THE CYPRUS INSTITUTE OF NEUROLOGY & GENETICS

A Center of Excellence

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THE CYPRUS INSTITUTE OF NEUROLOGY & GENETICS
ΙΝΣΤΙΤΟΥΤΟ ΝΕΥΡΟΛΟΓΙΑΣ
&
ΓΕΝΕΤΙΚΗΣ ΚΥΠΡΟΥ
KIBRIS GENETİK
&
NÖROLOJİ ENSTİTÜSÜ
THE CYPRUS INSTITUTE
OF
NEUROLOGY & GENETICS

The Cyprus Institute of Neurology and Genetics

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Message from the President of the Board of Directors

Mr Chris Phylactou

Our Objective in issuing and distributing this “CING profile booklet” is to raise awareness and provide useful information to interested Entities/Individuals as well as to share with them the Mission and Vision of The Cyprus Institute of Neurology and Genetics (CING). We are aiming also to inform the readers of our current scientific interests, areas of work and some of the results accomplished so far, as well as to share some of the work in progress that falls within our short term plans.

In the core of our mission is the “Human and its Well Being”. Our prime role and objective within the scope of our specialized services and research work in the Biomedical and NeuroGenetics Sciences is to keep people healthier, happier and more productive in life.

Our vision is to maintain and improve upon our position as a Centre of Excellence in the Biomedical Sciences by giving equal opportunities, encouragement and support to all of the CING people irrespective of ethnic origin, gender, language, color or religion to succeed and excel in their respective area of activity and specialization.

Within the same spirit and values, as a non profit/non Government medical, research and academic Institution we remain dedicated and will spare no effort to continue serving in excellence all patients and the society in general in Cyprus, as well as people from other neighboring countries who are in need of our expertise.

Message from the Chief Executive Medical Director

Dr Philippos C. Patsalis

The Cyprus Institute of Neurology and Genetics continues on its journey through time, true to its vision and its goals to operate as a National and Regional Centre of Excellence - offering specialised services, advanced research, and post-graduate education in the areas of Neurology, Genetics and Biomedical Sciences. These goals were set by its Founders and all those who worked so hard to make this Institute a reality. We are here to continue these endeavours and advance them even further. We are here to continue upgrading and modernizing the state-of-the-art infrastructure and work of the Institute, making it even more competitive, with a leading role in the Region and an International reputation. We are well aware of our role, and the responsibility that we undertook with the founding of this Institute and we would like to assure all the people of Cyprus that we will continue to work hard, with zeal, passion and determination, in order to achieve all its goals and keep the Institute at the front line of the international scientific arena.

The Cyprus Institute of Neurology and Genetics

The Cyprus Institute of Neurology and Genetics (CING) is a bicommunal, non-profit, academic Institution.

The Vision of the CING is to function as a National Centre of Excellence and a Regional Referral Centre in the areas of Neurology, Genetics, Biomedical, Medical and other similar and related Sciences.

The Mission of the CING is to develop and provide high level clinical and other laboratory services, develop and pursue advanced research and provide education in the areas of Neurology, Genetics, Biomedical, Medical and other similar and related Sciences.

Its ultimate scopes are to improve and upgrade the quality of life of all Cypriot citizens, irrespective of religion or national origin, and strengthen its international role in the areas of its specialty.

The First Lady of the Republic of Cyprus Mrs Elsi Christofia is the Honorary Patron of The Cyprus Institute of Neurology and Genetics

Scientific Research

The Cyprus Institute of Neurology and Genetics has the largest and most technologically developed research infrastructure in Cyprus and the neighboring area in the sectors of Neurology, Genetics, Biomedical and Medical Sciences.

The Institute makes important contributions towards basic and translational research. CING research scientists are characterized by their enthusiasm and devotion to the advanced research carried out within the CING, resulting in the Institute becoming an important regional research resource.

Over the last few years, the number of research grants obtained from funding organizations in Cyprus and abroad has increased, i.e. there are approximately 40 ongoing research grants with a total funding of approximately €6.000.000.

The results of the successful completion of research programs are depicted in the number of publications in international peer review scientific journals and books. The publications in high impact factor journals of peer reviewed articles are approximately 45 per year. Moreover, more than 25 national and international awards for scientific work have been granted to CING by various scientific organizations and authorities in Cyprus and abroad.

The CING obtains the majority of competitive grants of the country in the health sector and provides very competitive and pioneering biomedical research. The CING has established more than 100 international research collaborations with universities and research institutes abroad.

Educational Programs and Activities

The Cyprus Institute of Neurology and Genetics has developed the facilities and an atmosphere enabling education and training activities within the Institute.

The CING promotes and provides training of doctors, scientists and students, as well as educational programs and studies. Up until today, several doctoral theses resulting in the award of the PhD title have been completed. The doctoral studies were completed in collaboration with universities in Cyprus and abroad. Today 18 doctoral students are working towards their PhD studies. The CING is recognized for the completion of PhD studies by several universities in Cyprus and abroad, i.e. University of Cyprus, University of Athens, University of London, Imperial College of London, University of Bristol, etc. The CING has also been recognized by European Universities for the completion of the final thesis of Biology degree students.

Moreover, the CING provides education and specialization to graduate students, doctors and scientists from Cyprus and abroad in specialized fields of Genetics and Laboratory Medicine.

A substantial number of neurologists from Cyprus and abroad have completed their specialization training at CING and continue specializing in Clinical Neurology and Electromyography. Also, the CING has established a training program (approved and accredited by the Cyprus Ministry of Health) for the acquisition of the one year medical specialty in Neurology.

In addition to the above, the CING organises lectures on a weekly basis within the CING, as well as national and international scientific meetings, conferences and courses in Cyprus and abroad. These academic activities are approved by the Cyprus Medical Association for awarding points for continuing education of medical doctors.

Since 2004, the CING has been recognized by the European School of Genetics Medicine as a regional centre of education in the sector of Medical Genetics and to date, 7 European congresses have been organized at the CING.

The CING is considered to be the most advanced tertiary medical academic centre in our country in the health sector as it provides education and training to doctors, scientists, students and paramedical personnel.

Specialized Medical, Biomedical and other Services

The Cyprus Institute of Neurology and Genetics provides a wide range of highly specialized clinical and laboratory medical and biomedical services to all Doctors, Clinics and Hospitals in the Government and Private sector, offering diagnostics for common and rare diseases to the Cypriot community and to countries of the region. The CING also provides forensic services to the Government and Private sector.

The CING provides approximately 65.000 examinations (clinical and laboratory services) per year. The cost of these examinations is approximately €6.000.000, per year. The CING is the only Institute in Cyprus that has the technology, know-how and expertise to provide more than 90% of these examinations.

The Institute has also established collaborations with Centers and Universities of the neighboring area and provides diagnostic services as a Regional Referral Center.

Several services offered by CING are accredited or certified thereby ensuring their high quality. All CING laboratories currently participate in international external quality control schemes.

The CING plays a leading role in Cyprus in the fields of Neurology, Genetics, Biomedical and Medical Sciences. It has introduced and applied clinical and laboratory services with great success, and has undertaken the responsibility of several national diagnostic and screening programs in these sectors.

Brief history of the Cyprus Institute of Neurology and Genetics

The Cyprus Foundation for Muscular Dystrophy Research is the parent organization of the Cyprus Institute of Neurology and Genetics. It was established in 1987 under the name Muscular Dystrophy Research Trust of Cyprus (MDRTC) by the Cyprus Muscular Dystrophy Association, Lady Langley (wife of the then Commander of the British Bases in Cyprus) and Dr Lefkos T. Middleton (first Medical Director of the Institute). In 1991, the Trust created the Cyprus Institute of Neurology and Genetics and in 1995, it was renamed as the Cyprus Foundation for Muscular Dystrophy Research (CFMDR).

CING the initial stages (1991-1995)

In the initial stages of establishment (1991–1995), the CING was functioning in a space of 300m^2 at the Makarios Hospital in Nicosia with basic equipment, and a staff of approximately 20 individuals (scientific and administration). This space was generously provided by the Cyprus Government, who also donated the land for building CING's new premises. Moreover, the United States Government donated to CING, through the Cyprus office of the United Nations High Commission for Refugees, an amount for running the Institute during the years 1991-1995, as well as for the establishment of its new premises. Using part of this initial one-off funding, the CING established the Departments and Clinics at Makarios Hospital, employed a small number of employees and purchased basic equipment. These small scientific groups (Departments and Clinics) managed to attract the first external competitive research grants and published the first scientific papers of the Institute.

CING new premises (1995-2009)

In 1995, the CING moved to its own purpose-built premises made up of an area of approximately 10.000m^2. Due to the lack of a medical center in Cyprus with the infrastructure and know-how to provide specialized laboratory and clinical services, the Cyprus Government offered to fund the CING annually, in return for the provision of specialized clinical and diagnostic services to Government Hospitals. This annual funding has been the major backbone of the CING budget for all these years, and has helped it to survive financially and expand further.

CING today

The CING receives international recognition and plays an active and essential role as a national, regional and international center of excellence for the provision of high quality services, research and education. The dynamic success of the Institute is based on the development of medical services and research programs which are directly related to the needs of Cyprus and the countries of the region.

Today the CING is one of the very few innovative organizations in Cyprus that has developed a critical mass, and contributes actively in the research and development of new knowledge.

The CING has available appreciable human potential, laboratory infrastructure unique for Cyprus, excellent relations and collaborations with countries of the Middle East, Northern Africa, Europe and America, and is successfully competing at the national and international level.

External Evaluation of the CING

An External Evaluation Team, consisting of eight world renowned scientists (seven members of the International Scientific Advisory Committee and one member recommended by the Planning Bureau of the Republic of Cyprus) conducted the On-Site External Evaluation. The evaluation was based on high international standards and included interviews with the Chief Executive Medical Director and all Heads of Departments, Clinics and Group. The External Evaluation Team also met with members of the Board of Directors. Following completion of interviews and a tour of the CING Departments and Clinics, the Team prepared a detailed evaluation report, the outcome of which was outstanding.

