34**, 336-344
33. Janikashvili, N., Larmonier, N., and Katsanis, E. (2010) *Immunotherapy* **2**, 57-68

34. Larmonier, N., Fraszczak, J., Lakomy, D., Bonnotte, B., and Katsanis, E. (2010) *Cancer Immunol Immunother* **59**, 1-11
35. Larmonier, N., Janikashvili, N., LaCasse, C. J., Larmonier, C. B., Cantrell, J., Situ, E., Lundeen, T., Bonnotte, B., and Katsanis, E. (2008) *J Immunol* **181**, 6955-6963
36. Prasad, S. J., Farrand, K. J., Matthews, S. A., Chang, J. H., McHugh, R. S., and Ronchese, F. (2005) *Journal of immunology* **174**, 90-98
37. Yu, P., Lee, Y., Liu, W., Krausz, T., Chong, A., Schreiber, H., and Fu, Y. X. (2005) *J Exp Med* **201**, 779-791
38. Appelbaum, F. R. (2001) *Nature* **411**, 385-389
39. Chen, B. J., Cui, X., Sempowski, G. D., Liu, C., and Chao, N. J. (2004) *Blood* **103**, 1534-1541
40. Janikashvili, N., LaCasse, C. J., Larmonier, C., Trad, M., Herrell, A., Bustamante, S., Bonnotte, B., Har-Noy, M., Larmonier, N., and Katsanis, E. (2011) *Blood* **117**, 1555-1564
41. LaCasse, C., Janikashvili, N., Larmonier, C., Alizadeh, D., Hanke, N., Kartchner, J., Situ, E., Centuori, S., Bonnotte, B., Katsanis, E., and Larmonier, N. (2011) *J immunol (in press)*

Meet with Hellenes Investigators from around the World

Research Activities of the Advanced Center for Detection of Cancer

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INTRODUCTION

Our laboratory was established in 1988 and is currently focusing on nine areas of research:

1. Kallikrein enzyme biology and pathophysiology
2. Proteomics
3. Tumor markers
4. Mechanisms of carcinogenesis and metastatic progression
5. Translational research
6. Cancer therapeutics
7. Male infertility
8. Pathobiology and biomarkers of autoimmune diseases
9. Neurodegeneration

From the point-of-view of human disease research, our major interest is cancer, but other diseases, including neurodegeneration, inflammation, autoimmunity, maternal/fetal health and skin disorders are also of interest. Our laboratory integrates basic, cell biology and translational research under one roof.

All publications of our laboratory can de accessed online (1).

Kallikrein Biology and Pathophysiology

Our laboratory has cloned numerous novel genes, in particular those that belong to the kallikrein gene family. The kallikreins are a group of related serine proteases, clustered in tandem on human chromosome 19q13.4. The locus map and theoretical 3-dimensional molecular models, as well as the annotated genomic sequences of KLKs can be found in the cited link (2).

A schematic of the KLK locus and the genomic and proteomic structure of KLKs are shown in Figure 1.

Three reviews by our group summarize the progress in this field, over the last 15 years (3-5).

Our research interests related to kallikreins include the following:

1. Kallikrein gene structure and transcriptional regulation.
2. Kallikrein protein function and enzymology.
3. Discovery of physiological pathways involving kallikreins (including enzymatic cascades).
4. Identification of physiological substrates for kallikreins.
5. Kallikrein gene rearrangements in cancer.
6. Kallikreins as diagnostic and therapeutic targets.
7. Kallikreins and Proteinase-Activated Receptor (PAR) signalling

To achieve these goals we continue to develop innovative tools for kallikrein research such as recombinant proteins, monoclonal antibodies, immunological and molecular assays and immunohistochemical procedures. Also, through our collaborators, we use fluorogenic combinatorial libraries and phage-display technology to delineate kallikrein

substrates and function. More recently, we are using mass spectrometric techniques to discover novel kallikrein targets and inhibitors.

A large number of international research laboratories is also investigating the physiology and pathobiology of kallikreins. A bi-annual international conference on kallikreins and related peptidases is currently in place. The first international symposium was held in Lausanne, Switzerland on September 1-3, 2005, the second was held in the Island of Santorini, Greece on October 16-18, 2007, the third took place in Munich, Germany on August 30-September 2, 2009 and the fourth in the Island of Rhodes, Greece on September 2-4, 2011. Special issues of the journals *Biological Chemistry* and *Thrombosis and Hemostasis* had devoted space to summarize selected presentations from these international symposia.

Proteomics

We are working towards delineating the proteome of biological fluids, tissues and cancer cell lines. In particular, we are identifying the secreted proteins (secretome) of breast, ovarian, lung, prostate, colon, pancreatic and other cancer cell lines, in order to discover molecules that may represent novel cancer biomarkers. This research involves extensive use of tissue culture technologies, fractionation and purification with various chromatographic techniques and mass spectrometric analysis of fractionated proteins. Our laboratory operates several state-of-the-art mass spectrometers and has significant in-house bioinformatic expertise. Our laboratory was the first to delineate the proteomes of amniotic fluid and cervico-vaginal fluid and expanded the proteomes of other fluids such as seminal plasma, nipple aspirate fluid and ascites fluid. The secretomes of over 50 cancer cell lines has also been delineated. In the area of clinical proteomics, we are seeking to identify novel molecules or proteomic signatures that can be used for early detection of cancer.