The evaluation of our Institute provides an external peer review evaluation of our standards, which helps us to achieve our long and short term goals. Evaluation is a very useful tool for continuing self-improvement.

Telethon

Telethon is an international charitable campaign that began in the United States and subsequently extended to Europe. The countries in Europe that have adopted and successfully organize TELETHON are France, Italy, Belgium, Switzerland, Luxemburg and Cyprus.

The main aims of TELETHON are:

- To increase public awareness of the problems of patients who suffer from neurological, neuromuscular and genetic diseases.
- To project the scientific work carried out at the CING.
- To financially support the research activities of the CING on neurological, neuromuscular and genetic diseases.
- To financially support the Cyprus Muscular Dystrophy Association, the efforts of which are focused on the continuous improvement of the quality of life of its members.

The Cyprus TELETHON includes many fundraising events that take place throughout the year.

The Cyprus TELETHON is being organized annually by the Cyprus Institute of Neurology and Genetics in collaboration with the Cyprus Muscular Dystrophy Association, since 1994.

Organization and Structure

Board of Directors

The Board of Directors consists of 20 members. Ten members, including the President, are representatives of the Cyprus Government (eight are appointed by the Council of Ministers, one by the Ministry of Health and one by the Ministry of Education). Nine members are representatives of patient associations, the CING Scientific Council, the United States Government, the British Bases in Cyprus and the Turkish-Cypriot community. One member is the CING Chief Executive Medical Director.

The Board of Directors exercises the following powers and executes the following duties: a) administers and controls the affairs of the Institute and all its property, and in general deals with all related matters, b) acts in regard to the above matters and property in a way that best promotes the interests and aims of the Institute, c) exercises all other activities and undertakes acts and actions which are conducive or essential, for the achievement of the aims of the Institute.

President	**Mr Phylactou Christos** (Cyprus Government representative)
Vice President	**Mr Agapiou Yiannakis** (Cyprus Government representative)
Treasurer	**Mr Voskos Panicos** (Cyprus Government representative)
Secretary	**Dr Patsalis Philippos** (CING Chief Executive Medical Director)
	Dr Angastiniotis Michael (Pancyprian Antianemic Association)
	Dr Constantinou George (CING Scientific Council representative)
	Dr Demetriou Andreas (CING Scientific Council representative)
	Dr Djavit Ahmed (Cyprus Government representative)
	Mr Eliades Christos (Cyprus Government representative)
	Dr Hami Mustafa (Turkish-Cypriot representative)
	Mr Ioannou Ioannis (Cyprus Government representative)
	Dr Kaimakliotis Ioannis (US Government representative)
	Dr Malisan Lucy (US Government representative)
	Dr Polynikis Andreas (Ministry of Health representative)
	Mrs Santama Niki (Ministry of Finance representative)
	Mr Stylianou Stelios (Muscular Dystrophy Association)
	Mr Theophilou Theophilos (Cyprus Government representative)
	Mrs Tiggiridou Sylva (Cyprus Government representative)
	Mr Varoglu Ahmet (Turkish-Cypriot representative)
	Vacant position (British Bases representative)

Chief Executive Medical Director

The Chief Executive Medical Director, who is also the Chairman of the Scientific Council, heads all medical, scientific and other services of the Institute.

Dr Philippos C. Patsalis, BSc, MA, MPh, PhD, HCLD

Scientific Council

The Scientific Council consists of the Chief Executive Medical Director who is the Chairman of the Scientific Council, the Financial and Administrative Director and the Heads of Departments and Clinics of the Institute.

The Scientific Council is in charge of the academic and scientific work of the Institute both in the field of medical and laboratory services and in the area of research and post-graduate training. More particularly it, a) approves the academic research and training programs, and medical and laboratory services provided, b) submits to the Board of Directors proposals for the allocation of the budget and the Institute's requirements concerning medical and other equipment, c) makes suggestions to the Board of Directors regarding the establishing or abolishing of medical and scientific teams, laboratories, Departments or Clinics, d) sets up committees from among its members and may delegate to such committees, on any terms and conditions it deems fit, any of its powers, e) carries on any activities, and carries out any duties granted to it or imposed on it by the Articles of Association or the Institute's Regulations and f) regulates its own proceedings subject to the provisions of the Articles of Association and the Institute's Regulations.

Chairman	**Dr Patsalis C. Philippos**, BSc, MA, MPh, PhD, HCLD
Secretary	**Dr Phylactou A. Leonidas**, BSc, PhD
	Dr Cariolou Marios, BSc, PhD
	Dr Christodoulou G. Christina, BSc, MSc, DEA, Dipl. Virol., PhD
	Dr Christodoulou Kyproula, BSc, MSc, PhD
	Dr Christophidou Anastassiadou Violetta, MD (in attendance)
	Dr Drousiotou Anthi, BSc, PhD, ARCSc
	Mr Flouros Marios, BSc, MHA, FCA
	Dr Kleanthous Marina, BSc, PhD
	Dr Kleopa A. Kleopas, MD
	Dr Kyriacou Kyriacos, BSc, PhD, FRMSoc
	Dr Kyriakides Theodoros, MB, ChB, BSc (Hons), FRCP (Lon)
	Dr Pantzaris Marios, MD
	Dr Papacostas Savvas, MD
	Dr Zamba Papanicolaou Eleni, MD

International Scientific Advisory Committee

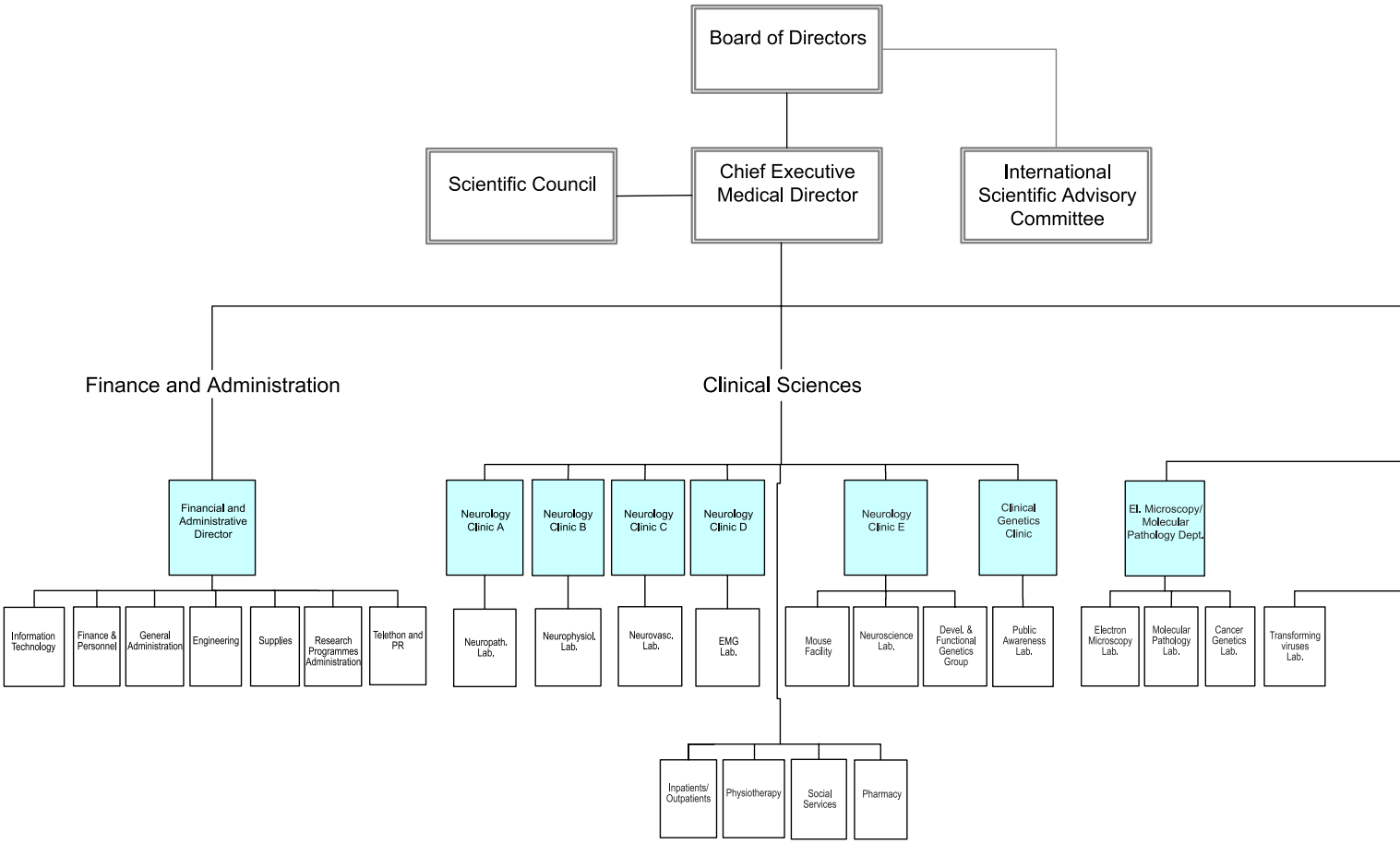
The International Scientific Advisory Committee consists of 10 internationally-renowned scientists appointed by the Board of Directors. The International Scientific Advisory Committee has the following competencies: a) to advise the Board of Directors on matters of scientific policy, b) to provide assistance to the Scientific Council on scientific matters and c) to carry out assessments and evaluations on any matter forwarded to it by the Board of Directors or the Scientific Council.