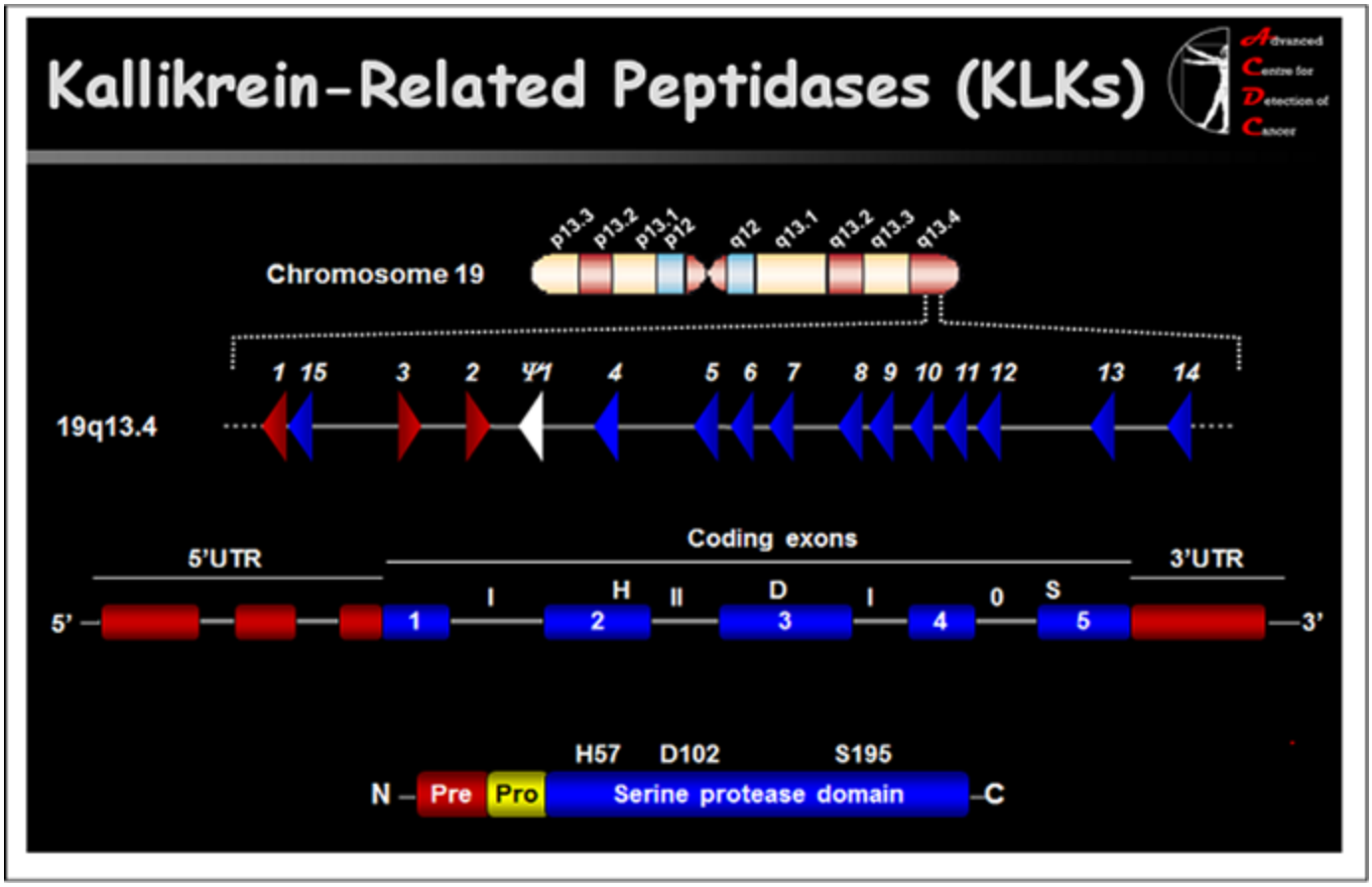

Figure 1. The human tissue kallikrein family of genes is located on chromosome 19q13.4. The 15 kallikrein genes and their direction of transcription are shown by arrows. The white arrow represents a kallikrein pseudogene. All kallikrein genes have a common structure with untranslated 5'UTR (red color) and 3'UTR, as well as 5 coding exons. The amino acids of the catalytic triad of all kallikreins, H (histidine), D (aspartic acid) and S (serine) are shown. The lower panel represents the enzyme structure, which is synthesized as a prepro-enzyme. The pre segment is removed intracellulary and all kallikreins are secreted as proforms. During activation, the pro-segment is removed. For more details, please see the cited reviews (3-5).

Three reviews describe in detail our work to date (6-8).

In the most recent version of our discovery approach for novel biomarkers, we are using an integration of various techniques and sources, including proteomics of tumor tissues, serum, cancer cell lines, proximal fluids, as well as animal models and microarray profiling. This integrated approach has recently been described in detail (8). Our proteomic biomarker pipeline includes steps such as discovery (by using tandem mass spectrometry), candidate selection (by using bioinformatic analysis), candidate verification (by using ELISA and mass spectrometry), biomarker validation (ELISA/MS), clinical trials and commercialization (ELISA) and FDA approval. A schematic of our proteomic biomarker pipeline and the techniques used are shown in Figure 2.

Tumor Markers

Our laboratory has already developed novel tumor markers for early cancer diagnosis, prognosis and monitoring. Dr. Eleftherios P. Diamandis is the Principal Investigator of the Ontario Cancer Biomarker Network (OCBN), a consortium which aims to discover, use and commercialize novel cancer biomarkers. For more information, please visit the website of the Ontario Cancer Biomarker Network (www.ocbn.ca/).

We are interested in discovering and validating novel cancer biomarkers that will aid in the early diagnosis, prognosis and monitoring of various forms of cancer, especially endocrine-related cancers such as breast, ovarian and prostate cancer. Examples of such discoveries can be found in the cited literature (6-10).

Mechanisms of Carcinogenesis and Metastatic Progression

We deploy mass spectrometry-based proteomic strategies to investigate pathophysiological pathways involved in carcinogenesis. We are using the in-vitro cell culture model in the context of microenvironment alteration experiments (e.g. stimulation with growth factors, hormones, or other soluble factors, drugs and/or chemical analogs that affect various pathophysiological processes) in combination with the SILAC approach, to identify key mediators that affect cancer-related processes such as tumor cell invasion and metastasis, angiogenesis, proliferation, evasion of apoptosis, resistance to antiproliferative signals/chemotherapy and cell survival.

Our specific research interests are:

1. Investigation of players involved in the metastasis cascade (mediators of epithelial-to-mesenchymal transition, invasion, migration, motility and angiogenesis), by performing differential proteomic analysis between primary and metastatic or between malignant and non-malignant cell lines
2. Investigation of the hormonal dependence in breast and prostate cancers, by stimulating cell lines with androgens or estrogens and performing differential proteomic analysis to identify affected genes and pathways
3. Investigation of tumor-host cell interactions (desmoplasia, angiogenesis, inflammation), by using co-culture systems, including cancer and stromal cells, followed by quantitative proteomic analysis of the conditioned media.

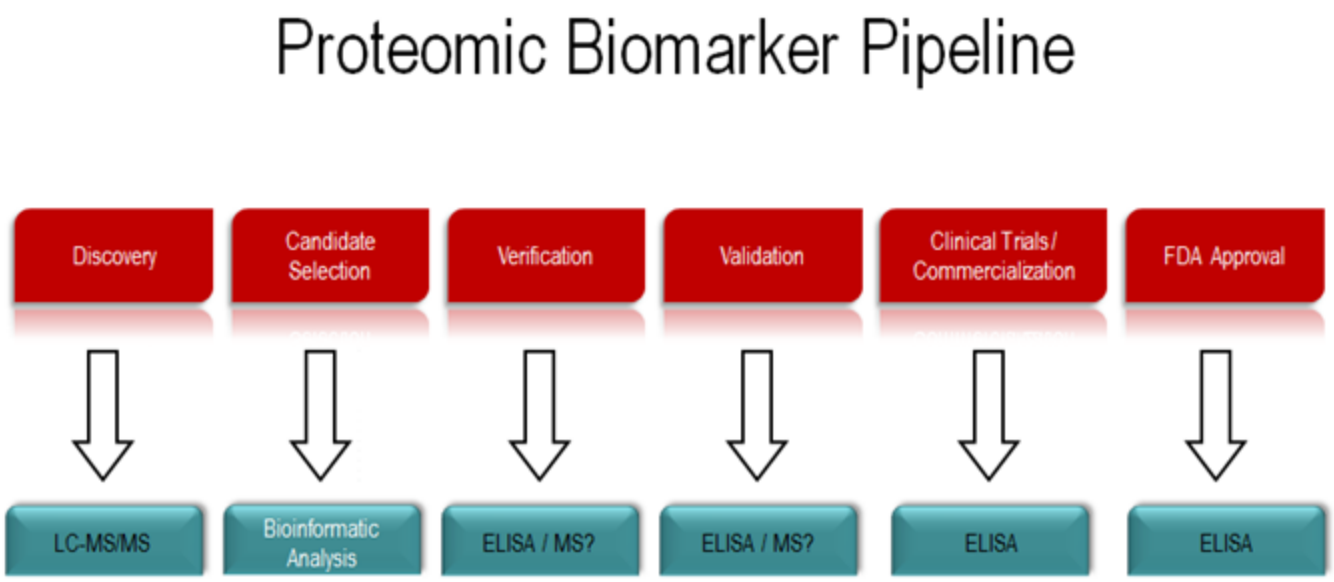

Figure 2. The proteomic biomarker pipeline of the ACDC Laboratory. For more details, see text and references 6-8.

Our recent review summarizes our experimental approaches (11).

Translational Research

We have access to large biorepositories of biological fluids, tissues and nucleic acids, which are invaluable in our efforts to identify novel cancer biomarkers and new ways for diagnosing and monitoring human disease. An international group of investigators is working closely with us by providing valuable clinical material for translational research.

Some of our translational research interests include:

1. Identification of potential clinical applications of kallikreins (diagnostic markers, therapeutic targets, predictors of prognosis and therapeutic response)
2. Involvement of kallikreins in non-malignant diseases (neurodegeneration, skin diseases, *etc*.)
3. Identification of non-kallikrein biomarkers that could be used for diagnosis, therapy and monitoring of cancer and other diseases

Cancer Therapeutics

We are using high-throughput technologies to screen candidate drug molecules from large chemical libraries. Recently, we screened libraries such as Spectrum, Prestwick and LOPAC and identified members of the cardiac glycoside family as potential anti-cancer agents. Our efforts to identify therapeutic molecules which could act either alone, or in a synergistic way, against cancer are continuing.