Prof. John Christodoulou	Director, Western Sydney Genetics Program The Children's Hospital Westmead The University of Sydney Australia
Prof. V.M. Der Kaloustian	Professor of Pediatrics and Human Genetics Clinical Director, Division of Medical Genetics McGill University Health Center Montreal, Canada
Prof. Douglas Higgs	Director of the Molecular Haematology Unit and Hon. Consultant Haematologist MRC Molecular Haematology Unit Institute of Molecular Medicine John Radcliffe Hospital University of Oxford Oxford, U.K.
Prof. Peter Karayiannis	Reader in Molecular Virology Department of Medicine, Hepatology Section Division of Medicine Imperial College London London, U.K.
Prof. James R. Lupski	Cullen Professor of Molecular and Human Genetics and Professor of Pediatrics Baylor College of Medicine Houston Texas, U.S.A.
Prof. Dimitris P. Mikhailidis	Academic Head of Department Department of Clinical Biochemistry (Vascular Disease Prevention Clinics) Royal Free Hospital Royal Free University, College School of Medicine University College London London, U.K.
Prof. Konstantin Miller	General Secretary of the European Cytogenetics Association Director of Cytogenetics Institute of Human Genetics Hannover Medical School Hannover, Germany

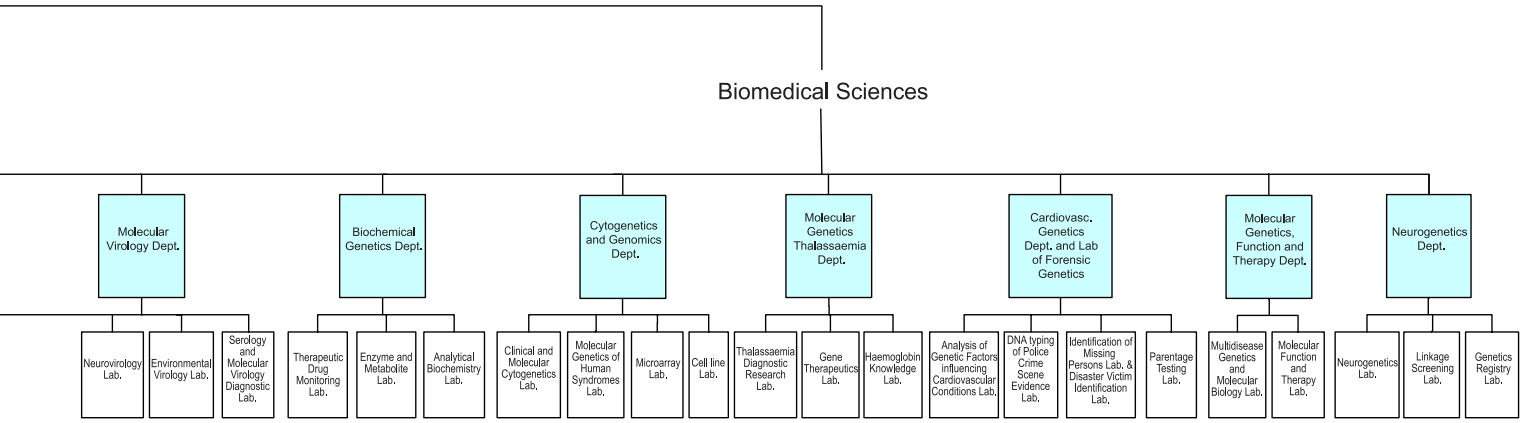
Prof. Jahn M. Nesland	Vice President of International Academy of Pathology Director of Division of Pathology The Norwegian Radium Hospital University of Oslo Oslo, Norway
Prof. Timothy Pedley	Chairman The Neurological Institute Columbia University New York, U.S.A.
Prof. Demetris Vassilopoulos	Professor of Neurology University of Athens Neurology Clinic Aiginitio Hospital University of Athens Athens, Greece

THE CYPRUS INSTITUTE OF NEUROLOGY AND GENETICS

ORGANIZATIONAL CHART



Dept/Clinics represented in the Scientific Council


Biomedical Sciences
Molecular Virology Dept.
Neurovirology Lab.
Environmental Virology Lab.
Serology and Molecular Virology Diagnostic Lab.
Biochemical Genetics Dept.
Therapeutic Drug Monitoring Lab.
Enzyme and Metabolite Lab.
Analytical Biochemistry Lab.
Cytogenetics and Genomics Dept.
Clinical and Molecular Cytogenetics Lab.
Molecular Genetics of Human Syndromes Lab.
Microarray Lab.
Cell line Lab.
Molecular Genetics Thalassaemia Dept.
Thalassaemia Diagnostic Research Lab.
Gene Therapeutics Lab.
Haemoglobin Knowledge Lab.
Cardiovasc. Genetics Dept. and Lab of Forensic Genetics
Analysis of Genetic Factors influencing Cardiovascular Conditions Lab.
DNA typing of Police Crime Scene Evidence Lab.
Identification of Missing Persons Lab. & Disaster Victim Identification Lab.
Parentage Testing Lab.
Molecular Genetics, Function and Therapy Dept.
Multidisease Genetics and Molecular Biology Lab.
Molecular Function and Therapy Lab.
Neurogenetics Dept.
Neurogenetics Lab.
Linkage Screening Lab.
Genetics Registry Lab.

Finance and Administration Department

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Personnel

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Kyrialli Kristiana, BSc, MSc
Miltiadous Andreas

Finance and Personnel
Kazandjian Vera, BA, MBA – Financial and Personnel Services Manager
Deligeorgi Triantafillia, BA, MA
Shakalli Maro
Photiou Elena

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Odysseos Maria, BSc, MBA – Administrative Services Manager
Loizou Maria, BA, MBA
Damianou Maria
Hadjiyianni Christina
Polycarpou Elena
Kyriacou Elena
Ellina Maria
Mouzourkou Maria
Efstathiou Frederikos
Andreou Stavros
Savvidou Eliana
Chrysaphiades Polycarpos
Andreou Jenny
Eliadou Eleni

Engineering
Gerolakkitis Michalis, BSc – Senior Engineer
Polycarpou Neophytos
Apostolides Georgios

Supplies
Vlachou Amal, BSc, MPH – Purchasing and Store Manager
Ioannou John, PgDip, MCIPS
Pashiali Eleni

Research Programmes Office
Ioannidou Elena, BSc, MBA – Research Programmes Officer

Telethon and PR
Karanikis Kypros, Dip (HM) – Telethon and PR Manager
Vatiliotis George, Dip (HM)

Activities

The Finance and Administration Department is responsible for the financial and administrative matters of the Institute. Its mission is to support the service, research and education activities of the Institute through the provision of high quality administrative services to all the spectrum and levels of the Institute hierarchy, its patients and the public. The Finance and Administration Department comprises of seven sections:

- General Administration
- Finance and Personnel
- Supplies
- Engineering
- Information Technology
- Research Programmes Office
- Telethon and PR


GILSON

CING Clinical and Biomedical Sciences Departments and Clinics

Clinical Sciences

Personnel
Clinical Sciences Co-ordinator
Dr Kyriakides Theodoros, MB, ChB, BSc (Hons), FRCP (Lon)

Inpatients
Toufexis Judith
Kazakeou Mary
Deneva Rayna
Hanghiuc Mariana
Kukova Krassimira
Stylianou Olga
Charalambous Dimitrinka
Charalambous Kyriaki
Kaplani Svetlana
Chroidou Galini
Askalidou Electra
Gencheva Lilyana
Chkheidze Ekaterine

Outpatients
Gagglia Eftychia
Papadopoulou Eleni
Chryseliou Marina
Symeou Maria

Physiotherapy
Ormiston Annita, MCSP
Zannettou Irini, BSc

Social Services
Pavlou Marina, BSc

Pharmacy
Kkolou Eleni, BSc
Ploutarchou Andry, BSc

Activities

The Clinical sciences consist of five Neurology Clinics with their associated laboratories (Clinics A-E), a Clinical Genetics Clinic and a common outpatient/inpatient infrastructure facility.

The Neurology Clinics provide tertiary medical care to patients with neurological disorders such as muscular dystrophy, myasthenia gravis, multiple sclerosis, epilepsy, neurovascular diseases, movement disorders, Alzheimer's disease and others. The referrals are from government neurologists and neurosurgeons, the private sector and from abroad. Each of the Clinics has its main service and research interests which will be outlined below. The Clinical Genetics Clinic provides diagnoses and counselling to a variety of congenital and genetic disorders.

The outpatient infrastructure consists of a pharmacy, physiotherapy service, a social worker, an outpatient nurse as well as receptionists and secretarial support. One of the basic principles of the Clinical Sciences is the provision of multidisciplinary care and therefore a variety of specialty clinics are provided on site. These include cardiology, chest medicine, gastroenterology, orthopedics, endocrinology, psychology, speech pathology and a dietitian.

The inpatient infrastructure consists of a 12 bedded ward which operates on 24 hour basis for cold admissions. The latter include patients for investigation and treatment, video-EEG monitoring and on rare occasions terminal care.

The Clinics of the Clinical Sciences see, investigate and treat more than 5.000 patients annually with a steadily increasing number of referrals. They also participate in education by having Psychiatry and Neurology residents from Cyprus and Greece.

Neurology Clinic A

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Personnel
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Neuromuscular Laboratory
Papacharalambous Revecca, BSc
Polycarpou Pavlos, BSc

Activities

The study and treatment of neuromuscular diseases has been the original aim of the CING and this continues to be the main priority of this Clinic. It serves as a national tertiary referral centre for neuromuscular disorders and houses the only neuropathology laboratory in Cyprus that processes muscle and nerve biopsies. A wide variety of neuromuscular disorders are investigated and treated including muscular dystrophy, inflammatory myopathies, inherited and acquired neuropathies, amyotrophic lateral sclerosis and others. A multi-disciplinary approach to therapy is followed. Demyelinating disease including Multiple sclerosis is another interest of the Clinic although a large number of challenging general neurology patients is also seen. The Clinic also established and functions the Neuromuscular Laboratory.