Cardiac glycosides such as digoxin, digitoxin, peruvoside, etc. have been identified by our group as potent inhibitors of human kallikrein expression (12). These findings may have implications for cancer therapies. We have further reviewed the literature describing therapeutic applications of cardiac glycosides (13). More recently, we have identified novel synergistic interactions between cardiac glycosides and other molecules, by using high-throughput screening (our unpublished data). We have further delineated that digitoxin-induced cytotoxicity of cancer cells is mediated through distinct kinase and interferon signalling networks (14).

Male Infertility

In collaboration with Dr. Keith Jarvi from the Murrray Koffler Urologic Wellness Centre, we are delineating the proteomes of seminal plasma and associated fluids in our efforts to identify biomarkers of infertility and urological diseases such as prostate cancer. In collaboration with Dr. Alex Zlotta, we are studying genomic, proteomic and transcriptomic signatures of prostate cancer.

Our seminal plasma proteome is the largest ever reported proteome for this fluid. Taking advantage of this knowledge, and our ability to develop selected reaction monitoring (SRM) assays for various analytes, we have shown that combination of very few biomarkers (between 2 and 10) can discriminate obstructive from non-obstructive azoospermia with 100% sensitivity and specificity. Additionally,with inclusion of more markers, we were able to distinguish various forms of non-obstructive azoospermia, leading to avoidance of testicular biopsies in patients with male infertility (Ref. 15 and our unpublished data).

Pathobiology and Biomarkers of Autoimmune Diseases

In collaboration with Dr. Dafna Galdman and Dr. Vinod Chandran, Professors at the Department of Medicine, Division of Rheumatology, Center for Prognostic Studies in the Rheumatic Diseases, Toronto Western Hospital, University Health Network, we are conducting proteomic studies to identify novel biomarkers of autoimmune and rheumatic diseases including psoriasis, psoriatic arthritics, systemic lupus erythematosus, etc. In such studies, we also collaborate with Drs. Morley Hollenberg, University of Calgary and Dr. Martin Steinhoff, Center for the Neurobiology of Digestive Diseases, University of California, San Francisco, USA.

We have recently found that a kallikrein signature in both synovial fluid and serum of patients with psoriasis can effectively discriminate between psoriasis and non-psoriasis patients with or without psoriatic arthritis (our unpublished data).

Neurodegeneration

One research interest of the ACDC Laboratory is identification of biomarkers of early diagnosis of neurodegenerative diseases such as Alzheimer's and Parkinson's Disease. Some of our local and international collaborators on this project include Dr. Anthony Lang, Toronto Western Hospital, University Health Network

and Dr. Ana-Maria Simundic, University Hospital "Sestre Milosrdnice", Zagreb, Croatia.

In our efforts to discover biomarkers of Alzheimer's disease, we have already delineated the proteome of cerebrospinal fluid from normal and Alzheimer's disease patients. We are further studying intensely, differential glycosylation patterns of various proteins in Alzheimer's and non-Alzheimer's patients. Additionally, we are investigating the role of one kallikrein that is highly expressed in central nervous system, KLK6, as a biomarker of Alzheimer's disease. Recently, we summarized Alzheimer's disease in a review article (16).

Concluding Remarks

The Advanced Center for Detection of Cancer has diverse interests. However, close examination of these projects reveals that all of them are evolving around the analytical strengths of the laboratory, which include separation technologies, immunological assay development, molecular biology techniques, and most prominently, qualitative and quantitative mass spectrometry and bioinformatic analysis. The laboratory is interested to recruit high-quality national and international students. A video of the Laboratory Director outlines his philosophy and approach towards accepting new graduate students (17). In addition to high scientific standards, the laboratory also promotes other recreational activities, including music and sports. The laboratory is also posting an annual video which captures those working in the laboratory at that time. The videos can be found on our website or YouTube.

REFERENCES

1. http://www.utoronto.ca/acdclab/pubs.htm
2. http://www.utoronto.ca/acdclab/annotations/index.htm
3. Yousef GM, Diamandis EP. The New Human Tissue Kallikrein Gene Family: Structure, Function, and Association to Disease. Endocrine Reviews 2001; 22: 184-204.
4. Borgoño CA, Diamandis EP. The Emerging Roles of Human Tissue Kallikreins in Cancer. Nature Reviews Cancer 2004; 4: 876-890.
5. Sotiropoulou S, Pampalakis G, Diamandis EP. Functional Roles of Human Kallikrein-related Peptidases. J Biol Chem. 2009; 284:32989-94.
6. Diamandis EP. Mass spectrometry as a diagnostic and a cancer biomarker discovery tool: Opportunities and potential limitations. Mol Cell Proteomics 2004;3:367-378.
7. Kulasingam V, Diamandis EP. Strategies for discovering novel cancer biomarkers through utilization of emerging technologies. Nat Clin Pract Oncol 2008;5:588-599.
8. Kulasingam V, Pavlou M, Diamandis EP. Integrating high-throughput technologies in the quest for effective biomarkers for ovarian cancer. Nat Rev Cancer 2010;10:371-378.
9. Kulasingam K, Diamandis EP. Tissue culture-based breast cancer biomarker discovery platform. Intl J Cancer 2008;123:2007-12.
10. Makawita S, Smith C, Batruch I, Zheng Y, Reuckert F, Grutzmann R, Pilarsky C, Gallinger S, Diamandis EP. Intergrated proteomic profiling of cell line conditioned media and pancreatic juice for the identification of pancreatic cancer biomarkers. Mol Cell Proteomics 2011 [Epub ahead of print].
11. Karagiannis GS, Pavlou MP, Diamandis EP. Cancer secretomics reveal pathophysiological pathways in cancer molecular oncology. Mol Oncol 2010;4:496-510.
12. Prassas I, Paliouras M, Datti A, Diamandis EP. High-throughput screening identifies cardiac glycosides as potent inhibitors of human tissue kallikrein expression: Implications for cancer therapies. Clin Cancer Res 2008;14:5778-5784.
13. Prassas I, Diamandis EP. Novel therapeutic applications of cardiac glycosides. Nat Rev Drug Discov 2008;7:926-935.
14. Prassas I, Karagiannis GS, Batruch I, Dimitromanolakis A, Datti A, Diamandis EP. Digitoxin-induced cytotoxicity in cancer cells is mediated through distinct kinase and interferon signalling networks. Mol Cancer Ther 2011 [Epub ahead of print].
15. Batruch I, Lecker I, Kagedan D, Smith CR, Mullen B, Grober E, Lo K, Diamandis eP, Jarvi KA. Proteomic analysis of seminal plasma from

normal volunteers and post-vasectomy patients identifies over 2000 proteins and candidate biomarkers of the urogenital system. J Proteome Res 2011;10:941-953.

16. Pasic MD, Diamandis EP, McLaurin J, Holtzman DM, Schmitt-Ulms G, Quirion R. Alzheimer Disease: Advances in Pathogenesis, Diagnosis, and Therapy. Clin Chem 2011;57:664-669.
17. http://www.utoronto.ca/acdclab/videos/index.html

Hellenic Bioscientific Association in the USA

2nd Panamerican Conference of the HBA-USA
"Moving from basic to translational research via novel technologies"

October 15-16, 2011 - Columbia University
New York

The Hellenic Bioscientific Association in USA (HBA-USA) organized the second Pan-American Congress at Columbia University in New York on October 15th-16th. The conference theme was "Moving from basic to translational research via novel technologies" and was supported by the Columbia University Hellenic Association. About 100 Greek researchers in the field of biosciences from 15 states attended the conference. The first day included the opening ceremony and talks from the President of the HBA-USA, Dr. Thomas Thomou (Harvard University, MA), the representative of the Columbia University Hellenic Association, Mr. Thomas Nikolakaki and general consuls of Greece and Cyprus in New York, Mrs Agi Balta and Mrs. Koula Sofianou.

Following the opening ceremony, Mr. Stavros Vougiouklakis and Niki Sideri, who passed away unexpectedly 3 days before the start of the conference, were nominated as honorary members of the Association. This was followed by the award to Professor Vassilis Zannis (Boston University, MA) for his contributions to education in the field of biosciences and the award to Professor Charalambos Gavras (Boston University, MA) for his contributions in biomedical research. The next section of the first day of the conference included presentations by Dr. Iannis Aifantis (New York University, NY), Dr. Poulikos Poulikakos (Memorial Sloan Kettering, NY) and Dr. Nick Vlahakis (Mayo Clinic, MN), whose published scientific papers were the best among the scientific publications of the members of the Association during the last year. The first day of the conference ended with a reception where all the attendees of the conference had the chance to interact with each other.

The program of the 2nd day of the conference included only scientific talks. The first session focused on the implementation of new technologies in research and started with the distinguished lecture given by Dr. Nikos Kyrpides (head of the Genome Biology Programm U.S. Department of Energy, CA) followed by two lectures by Dr. Nikos Chronis (University of Michigan, MI) and Dr. Maria Liberis (University of Pennsylvania, PA). The session was opened by Deputy Ambassador of the Permanent Representation of Greece to the United Nations (UN), Mr. Dimitris Karamitsos-Tziras, who focused on the particular value of the role of expatriate Greek scientists in Greece ravaged by the economic crisis.

The next session focused on research related to metabolism and cardiovascular diseases. Dr. Litsa Kranias (University of Cincinnati, OH) gave the distinguished lecture on the mechanisms that cause calcium disorders which affect heart function leading to the onset of heart failure. In the same session, Dr. Chris Vlahos (Lilly Research Laboratories, IN) discussed the process for the design and manufacture of drugs in the industry and Dr. Tasos Lymperopoulos (Nova Southeastern University, FL) talked about new therapeutic targets in heart failure.

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The last scientific session focused on cancer research. Dr. John Kyriakis (Tufts University) presented the distinguished lecture in this session on the identification and mechanisms of action of a tumor suppressor protein, followed by Dr. Constantine Stratakis (Director of the Endocrinology & Genetics at the National Institute of Child Health and Human Development, MD) who described mechanisms that contribute to the development of adrenal tumors. This session ended with the talks of Dr. Gabriela Chiosis (Memorial Sloan-Kettering, NY) and Dr. Dimitris Iliopoulos (Harvard, MA) who discussed novel approaches for finding new therapeutic treatments for cancer patients.