Research Interests

- Epidemiology and molecular pathology of Familial Amyloidotic neuropathy Type I.
- The role of oxidative stress and apoptosis in the pathophysiology of mitochondrial encephalomyopathies.
- Therapeutic trials of different molecules in the G93A transgenic animal model of ALS.
- The role of oxidative stress in the pathophysiology of dystrophinopathies.
- The investigation of HyperCKemia.

Selected Publications

- Dardiotis E, Koutsou P, Zamba-Papanicolaou E, Vonta I, Hadjivassiliou M, Hadjigeorgiou G, Cariolou M, Christodoulou K, Kyriakides T. Complement C1Q polymorphisms modulate onset in familial amyloidotic polyneuropathy TTR Val30Met. J Neurol Sci. 2009 Jun 2. [Epub ahead of print]

- Pantelidou M, Zographos SE, Lederer CW, Kyriakides T, Pfaffl MW, Santama N. Differential expression of molecular motors in the motor cortex of sporadic ALS. Neurobiol Dis. 2007 Jun;26(3):577-89. Epub 2007 Feb 16.

- Kleopa KA, Drousiotou A, Mavrikiou E, Ormiston A, Kyriakides T. Naturally occurring utrophin correlates with disease severity in Duchenne muscular dystrophy. Hum Mol Genet. 2006 May 15;15(10):1623-8. Epub 2006 Apr 4.

- Kleopa KA, Zamba-Papanicolaou E, Alevra X, Nicolaou P, Georgiou DM, Hadjisavvas A, Kyriakides T, Christodoulou K. Phenotypic and cellular expression of two novel connexin32 mutations causing CMT1X. Neurology. 2006 Feb 14;66(3):396-402.

- Sivakumar K, Kyriakides T, Puls I, Nicholson GA, Funalot B, Antonellis A, Sambuughin N, Christodoulou K, Beggs JL, Zamba-Papanicolaou E, Ionasescu V, Dalakas MC, Green ED,

Fischbeck KH, Goldfarb LG. Phenotypic spectrum of disorders associated with glycyl-tRNA synthetase mutations. Brain. 2005 Oct;128(Pt 10):2304-14. Epub 2005 Jul 13.

- Kleopa KA, Kyriacou K, Zamba-Papanicolaou E, Kyriakides T. Reversible inflammatory and vacuolar myopathy with vitamin E deficiency in celiac disease. Muscle Nerve. 2005 Feb;31(2):260-5.

- Kleopa KA, Kyriakides T. A novel movement disorder of the lower lip. Mov Disord. 2004 Jun;19(6):663-6.

- Christodoulou K, Zamba E, Tsingis M, Mubaidin A, Horani K, Abu-Sheik S, El-Khateeb M, Kyriacou K, Kyriakides T, Al-Qudah AK, Middleton L. A novel form of distal hereditary motor neuronopathy maps to chromosome 9p21.1-p12. Ann Neurol. 2000 Dec;48(6):877-84.

Neurology Clinic B

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Personnel
Head, Papacostas Savvas, MD
Themistocleous Despina, MA (PhD Candidate)

Neurophysiology Laboratory
Papathanasiou Eleftherios, PhD
Myrianthopoulou Panayiota, BSc

Activities

This Clinic specializes in behavioral neurology and dementias like Alzheimer's disease and neurodegenerative disorders or behavioral symptoms of brain disease. Also, we participate in regional/international studies of new treatments.

We evaluate patients with epilepsy who do not respond to traditional medical therapies. Patients undergo thorough evaluation and, in selected cases, video-EEG recording to assess whether they could improve or become seizure free with surgery. Other specialized neuropsychological evaluations include Wada tests to assess the location of memory and language in the brain. Selected patients are either referred abroad, or operated locally by collaborating surgeons from the United States. Patients may be offered alternative treatments such as Ketogenic Diet or implantation of a Vagus Nerve Stimulator, a method that controls seizures and improves quality of life. Patients may participate in studies with new anti-epileptic medications.

The Clinic established and operates the Clinical Neurophysiology Laboratory which performs electroencephalography, video-EEG, and evoked potentials to evaluate the function of sensory symptoms in the upper and lower extremities, the eyes and the ears. Sleep studies are performed to evaluate sleep-related problems or excessive daytime sleepiness.

Clinic B serves as the national contact point for the surveillance of Creutzfeldt-Jacob disease, a program sponsored by the European Union. The consortium's diagnostic criteria have been adopted by the World Health Organization.

Between 2007-2008 three University of Cyprus students obtained Masters Degrees in Clinic B. Their topics, currently prepared for publication were; "Quality of life and working memory in patients with temporal lobe epilepsy"; "Neuropsychiatric and memory disturbances in pharmacoresistant epilepsy"; "Translation and validation into Greek are the Epilepsy Foundation Concerns Index and co-administration with Beck's depression scale and anxiety scales". All of the above have been presented in international and local meetings. The Clinic Head participates in the Technological University of Cyprus Advisory Committee for the creation of a School for Health Sciences and teaches at the University of Cyprus.

Research Interests

- Comparison of psychogenic with epileptic seizure patients.
- Psychological, Cognitive and quality of life issues in patients with epilepsy.
- Sudden Unexpected Death in epilepsy during video-EEG monitoring (MORTEMUS Study).
- Neurogenic vestibular evoked potential cortical representations.
- Neurophysiological correlates of developing intelligence – Collaboration with the

University of Cyprus.

- Efficacy and safety of new anti-epileptic and dementia drugs.
- Neurophysiology of Multiple Sclerosis.

Selected Publications

- Papacostas SS, Malikides A, Petsa M, Kyriakides T. “10-year mortality from Creutzfeldt-Jakob disease in Cyprus”. WHO – Eastern Mediterranean Health Journal, 14(3): 715-719, 2008.

- Papathanasiou ES, Papacostas, SS.” Flash electroretinography: Normative values with surface skin electrodes and no pupil dilation using a standard stimulation protocol”. Documenta Ophthalmologica 2008;116:61-73.

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Neurology Clinic C

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Activities

A national Multiple Sclerosis (MS) Clinic was established at the Cyprus Institute of Neurology and Genetics in 1989, when it became apparent that the prevalence of MS in Cyprus was high and approaching that of northern European populations.

Epidemiological research at the Institute has shown a high prevalence in the Greek Community with 180 cases per 100.000. The Clinic cares for over 800 patients with access to inpatient, neurophysiology and physiotherapy facilities. Drug therapy, including the administration of corticosteroids, interferons, mitoxandrone and the newer monoclonal antibodies is supervised by the clinic.

The Clinic established and functions the Neurovascular Laboratory. The laboratory serves as a regerence lab for the study of the extracranial carotid arteries, the extracranial vertebral arteries and the intracranial arteries (the only laboratory in our country that offers the last service). Carotid artery atherosclerosis is the major cause of ishaemic brain damage (ischaemic stroke), so the study of the carotids with ultrasound offers significant clinical data for both primary and secondary stroke prevention. The laboratory offers unique and experienced diagnostic service in arterial dissection, both in the territory of the internal carotid and vertebral arteries. Transcranial study of the intracranial brain arteries offer diagnostic services for intracranial arterial stenosis, intracranial aneurysms, arterial vasospasm following subarachnoin haemorrhage and also transcranial monitoring for emboli detection as well as for arterial reserve study (CO2 reactivity test).

Research Interests

- Development of databases for epidemiological and clinical data for Multiple Sclerosis and Stroke.
- Development of automated computer programmes to identify and evaluate the arterial wall thickness and plaque delination in carotid atherosclerotic disease.
- Qualitative study of the carotid wall changes and carotid atherosclerotic plaques and the evaluation of future events (stroke and carotid stenosis).
- Quantitative and qualitative study of the demyelinating plaques in the brain and the evaluation of prognostic factors in Multiple Sclerosis prognosis.

Selected Publications

- C.P. Loizou, M. Pantziaris, M.S. Pattichis, E. Kyriakou, C.S. Pattichis, “Ultrasound image texture analysis of the intima and media layers of the common carotid artery and its correlation with age and gender,” Computerized Medical Imaging and Graphics, vol. 33, no.4, pp. 317-324, 2009.

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segmentation of atherosclerotic carotid plaque," IEEE Trans. on Inform. Techn. in Biomedicine," vol. 11, no. 6, pp. 661-667, Nov. 2007.

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- C.P. Loizou, C.S. Pattichis, C.I. Christodoulou, R.S.H. Istepanian, M. Pantziaris, and A. Nicolaides "Comparative evaluation of despeckle filtering in ultrasound imaging of the carotid artery," IEEE Trans. Ultrasonics Ferroelectrics and Frequency Control, vol. 52, no. 10, pp. 1653-1669, 2005.

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Activities

Clinic D provides outpatient clinic services in the fields of neurogenetic diseases including Spino Cerebellar Ataxias (SCA), Friedreich's Ataxia, Charcot-Marie-Tooth Polyneuropathies (CMT), Huntington's disease, Myotonic Dystrophy and Spinal Muscular Atrophy (SMA). These services also cover a number of neuromuscular disease patients including Myasthenia Gravis (MG) and Motor Neuron Disease (MND). A special Botulinum Toxin treatment clinic is offered to a number of patients with focal dystonias and spasticity.

The Clinic functions the EMG Laboratory. The EMG laboratory provides services for the investigation of the peripheral nervous system including neuropathies, rediculopathies, plexopathies, myopathies and neuromuscular junction defects. Some of the services are Nerve Conduction Studies, Blink Reflex, Jaw Jerk Reflex, Masseter Inhibitory Reflex, Repetitive stimulation, Mixed nerve, Inching technique, Autonomic testing, H-reflex, Electromyography, Quantitative EMG, Single fibre EMG.