Dr. Thomas Thomou, president of the Hellenic Bioscientific Association in the USA

The conference ended with the presentation of collaborative educational programs between the U.S., Greece and Cyprus by Dr. Vassilis Zannis (Boston University, MA), Dr. John Evans (Harvard University, MA) and Mr. Leon Stavrou (the Next Generation Initiative). The President of the Association, Dr. Thomas Thomou, presented the Science Teaching Exchange Program (STEP) with the Aristotle University of Thessaloniki and the University of Ioannina in Greece, which was just launched with the support of Greek expatriates, the Maritime Administration of Thessaloniki, and the think tank Strategy International. Finally, Dr. Stelios Papadopoulos delivered the final talk in the session with the presentation of Fondation Santé, which provides scholarships to young scientists from Greece and Southeast Europe for training in pharmaceutical companies.

The conference was concluded with a summary speech by Dr. Athanasios Vasilopoulos (Vanderbilt University, TN), Vice-President of the HBA-USA, who emphasized the value of volunteer work of the members of the Association which contributed to the success of the conference as well as the high scientific level of the research findings presented by all speakers indicating the great impact of the Greek bioscientists in the USA on the scientific community worldwide.

The Board of Directors renewed the appointment with the members of the Association in 2 years, when the 3rd Pan-American conference of the HBA-USA will take place.

Mrs. Aghie Balta, Consul General of Greece in New York

Prof. Haralambos Gavras 2011 Aristoteles Award recipient for outstanding contribution in Biomedical Research

Prof. Vassilis Zannis Recipient of the 2011 Award for outstanding contribution in Biosciences Education

Mrs. Koula Sophianou, Consul General of Cyprus in New York

January 2012

Volume 3, Issue 1

World Hellenic Biomedical News

- WHBA Societies News

Hellenic Medical Society of New York

Announcements

The Hellenic Medical Society of New York invites your **nominations for The Maria Kalopothakes, M.D. - Distinguished Female Physician of the Year Award 2012**. Please direct your responses to the Administrator of the Society.

Past Events

(1) Thursday, January 12th 2012: Traditional Cutting of Vasilopita

(2) Diabetes Dinner Symposium with a scientific lecture by Spyros G. E. Meztis, M.D., Ph.D.: "A New DPP-4 Inhibitor for the Treatment of Adult Patients with Type 2 Diabetes Mellitus", Thursday, October 18th, 2011 at Thalassa Restaurant, Tribe, NY

(3) Lectures by Dr. Spyros Mezitis: "Thyroid Disease" and Dr. Nicholas Mezitis: "Diabetes Prevention" on November 11th 2011 at the Pan-Macedonian Studies Center, Queens, NY

(4) **Scientific Symposium 2011: Fellowship Awards, Scholarship Awards and Student Grants**, Thursday December 1, 2011

Scientific Symposium 2011

Demetrios Kotsilimbas Memorial Scholarship recipient Costas Stavrakis, **Dr. Nicholas Mezitis** (President of the HMSNY) and **E-Trade Financial Scholarship** recipient Paul Petrakos

A $ 40,000 medical school scholarship in memory of Mr. Stavros Hartofilis, friend of our Society, was made by his wife Mrs. Aristea Angelopoulou.

- WHBA Societies News

Dr. Spyros G.E. Mezitis and his wife Mrs. Vivian Kartsonis- Mezitis contributed $25,000 for a named medical school scholarship.
Dr. Pavlos Kymissis, former president of the WHBA, was honored as the Distinguished Colleague of 2011 for his services in creating the first medical school on the island of Cyprus, in collaboration with St. George's University London. The school is the only location in the Middle East where students can sit for the MCAT examination, used by U.S. medical schools in their evaluation of candidates for post graduate training.
The Circles distinguished levels of contribution were introduced this year to honor members for their donations and for securing donations from the community.

The Hellenic Medical Society of New York DIAMOND JUBILLE 75th Anniversary Celebration, Friday December 2, 2011.

Gala Honorees: Dr. Pavlos Kymissis (former president of the WHBA), Dr. John Golfinos and Mr. Ernie Anastos

President's Address - 'Diamond Jubilee'
Distinguished Guests and Members of the Hellenic Medical Society of New York
This is a very special evening indeed.
And you are a very special group of individuals gathered here this evening, to celebrate the Hellenic Medical Society of New York 'Diamond Jubilee'. Each one of you, either through service or support, has collaborated in realizing the mission of our Society and in spreading its message: Health, Education, Hellenism
This message, this triptych, was the vision of the Founders of the Society 75 years ago.
We share the vision - We accept the obligations of the torch we carry - We realize the message.
Tonight, we honor three personalities who exemplify the unique gifts of Greece to humanity through the centuries:
EPISTIMI – Science, TECHNI – Arts, KOINA - Public Service
These gifts are lasting. These gifts are the Greek treasure. These gifts express the timelessness of the Greek legacy through its civilization in its offspring. These gifts bear witness to the truth in the words of the poet of the National Resistance - Yannis Ritsos :"On these marbles evil rust has no domain..." ('Σε τουτα εδώ τα μάρμαρα κακιά σκουριά δεν πιάνει...')
Ladies and gentlemen, the Executive Board of the Hellenic Medical Society of New York will now introduce to you our distinguished honorees for 2011:
Dr. John G. Golfinos - Distinguished Physician 2011
Ernie Anastos - Distinguished Hellene 2011
Dr. Paul Kymissis - Distinguished Colleague 2011

The Scholarship Scientific Symposium and the Diamond Jubilee Gala emphasized the new collaborative approach to affairs represented by the Executive Board 2011 - 2013, through its President. All Executive Board members participated in the program and the awards ceremony. 6 past presidents (Dr. Marinos Petratos, Dr. Apostolos Tambakis, Dr. Antoine Harovas, Dr. George Yatrakis, Dr. Spyros Mezitis, and Dr. George Tsioulias) joined the current president, Dr. Nicholas H.E. Mezitis, for commemorative photographs.