Research Interests

Clinic D is interested and involved in a number of research projects on neurogenetic diseases including:

- Charcot-Marie-Tooth polyneuropathies.
- Spino Cerebellar Ataxias.
- Hereditary motor neuronopathy type Jerash, FSHD.
- Spinal Muscular Atrophy.

Selected Publications

- Paschalis Nicolaou, Anthi Georghiou, Christina Votsi, Lefkos T Middleton, Eleni Zamba-Papanicolaou and Kyproula Christodoulou. A novel c.5308_5311delGAGA mutation in Senataxin in a Cypriot family with an autosomal recessive cerebellar ataxia. BMC Medical Genetics 2008, 9:28; doi:10.1186/1471-2350-9-28.

- Eleftherios S. Papathanasiou, Eleni Zamba-Papanicolaou. Differential Orbicularis Occuli involvement in Neuromuscular Junction Dysfunction. Journal of Clinical Neurophysiology Vol 25, No.5 Oct 2008; 293-298.

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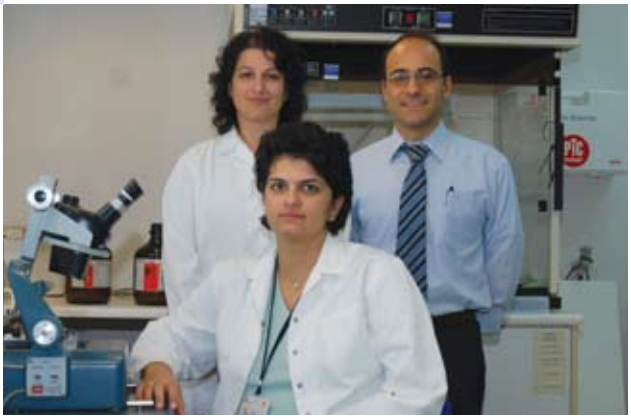
Neurology Clinic E



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Activities

Neurology Clinic E provides specialized services for a broad spectrum of neurological disorders focusing on neuromuscular disorders and electromyography. The Clinic provides care for outpatients and inpatients with myasthenia gravis, inherited and acquired peripheral neuropathies and myopathies, motor neuron disease, and other degenerative, autoimmune and metabolic neurological diseases, including inherited and acquired demyelinating disorders of the peripheral and central nervous system. We also perform regularly nerve conduction studies and electromyography for adults and children. The Clinic Head also oversees the activities of the Mouse Facility.

Our research group in the Neuroscience Laboratory has been active both in clinical as well as basic research with emphasis on translational aspects of neuroscience and generating models of neurological disease. We generate and study cellular and mouse models of inherited neuropathies caused by gap junction mutations and gene therapy applications are being designed. The study of molecular mechanisms in inherited and autoimmune disorders of ion channels and related molecules has been another focus of our activities. Furthermore, we have started the investigation of gap junction pathology in post-mortem human brain from multiple sclerosis patients, as well as in Experimental Autoimmune Encephalomyelitis mouse models generated in our lab.

The Developmental and Functional Genetics Group is interested to understand the function of factors that determine lineage commitment of uncommitted progenitors to either the neuronal or glial fates in the CNS. We are studying the developmental origin of these cells and develop genetic tools to label stem cells in vivo in various tissues and use them to isolate and propagate these cells in vitro.

Research Interests

- Generating cellular and animal models of inherited neuropathies.
- Studying mechanisms of axonal degeneration in disease models of neuropathy.
- Generating disease models of multiple sclerosis.
- Studying pathological mechanisms in multiple sclerosis brain.
- Developing new therapeutic approaches with gene replacement for inherited neuropathies and leukodystrophies.

- Studying disorders of nerve and brain excitability.
- Investigating molecular mechanisms of neuronal dysfunction caused by ion channel and cell adhesion molecule defects.
- Investigation of genetic and molecular mechanisms of neurodegenerative disorders such as Parkinson's disease and Motor Neuron disease.
- Clinical and genetic investigation of families with inherited neuropathies and other neurogenetic disorders.
- Clinical and epidemiological study of myasthenia in Cyprus and investigation of new treatments.
- Understanding the role of SOX1/21, SOXB during neuronal commitment.
- Understanding the role of SOX1, PAX6 and Notch signalling during oligodendrocyte specification in the ventral spinal cord in mice.
- Studying stem cells in vitro isolated from animal models using cell-tagging approaches.

Selected Publications

- Sargiannidou I, Vavlitou N, Aristodemou S, Hadjisavvas A, Kyriacou K, Scherer SS, Kleopa KA (2009). Connexin32 mutations cause loss of function in Schwann cells and oligodendrocytes leading to PNS and CNS myelination defects. J Neurosci, 29:4736-4749.

- Genethliou N, Panayiotou E, Panayi H, Orford M, Mean R, Lapathitis G, Malas S. Spatially distinct functions of PAX6 and NKX2.2 during gliogenesis in the ventral spinal cord. Biochem Biophys Res Commun. 2009 Apr 24;382(1):69-73.

- Savvaki M, Panagiotaropoulos T, Stamatakis A, Sargiannidou I, Karatzioula P, Watanabe K, Stylianopoulou F, Karagogeos D, Kleopa KA (2008). Impairment of learning and memory in TAG-1 deficient mice associated with shorter CNS internodes and disrupted juxtaparanodes. Mol Cell Neurosci, 39:478-490.

- Kleopa KA, Zamba-Papanicolaou E, Alevra X, Nicolaou P, Georgiou D-M, Hadjisavvas A, Kyriakides T, Christodoulou K (2006). Phenotypic and cellular expression of two novel Connexin32 mutations causing CMT1X. Neurology, 66:396-402.

- Kleopa KA, Drousiotou A, Mavrikiou E, Ormiston A, Kyriakides T (2006). Naturally occurring utrophin correlates with disease severity in Duchenne Muscular Dystrophy. Hum Mol Genet, 15:1623-8.

- Kleopa KA, Elman L, Lang B, Vincent A, Scherer SS (2006). Neuromyotonia and limbic encephalitis sera target mature Shaker-type K+ channels: subunit specificity correlates with clinical manifestations. Brain, 129:1570-84.

- Vincent A, Lang B, Kleopa KA (2006). Autoimmune channelopathies and related neurological disorders. Neuron, 52:123-138.

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Activities

Clinical Genetics is a specialized health care clinic which provides diagnosis, management and genetic counselling services to people affected by or who may be at risk for a genetic condition. Clinical genetics aims to help patients and their families attain the best possible quality of life and reproduction.

At the Cyprus Institute of Neurology and Genetics, the Clinical Genetics Clinic offers diagnostic assessment, management and genetic counselling for the whole spectrum of genetic conditions at any age for any system. The service provided includes dysmorphology, neurogenetics, cancer genetics, prenatal genetics, teratology and other fields of medical genetics. The process of genetic counselling involves not only the exchange of information relating to the genetic disorder and relevant laboratory results but also supportive counselling to both patients and their families/ carers.

The clinical genetics team consists of one clinical geneticist, two genetic counsellors and a genetics nurse. Clinics are held both at CING and the Archbishop Makarios III Hospital in Nicosia. Families are referred by many healthcare and other professionals as well as through self-referrals. The Clinic serves as a reference centre for the whole of the island.

A genetic registry is established and in progress, used for studies on the epidemiological data regarding genetic disorders in Cyprus.

Educational activities are an integral part of the clinic's activities, addressing nurses, residents in medical specialties and other health professionals and students. Our experience in cross-cultural aspects of genetic counselling and also from the application of genetics at the community level is the basis of the clinic's contribution to the curriculum of the European Genetics Foundation course on "Genetic Counselling in Practice" which now runs for nine years.

The clinic staff runs a public awareness laboratory which researches ways on raising public and professional education and sensitization about genetics. This laboratory is very active in bicommunal efforts and has already produced a number of trilingual leaflets on several genetic disorders and a trilingual website.

The clinic is active on various local and European committees and bodies such as the Rare Disease Task Force.

Research Interests

Research activities include projects on:
- Epidemiology of genetic disorders in Cyprus.
- Rare mental retardation syndromes.

- Rare syndromes and genetic diseases specific to the Cypriot population, both in general and in isolated communities.
- Genetic and linguistic factors in specific patterns of speech development.
- Genodermatoses in Cyprus as part of a European network of collaboration.
- Ethical and anthropological studies on the reflection of applications from the new genetics within the Cypriot society.
- Development of models for raising public awareness in a culturally specific manner.

Selected Publications

- Sismani C, Kitsiou-Tzeli S, Ioannides M, Christodoulou C, Anastasiadou V, Stylianidou G, et al. Cryptic genomic imbalances in patients with de novo or familial apparently balanced translocations and abnormal phenotype. Mol Cytogenet, 1:15, 2008.

- Loizidou M, Marcou Y, Anastasiadou V, Newbold R, Hadjisavvas A, Kyriacou K. Contribution of BRCA1 and BRCA2 germline mutations to the incidence of early-onset breast cancer in Cyprus. Clin Genet 2007;71:165-70.

- Hadjisavvas A, Papasavva T, Loizidou M, Malas S, Potamitis G, Christodoulou C, Pavlides G, Papamichael D, Klonis C, Nasioulas G, Anastasiadou V, Kyriacou K. Novel germline mutations in the APC gene of Cypriot patients with familial and sporadic adenomatous polyposis. Clin Genet., 69(5):404-9, 2006.

- Neocleous V, Aspris A, Shahpenterian V, Nicolaou V, Panagi C, Ioannou I, Kyamides Y, Anastasiadou V, Phylactou LA. High frequency of 35delG GJB2 mutation and absence of del(GJB6-D13S1830) in Greek Cypriot patients with nonsyndromic hearing loss. Genet Test, 10(4):285-9, 2006.