2011 collective achievements of the HMSNY

- A $200,000 2-year Fellowship in Ophthalmology at the Harkness Eye Institute of Columbia University was initiated by the HMS NY in honor of Dr. Apostolos Tambakis, a major benefactor of our Society, who has also donated his office in Brooklyn to the Society.
- The Hellenic Medical Society of New York launched its Partners in Medical Practice ProgramTM this year, according a growing number of non-medical professionals and businesses special status in joining the Society to promote their services, attend events and avail themselves of our offerings.
- The HMS NY featured its Yearbook 2011 with material from its monthly e-new bulletins that are sent to over 1000 recipients on their PCs, pads or smart-phones.
- The HMS NY Health Insurance Plan was launched this year and has generated great interest in the Omogenia.
- The HMS NY Private Banking international relationship with HSBC Bank for all members' personal and business accounts was launched this year.
- The HMS NY website has been completely revised and will feature a Physicians' Hotline to direct patients nationally and internationally to the finest physicians in all specialties, who are members of the Society.
- Physicians from Greece are also contacting the Society directly for training opportunities, arranged with our members at academic institutions.
- Scholarships for medical students and grants to medical students and high school students were awarded for specific projects. Dr. Theo Diktaban retired from his position as Chair of the Scholarship Committee for over 20 years and was honored at our Gala.
- The Dr. Mary Kalopothakes Annual Distinguished Female Physician Award was launched this year. Dr. Stella Lymberis was honored for her service in organizing this event. The event was held in a spacious new historic landmark venue at 583 Park Avenue with state-of- the-art acoustics and lighting and excellent cuisine. It was fully subscribed with over 300 representatives from academia, the diplomatic corps, the business world, as well as presidents and representatives of other medical societies and Hellenic-American organizations in attendance. The attendance of many young physicians and past scholarship recipients was remarkable. TV coverage featured the event on the Fox 5 Evening News and on the Makedonia TV network. Videos of the entire event, as well as videos (2) on the history (Past Presidents) and on the future plans (Executive Board) for the Society, which were featured during the Gala will be posted on the new website, together with photographs from the event. A collector's hardcover large-size album with color photographs from the Diamond Jubilee will be available for purchase from the Society.
- Archives of the popular radio program 91.5 'ΥΓΕΙΑ ΚΑΙ ΖΩΗ' from COSMOS FM, hosted by the Mezitis Education Institute - Dr. Nicholas Mezitis and his associate Dr. Despina Komninou, producers, and featuring experts from the Society membership will be available on the website, as well.
- The Hellenic Medical Society of New York is confirming its trademark logo of Asklepios as a symbol of medical excellence, serving as an example for all medical societies of the Hellenic Disapora and as a shining beacon for Greece in a time of distress.

- WHBA Societies News

Hellenic Medical Society of Philadelphia

Ongoing Programs/Prior Events:

1) Hellenic Medical Society of Philadelphia attains **Tax exempt (501c3) status**: With the assistance of our lawyer, friend and NJ Federation President, Tassos Efstratiades of Obermayer, Rebmann, Maxwell and Hippel, IRS granted this status which opens further opportunity for community philanthropy.

2) Hellenic Medical Society of Philadelphia Student scholarship program: The HMS supports a medical student (MD, DO, DMD, DDS) and allied health student scholarship (RN, PharmD, RT, PT) each year. This Year's awards were given to two medical students: **Jonathan McNeill of University of Pennsylvania Medical School** and **Nicholas Kitsopoulos of the UMDNJ-school, of Osteopathic Medicine**. Many thanks to the Scholarship committee including Chair: Denis Hadjiliadis, Catherine Nicholaides, Eleni Pippis, Elias Iliadis and Sophia Pappas.

3) **Go Red for St Thomas AGORA**, October 6-9th, 2011, St Thomas Greek Orthodox Church, Cherry Hill NJ. HMS Philadelphia participated in cardiovascular health event during St Thomas AGORA, Cherry Hill NJ. Over 400 patrons had Blood pressure checked and over 90 received blood glucose and cholesterol results. This program serves to improve the health of the entire community.

4) Hellenic Medical Society of Philadelphia Fall **Social and Greek Wine Tasting**: in conjunction with the other Philadelphia professional societies and continuing with this successful collaboration, our fall event occurred on November 1st at Kuzina by Sofia, Cherry Hill NJ. Of course, the fellowship of the various society members made the evening an overwhelming success.