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- Georgiou T, Stylianidou G, Anastasiadou V, Caciotti A, Campos Y, Zammarchi E, Morrone A, D'azzo A, Drousiotou A. 'The Arg482His mutation in the beta-galactosidase gene is responsible for a high frequency of GM1 gangliosidosis carriers in a Cypriot village. Genet Test, 9(2):126-32, 2005.

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- Xenophontos SL, Pierides A, Demetriou K, Avraamides P, Manoli P, Ayrton N, Skordis N, Anastasiadou V, Miltiadous G, Cariolou MA. 'Geographical clustering of low density lipoprotein receptor gene mutations (C292X; Q363X; D365E & C660X) in Cyprus. Hum Mutat, 15:380, 2000.

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Activities

The Department of Biochemical Genetics is the reference centre in Cyprus for the laboratory investigation and monitoring of inherited metabolic disorders (inborn errors of metabolism) and neuromuscular diseases. There are more than 500 known inherited metabolic disorders which cumulatively affect approximately 1 in 500 newborns. Many of these conditions are severely disabling and some are fatal, but an increasing number of them can be treated, provided they are diagnosed promptly. The contribution of the laboratory investigation to the diagnosis of inherited metabolic disorders is crucial since most of these disorders present with non-specific symptoms and are difficult to diagnose clinically.

The Department of Biochemical Genetics has established a wide range of highly specialized biochemical and molecular tests for the diagnosis and monitoring of inherited metabolic disorders. It receives samples from the government and private sector as well as neighboring countries. Over the years many diagnoses were made and in many cases they resulted in the prevention of death or mental retardation.

The Department of Biochemical Genetics also provides therapeutic drug monitoring of immunosuppressive drugs for the Cyprus Transplantation Centre. These measurements are crucial to the success of the transplantation and the prevention of graft rejection.

The Department of Biochemical Genetics is certified by the European Research Network for evaluation and improving of screening, diagnosis and treatment of inherited disorders of metabolism (ERNDIM) and takes part in European External Quality Control Schemes. The department has started the process of accreditation.

Research Interests

- The epidemiology and molecular characterization of inherited metabolic disorders in Cyprus.
- The deciphering of the cellular events implicated in disease pathology in lysosomal storage disorders with an emphasis on ER- and oxidative stress.
- The epidemiology and molecular basis of galactosaemia in Cyprus.
- The molecular characteristics of Cypriot patients with hyperphenylalaninaemia and their response to tetrahydrobiopterin.
- The relationship between the levels of chitotriosidase and the frequency of the 24bp duplication in the Cypriot population with past malaria endemicity.

Selected Publications

- K. Kleopas*, A. Drousiotou*, E. Mavrikiou, A. Ormiston and Th. Kyriakides. Naturally occurring utrophin correlates with disease severity in Duchenne Muscular Dystrophy. Human Molecular Genetics, 15(10):1623-1628, 2006. (* Equal contribution)

- M. Kleanthous, Ph. Patsalis, A. Drousiotou, M. Motazacker, K. Christodoulou, M. Cariolou, E. Baysal, K. Khrizi, B. Moghimi, F. Pourfarzad, S. van Baal, C. Deltas, H. Najmabadi and G. Patrinos. The Cypriot and Iranian National Mutation databases. Human Mutation-Mutation in Brief #893 Online, 2006.

- T. Georgiou, G. Stylianidou, V. Anastasiadou, A. Caciotti, Y. Campos, E. Zammarchi, A. Morrone, A. D'Azzo and A. Drousiotou. The Arg482His mutation in the β-galactosidase gene is responsible for a high frequency of GM1 Gangliosidosis carriers in a Cypriot village. Genetic Testing, 9(2):126-132, 2005.

- A. Drousiotou, E.H. Touma, N. Andreou, J. Loiselet, M. Angastiniotis, B.C. Verelli and S.A. Tishkoff. Molecular characterization of G6PD Deficiency in Cyprus. Blood Cells, Molecules and Diseases, 33(1): 25-30, 2004.

- T. Georgiou, A. Drousiotou, Y. Campos, A. Caciotti, L. Sztriha, A. Gururaj, P. Ozand, E. Zammarchi, A. Morrone and A. D'Azzo. Four novel mutations in patients from the Middle East with the Infantile from of GM_1 Gangliosidosis. Human Mutation, 24(4): 352, 2004.

- B.C. Verelli, J.H. McDonald, G. Argyropoulos, G. Destro-Bisol, A. Froment, A. Drousiotou, G. Lefranc, A.N. Helal, J. Loiselet and S.A. Tishkoff. Evidence for Balancing Selection from Nucleotide Sequence Analysis of Human G6PD. Am J Hum Genet, 71:5, 1112-1128, 2002.

- S.A. Tishkoff, R. Varkonyi, N. Cahinhinan, S. Abbes, G. Argyropoulos, G. Destro-Bisol, A. Drousiotou, B. Dangerfield, G. Lefranc, J. Loiselet, A. Piro, M. Stoneking, A. Tagarelli, G. Tagarelli, E.H. Touma, S.M. Williams and A.G. Clark. Haplotype diversity and linkage disequilibrium at human G6PD: Recent origin of alleles that confer malarial resistance. Science, 293, 455-462, 2001.

- A. Drousiotou, G. Stylianidou, V. Anastasiadou, G. Christopoulos, E. Mavrikiou, Th. Georgiou, G. Kalakoutis, A. Oladimeji, Y. Hara, K. Suzuki, K. Furihata, I. Ueno, P. Ioannou and A. Fensom. Sandhoff disease in Cyprus: Population screening by biochemical and DNA analysis indicates a high frequency of carriers in the Maronite community. Human Genetics, 107, 12-17, 2000.

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Activities

The Department of Cardiovascular Genetics pursues research on identifying genetic and environmental factors that contribute to the development of cardiovascular disease. In this field it has developed diagnostic assays for thrombophilia and familial hypercholesterolaemia (FH). An epidemiological study carried out in Greek Cypriot males indicated the involvement of both environmental and genetic factors in the expression of myocardial infarction. Studies in the genetic diagnosis of FH led to the identification of genetic abnormalities that are associated with the geographical origin of Greek and Greek Cypriot FH patients. In collaborative studies, recombinant

high density lipoprotein molecules were designed to study changes in gene expression levels brought upon by oxidised low density lipoprotein. In collaboration with Cape Town University the Department has initiated studies to investigate the effect of a series of genes on athletic performance in ironman triathletes. High through-put strategies for genotyping are currently being developed that would allow powerful genetic analyses to be pursued in the future.

The Laboratory of Forensic Genetics (LabFoG) uses state of the art DNA-based typing methodologies to study evidence from civil, criminal, mass disaster and missing persons investigations. Since 1997, the LabFoG has been actively involved in the attempts to identify, through the analysis of skeletal remains, approximately 2000 (both Greek Cypriots and Turkish Cypriots) missing persons since 1963-1964 and 1974. Recently, the Laboratory has also pursued research which focused on skeletal remains from an archaeological site. The LabFoG is a Member of the European Network of Forensic Science Institutes DNA Working Group and undergoes external proficiency testing twice a year. The LabFoG maintains the National Criminal DNA database for the Cyprus Police Authorities.

Research Interests

- Study of candidate genes and environmental factors involved in cardiovascular disease.
- MALDI-TOF assisted SNP genotyping.
- The role of genes in athletic performance.
- MALDI-TOF in Forensic Genetics and Cardiovascular Disease.
- Transfer of cells in Forensic Genetics.

Selected Publications

- Irwin J, Saunier J, Strouss K, Painter C, Diegoli T, Sturk K, Kovatsi L, Brandstatter A, Cariolou MA, Parsons W, Parsons TJ (2008). Mitochondrial control region sequences from northern Greece and Greek Cypriots. Int J Leg Med 122(1): 87-89.

- Y-STR analysis on DNA mixture samples – Results of a collaborative project of the ENFSI DNA Working Group (2008). On behalf of the ENFSI DNA Working Group; Parson W, Niederstatter H, Lindinger A and Gill P. Forensic Sci Int: Genet. 2: 238-242.

- Xenophontos S, Hadjivassiliou M, Karagrigoriou A, Demetriou N, Miltiadous G, Markou I, Elisaf M, Mikhailidis DP, Cariolou MA (2008). Low HDL Cholesterol, Smoking and IL-13 R130Q Polymorphism are Associated with Myocardial Infarction in Greek Cypriot Males. A Pilot Study. The Open Cardiovascular Medicine Journal, Vol.2: 52 – 59.

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- Saunders CJ, de Milander L, Hew-Butler T, Xenophontos SL, Cariolou MA, Anastassiades LC, Noakes TD, Collins M (2006). Dipsogenic genes associated with weight changes during Ironman Triathlons. Hum Mol Genet 15 (20): 2980-2987.

- Miltiadous G, Xenophontos S, Bairaktari E, Ganotakis M, Cariolou MA, Elisaf M (2005). Genetic and Environmental Factors affecting the response to statin therapy in patients with molecularly defined familial hypercholesterolaemia. Pharmacogenomics and Genomics 15: 219-225.

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Activities

The Department of Cytogenetics and Genomics provides diagnostic services, research as well as education in the area of Cytogenetics and Genomics. It is accredited by the College of American Pathologists (CAP) and meets the European quality control standards in Cytogenetics and Molecular Genetics.

The Department consists of the following laboratories: Clinical & Molecular Cytogenetics, Molecular Genetics of Human Syndromes, Microarrays, and Cell Lines. It serves as a referral center for prenatal and postnatal diagnosis of chromosomal disorders (e.g. Down syndrome), Fragile X syndrome, as well as many other genetic diseases and syndromes which cause mental retardation, multiple congenital anomalies, developmental delay, etc.

One of the Department's main focuses is to investigate at high resolution the whole human genome through microarray technology (array-CGH) for the identification of small and cryptic copy number changes and copy number variations, which cause many genetic syndromes and conditions. In addition, the Department maintains the specialized facility for the establishment and cryopreservation of immortal cell lines of patients for future diagnostic and/or research purposes. It carries out very competitive research programs in the area of human genomics and publishes its scientific outcome in international peer review scientific journals.

Research projects receive funding from the Cyprus Research Promotion Foundation, the 5th, 6th and 7th European Union Framework Programs and other international organizations. The Department is involved in several research programs and has collaborators in Universities and Research Institutes in Europe and the US.

The Department is involved in the provision of education by providing lectures and laboratory training to scientists, medical doctors and students. Furthermore, PhD students have graduated or are currently carrying out their doctoral degree.

Research Interests

- Development of Non-Invasive Prenatal Diagnosis for Down Syndrome and other chromosomal and genetic disorders.
- Application of high-resolution microarrays in prenatal diagnosis.
- Genomic investigation of syndromes linked to X-chromosome abnormalities and characterization of the underlying structural rearrangements and genetic mechanisms.
- Development of exon specific array for the detection of microdeletions and microduplications in genes of the chromosome X.
- Genetic investigation of patients with X-linked mental retardation.
- Genomic investigation and characterization of unknown and rare genetic and neurological syndromes in the Cyprus population with high resolution microarrays.
- Investigation and characterization of the clinical significance of Copy Number Variations in the human genome.
- Mapping of Copy Number Variations in the Cyprus population.

Selected Publications

- Bashiardes S, Kousoulidou L, van Bokhoven H, Ropers HH, Chelly J, Moraine C, de Brouwer AP, Van Esch H, Froyen G, Patsalis PC. A new chromosome X exon-specific microarray platform for screening of patients with X-linked disorders. J Mol Diagn. 2009 Nov;11(6):562-8. Epub 2009 Sep 24.
- Papageorgiou E, Fiegler H, Rakyan V, Beck S, Hulten M, Lamnissou K, Carter PN and Patsalis PC. Sites of differential DNA methylation between placenta and peripheral blood: Molecular Markers for non-invasive prenatal diagnosis of aneuploidies. The American Journal of Pathology. 174: 1609-1618, May 2009.
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- Sismani C, Syrrou M, Christodoulou K, Hamel B, Chelly J, Yntema H, van Bokhoven H, Georgiou Y and Patsalis PC. A gene for Nonsyndromic X-Linked Mental Retardation (MRX77) Maps to Xq12-Xq21.33. American Journal of Medical Genetics, 122A:46-50, 2003._
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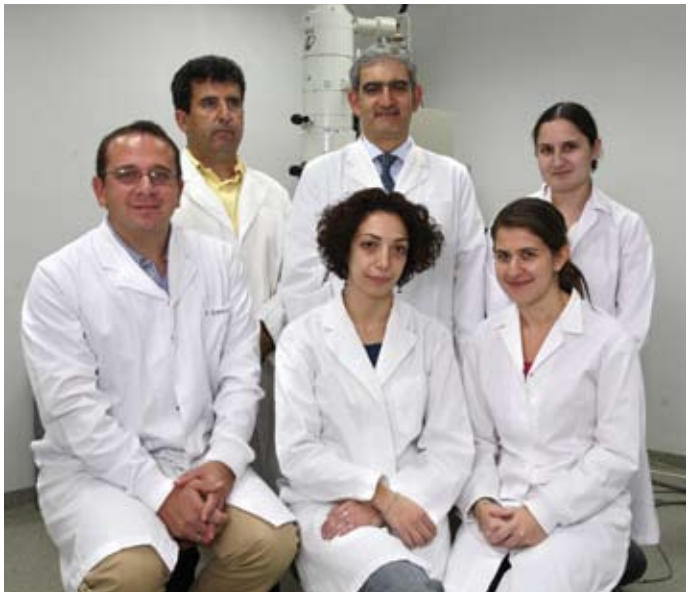

Activities

The Department operates the only Transmission Electron Microscope available in Cyprus. It offers a centralized ultrastructural diagnostic service in histopathology and deals with a range of human diseases, including neuromuscular, kidney and skin disorders as well as the diagnosis of undifferentiated neoplasms.

The Department offers a range of Molecular Genetic tests for diagnosing predisposition to common types of familial cancer, such as breast and colorectal cancer. A spectrum of predisposition genes are analysed including: BRCA1 and BRCA2 genes for hereditary breast and ovarian cancer; APC and MYH genes that predispose to the Familial Adenomatous Polyposis (FAP) syndrome; Mismatch repair genes (MLH1, MSH2, PMS1, PMS2 and MSH6) that predispose to the Hereditary Non-Polyposis Cancer syndrome known as HNPCC. Also performs mutation analysis of somatic DNA for establishing a pharmaco-genomics profile that determines the selection of patients targeted treatment.

An integral part of delivering the services outlined above, is the Cancer Genetics Clinic which has been established at CING in collaboration with the Clinical Genetics Clinic.

The Department participates in the European Molecular Genetics Quality Network (EMQN) assessment schemes, for evaluating the quality and standards of the services that are being offered, since 2000.

Research Interests

- Familial cancer genetics: Characterize pathogenic mutations in cancer predisposition genes in Cypriot families.
- Epidemiology of breast cancer: The Department is co-ordinating a National epidemiological study on breast cancer, in order to identify risk factors, and genetic polymorphisms that increase breast cancer risk.
- Functional studies on the role of the BRCA genes: BRCA mutations that have been identified in the Cypriot families are being cloned, expressed and functionally evaluated in cell cultures, in order to understand their clinical significance.
- Breast Cancer Proteomics and Biomarker Discovery: Investigation of the mechanisms of breast cancer progression, using proteomics. Aim to identify novel biomarkers in Cypriot breast cancer patients. This is carried out in collaboration with a major proteomics facility in the U.K.
- Mitochondrial myopathies: In collaboration with the Department of Neuropathology we are investigating the morphological and mitochondrial DNA defects that characterize Cypriot patients with mitochondrial myopathies.

Selected Publications

- M.A. Loizidou, T. Michael, S.L. Neuhausen, R.F. Newbold, Y. Marcou, E. Kakouri, M. Daniel, P. Papadopoulos, S. Malas, A. Hadjisavvas, K. Kyriacou. DNA-repair genetic polymorphisms and risk of breast cancer in Cyprus.Breast Cancer Res Treat. 2009 Jun;115(3):623-7. Epub 2008 Jun.

- I. Sargiannidou, N. Vavlitou, S. Aristodemou, A. Hadjisavvas, K. Kyriacou, S.S. Scherer, K.A. Kleopa. Connexin32 mutations cause loss of function in Schwann cells and oligodendrocytes leading to PNS and CNS myelination defects. J Neurosci. 2009 Apr 15;29(15):4736-49.

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- K. Voskarides, L. Damianou, V. Neocleous, I. Zouvani, S. Christodoulidou, V. Hadjiconstantinou, K. Ioannou, Y. Athanasiou, Ch. Patsias, E. Alexopoulos, A. Pierides, K. Kyriacou, C. Deltas. COL4A3/COL4A4 mutations producing focal segmental glomerulosclerosis and renal failure in thin basement membrane nephropathy. J Am Soc Nephrol, 18:3004-16, 2007.

- M. Loizidou, Y. Marcou, V. Anastasiadou, R. Newbold, A. Hadjisavvas, K. Kyriacou. Contribution of BRCA1 and BRCA2 germline mutations to the incidence of early-onset breast cancer in Cyprus. J of Clinical Genetics, 71:165-170, 2007.

- A. Hadjisavvas, T. Papasavva, M. Loizidou, S. Malas, G. Potamitis, C. Christodoulou, G. Pavlides, D. Papamichael, C. Klonis, G. Nasioulas, V. Anastasiadou, K. Kyriacou. Novel germline mutations in the APC gene of Cypriot patients with familial and sporadic adenomatous polyposis. J of Clinical Genetics, 69:404-409, 2006.

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- K. Christodoulou, E. Zamba, M. Tsingis, A, Mubaidin, K. Horani, S. Abu-Sheik, M. El-Khateeb, K. Kyriacou, T. Kyriakides, A.K. Al-Qudah, L. Middleton. A novel form of distal hereditary motor neuronopathy maps to chromosome 9p21.1-p12. Ann Neurol 48(6):877-84, 2000.

Department of Molecular Genetics, Function and Therapy

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Activities

The Department of Molecular Genetics, Function & Therapy (MGFT) carries out research, services and education in specific biomedical areas in order to achieve its mission in accordance with the wider mission of the CING. Regarding research, the department is interested in identifying the molecular causes of diseases, in studying the function of molecules which are involved in diseases and in the development of novel genetic approaches which may form the basis of therapy of diseases. Particularly, the use of regulatory RNA in research and the involvement of RNA in disease pathogenesis are priority research fields in MGFT. Moreover, there is interest in developing and exploiting genetic and biological tools for the appropriate implementation of the research projects. The department develops and applies, also, approaches (mainly genetic) for the diagnosis of several diseases which affect the people of Cyprus and the wider area. Some of these approaches are unique and provide novel findings about these diseases. MGFT participates in several quality control schemes for its services. The department has also educational activities and hosts full-time PhD students who are registered with the University of Bristol U.K. Finally, the department accepts undergraduate students to perform their final year dissertations.

Research Interests

- The involvement of RNA in diseases.
- The use of regulatory RNA as genetic tools for the study and development of therapeutic approaches of diseases.
- The study of the molecular pathogenesis of Myotonic Dystrophy and the restoration of the disease phenotype.
- Investigation of the pathway which leads to the formation of skeletal muscle cells.
- Induction of myogenesis in diseases.
- Induction of reversal of muscle cell differentiation and reactivation of muscle cells.
- Development of approaches for efficient delivery of genetic material in cells.
- Identification of genetic defects in diseases which affect the population of Cypriots.
- Development of new diagnostic methods.