5) Hellenic Medical Society **Fall Dinner Meeting**, on Tuesday November 15th, at OPA Restaurant, Philadelphia: Over 50 members and friends of the HMS attended the Dinner meeting. Discussion included the approval of the bylaws change and election of half the board each year which was unanimously approved. Committee report from Membership stated 285 members with 60% physicians and 40% allied health. Financial report stated that the society is healthy financially and growing in revenue. Lastly, our Education committee reported on the educational activity of the society including lectures regarding medical malpractice prevention and CME lectures to members. Finally, approval of the 2011 board was conducted unanimously with 3 new board members including Alexia Tsikouras PharmD, Stephanie Morris MD and Mike Moussattas MD. It was a wonderful night of socializing and advancing the HMS.

6) Hellenic Medical Society of Philadelphia supporting Greek American Chamber of Commerce event at Adelphia Restaurant, Wednesday November 16th at 6:30 pm entitled "Access of Public Documents for Business or Personal Use" Presented by Maria Efstratiades, President, GACC. Excellent and thought provoking lecture on the Public information and looking forward to more informative lectures from our Hellenic professionals.

7) HMS of Philadelphia participated in the joint Hellenic University Club, American Hellenic Lawyers Association, and Greek American Chamber of Commerce Christmas party at Union League, Philadelphia PA on December 11th.

Upcoming events:

1) Membership drive of the Hellenic Medical Society of Philadelphia: Please consider making this year's resolution to support your Society and its many programs through your dues which are our only source of income. This includes student scholarships, educational events and community service events. Please see our website page "Membership Dues" for electronic payment. The Hellenic Medical Society of Philadelphia (http://www.hmsphl.com/).

2) Hellenic Medical Society Standing Committees: Members needed to participate on the standing committees of the HMS. Committees are Education (planning of CME and non-CME events), Social (organizing spring, fall and winter social events), Membership (potential member recruitment). Please contact the society if interested.

3) Vasilopita and Winter Social with Hellenic University Club, American Hellenic Lawyers and Greek American Chamber of Commerce, on Wednesday January 25th at 6:30 pm at Estia Restaurant, Philadelphia. Cost: $50 per person for dinner and unlimited socializing with Hellenic Professionals. We are looking forward to a wonderful event.

- WHBA Societies News

Hellenic Medical Society of the United Kingdom

Past Events

The **Hippocratic Oration & Papanikolaou Prize competition** of the Hellenic Medical Society in the UK took place on Saturday 12th of November 2011, at the Hellenic Centre in London. The **Hippocratic orator** was **Professor Michael Gatzoulis**, the academic head of the Adult Congenital Heart Centre and Centre and the Centre for Pulmonary Hypertension at the Royal Brompton Hospital, as well as holding appointment as being a Professor of Cardiology and Congenital Heart Disease at the National Heart & Lung Institute, Imperial College, London. He is also the past president of the International Society for Adult Congenital Cardiac Disease (ISACCD) the largest professional body in the field and holds executive or advisory board positions in other professional bodies, including the International Committee of the American College of Cardiology. He gave the lecture: "**Congenital Heart Disease: Long-term Expectations for the Most Common Inborn Defect**".

Olga Kapellou, Dimitris Paschos (president of the HMS-UK), Michalis Gatzoulis with his son and Effrosyni Gkrania-Klotsas (president-elect) during the award ceremony

The judges noted that there was a very high quality of presentations by junior researchers also took place, which included:

- FGFR1 cleavage and nuclear translocation regulates breast cancer cell behavior, by Athina-Myrto Chioni.
- Effective connectivity during processing of facial affect: evidence for multiple parallel pathways, by Danai Dima.
- Molecular beacon-based multi-allelic real-time PCR for fast and accurate detection of pathogenic viruses and bacteria, by Andreas Hadjinicolaou.
- The effect of novel texture features of homogeneity and echolucency on carotid plaque characterization; results from the ACSRS study and subgroup analysis, by Gregory Makris.
- IκBα inhibits apoptosis at the outer mitochondria membrane through a novel, NF-κB–independent, interaction with VDAC1, by Evangelos Pazarentzos
- Accurate telemonitoring of Parkinson's disease symptom severity using nonlinear speech signal processing and statistical machine learning techniques, by Athanasios Tsanas.

Athina-Myrto Chioni and **Evangelos Pazarentzos** shared the **Papanikolaou Prize**.

Future Events

The Annual General Meeting and Vasilopitta Evening will take place at the boardroom at the Hellenic Centre in London, 7pm Friday 27th January 2012.

Hellenic Medical Association of Quebec, Canada

Past events

CME Events:

September 27th, 2011
Otolaryngology – "Pot-pourri" for the general practitioner
Apostolos Christopoulos MD, MSc, FRCSC
At: Mythos Ouzeri
Sponsored by: Merck

October 19th, 2011
Probiotics–Opportunities In Health
At: Mythos Ouzeri
Sponsored by: Ferring

November 29th, 2011
CME on:Cervical Cancer Update- New Preventive Measures (HPV Testing And Prophylactic Vaccination)
Dr Alex Ferenczy
At: Crescendo Restaurant
Sponsored by: Merck

February 21st, 2012
Lipids, New HDL therapy
Dr. M. Schweitzer
Lezvos West Restaurant

HMAQ CHRISTMAS PARTY
December 9th , 2011
Mythos Ouzeri
A relaxing and fun night was had by all attending members and their accompanying guests. We would like to thank all our members making 2011 another great year to be part of our longstanding academic and philanthropic institution. A special thanks to our sponsors and supporters over the years.