Selected Publications

- Youn-Bok Lee, Ioannis Bantounas, Do-Young Lee, Leonidas Phylactou, Maeve A. Caldwell, and James B. Uney. Twist-1 regulates the miR-199a/214 cluster during development Nucleic Acids Res. 2009 Jan; 37(1) 123-128.

- Nikolaos P. Mastroyiannopoulos, Elina Chrysanthou, Tassos C. Kyriakides, James B. Uney, Mani S.Mahadevan and Leonidas A. Phylactou. The effect of myotonic dystrophy transcript levels and location on muscle differentiation. Biochem Biophys Res Commun. 2008 Dec; 377(2): 526-31.

- Eleni Hjiantoniou, Mustafa Anayasa, Paschalis Nicolaou, Ioannis Bantounas, Masahiro Saito, Sachiko Iseki, James B. Uney & Leonidas A. Phylactou. Twist induces reversal of myotube formation. Differentiation; 2008 Feb;76(2):182-92.

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- Ioannis Bantounas, Colin PJ Glover, Sachiko Iseki, Leonidas A Phylactou, James B Uney. Assesing adenoviral hammerhead ribozyme and shRNA cassettes in primary neurons: inhibition of endogenous Caspase-3 activity and protection from apoptotic cell death. Journal of Neuroscience Research. 79(5):661-9, 2005.

- Theoni K. Georgiou, Maria Vamvakaki, Costas S. Patrickios, Edna N. Yamasaki and Leonidas A Phylactou. Nanoscopic Cationic Methacrylate Star Homopolymers: Synthesis by Group Transfer Polymerization, Characterization and Evaluation as Transfection Reagents. Biomacromolecules 2004, 5(6), 2221-2229.

- Leonidas A Phylactou. Ribozyme and peptide nucleic acid – based gene therapy. In Advanced Drug Delivery Reviews 44(2-3):97-108, 2000 (Elsevier Sciences, ed Mahato).

Department of Molecular Genetics Thalassaemia

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Activities

The Molecular Genetics Thalassaemia Department provides diagnostic services, research and education in the field of thalassaemia and other haemoglobinopathies.

The services include molecular and prenatal diagnosis of all forms of haemoglobinopathies, Preimplantation Genetic Diagnosis (PGD) for β-thalassaemia, Non-Invasive Prenatal Diagnosis (NIPD) test for the detection of the Y chromosome in the maternal plasma of pregnant women for severe X-linked disorders and NIPD for RHD status in Rhesus-negative pregnant women. The NIPD for β-thalassaemia that is provided as a service for the first time worldwide is rendering the Institute a pioneer in the field.

The research activities of the Department involve the development of microarrays for the diagnosis of haemoglobinopathies, studies for improving the NIPD methods for thalassaemia, studies for finding new HbF inducers for the drug therapy of thalassaemia, pharmacogenetic and pharmacogenomic studies for β-thalassaemia patients and studies aiming to establish a safe, therapeutically effective and clinically applicable gene therapy for β-thalassaemia. As coordinator

of the FP6 ITHANET project we developed and use e-Infrastructure tools such as the ITHANET portal, videoconference and video streaming tools for the organisation of e-learning courses and workshops.

The Department provides training on laboratory aspects, summer internships and supervises BSc and PhD theses.

Research Interests

- Improvement of thalassaemia diagnostic services: development of a new chip for the molecular diagnosis of thalassaemia, development of novel NIPD methods for β-thalassaemia, and the determination of the molecular basis of high HbF in Cyprus.
- Development of e-Infrastructure tools for thalassaemia: establishing the ITHANET portal, videoconference and video streaming tools for the organisation of e-learning courses and workshops.
- Drug therapy for thalassaemia: research into finding new chemical compounds with HbF inducing activity for the treatment of thalassaemia and pharmacogenetic/pharmacogenomic studies to determine patient responses to drugs.
- Gene therapy for β-thalassaemia: a new project aiming to enable gene therapy provision in Cyprus.

Selected Publications

- Papasavva T, Kalikas I, Kyrri A, Kleanthous M. Arrayed primer extension for the noninvasive prenatal diagnosis of beta-thalassemia based on detection of single nucleotide polymorphisms. Ann N Y Acad Sci. 2008 Aug;1137:302-8.

- Felekis X, Phylactides M, Drousiotou A, Christou S, Kyrri A, Kyriakou K, Kalogerou E, Christopoulos G, Kleanthous M. Hb Agrinio [alpha29(B10)Le-->uPro (alpha2)] in combination with --(MED I). Results in a severe form of Hb H disease. Hemoglobin. 2008;32(3):237-46.

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- M. Kleanthous, K. Kyriacou, A. Kyrri, E. Kalogerou, P. Vasiliades, A. Drousiotou, I. Kallikas, P. Ioannou, and M. Angastiniotis. Alpha-thalassaemia prenatal diagnosis by two PCR-based methods. Prenatal diagnosis 2001 21: 413-417.

- K. Kyriacou, M.T. Akbari, X. Feleki, A. Georghiou and M. Kleanthous. Five novel point mutations in the promoter and 5'UTR regions of the beta-globin gene. Blood Cells Molecules and diseases 2000; 26: 518-519.

- K. Kyriacou, A. Kyrri, E. Kalogirou, P. Vasiliades, M. Angastiniotis, P.A. Ioannou and M. Kleanthous. Hemoglobin Bart's levels in cord blood and α-thalassaemia mutations in Cyprus. Hemoglobin 2000; 24: 171-180.

Department of Molecular Virology

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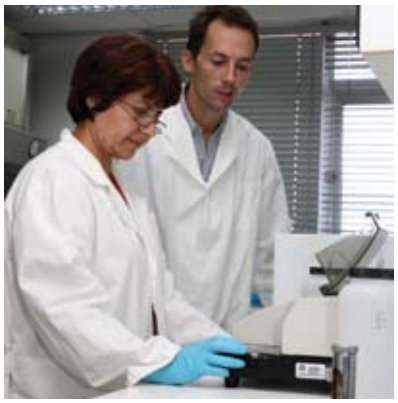

Activities

The Molecular Virology Department (MVD) was established in 1995. Our aim is to combine serological and molecular methods for specific and precise diagnosis of viral infections. Today, as Diagnostic Services, we provide tests to diagnose more than 20 viruses causing clinical symptoms in children, immunosupressed patients, pregnant women etc. (including Herpesviruses, enteroviruses, adenoviruses, parvoviruses). Each year, we perform hundreds of diagnostic tests evaluating the presence of antiviral antibodies and viral genomes.

Our Department is considered the Reference Laboratory for the Detection and Surveillance of enteroviruses since 1996. Routinely and also in emergency cases we are able to detect and type enteroviruses circulating in the population in order to prevent epidemics. For similar reasons, we prepared in-house protocols for Noroviruses, Adenoviruses and Rotaviruses. We consider it another major achievement of our Department to assist health officials to identify viral agents and offering support in preparedness to prevent epidemics.

We have also adapted protocols for a Real Time PCR based approach to detect and quantify viral loads for patient follow up. We have developed molecular diagnostic tests for the detection and quantification of HBV and HCV for diagnosis of patients and for following viral load fluctuations during treatment. In addition to hepatitis viruses, we ameliorated our protocol developed in the

MVD to detect and type HPV. Our Department offers HPV diagnostics and is able to type any of the approximately 100 types of HPV that may appear.

We pay particular attention to maintain the highest possible standards through internal and external quality control assessments and we therefore participate in multiple QCMD proficiency tests on a yearly basis.

Research Interests

- In Medical Virology we focus on the role of viruses in neurological syndromes with emphasis on Multiple Sclerosis (MS). We studied the possible role of herpesviruses in the onset and progression of MS. This work was funded by a competitive grant awarded by the American National Multiple Sclerosis Association.
- The Department is also involved in studying HPV infections in Cyprus. Our interest is focused on viral interactions with host proteins.
- Our department is the reference laboratory for enteroviruses in Cyprus. Surveillance of viruses and monitoring of their circulation/genetic evolution is possible to identify potential strains to cause epidemics and assist in the development of prevention strategies.
- In Environmental Virology, we investigate the presence and spreading of enteroviruses/ polioviruses, adenoviruses and hepatitis A in sewages, swimming pools water and seashore. These studies allow for: the surveillance of viral epidemics and the study of variants and emerging viruses.
- Very recently, in our clinical research, we started studying Helicobacter pylori infections in Cyprus and factors influencing clinical symptoms and patient management.

Selected Publications

- Bashiardes S, Richter J, Christodoulou CG. (2008) An in-house method for the detection and quantification of HCV in serum samples using a TaqMan assay real time PCR approach. Clin Chem Lab Med.;46(12):1729-31.

- Richter J, Bashiardes S, Koptides D, Tryfonos C, Pissarides N, Stavrou N, Papageorgiou GT, Christodoulou C. (2008). 2005 poliovirus eradication: poliovirus presence in Cyprus 2 years after. Water Sci Technol.;58(3):647-51.

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- Hadjisavvas A, Adamou A, O'Dowd Phanis C, Todd CM, Kitsios P, Kyriacou K, Christodoulou CG (2002). Q356R and S1512I are BRCA1 variants that may be associated with breast cancer in a Cypriot family. Oncol Rep. 9(2):383-6.

- Hadjisavvas A, Neuhausen SL, Hoffman MD, Adamou A, Newbold RF, Kyriacou KC, Christodoulou CG. (2001). BRCA1 germline mutations in Cypriot breast cancer patients from 26 families with family history. Anticancer Res;21(5):3307-11.

- Papageorgiou GT, Mocé-Llivina L, Christodoulou CG, Lucena F, Akkelidou D, Ioannou E, Jofre J. (2000) A simple methodological approach for counting and identifying culturable viruses adsorbed to cellulose nitrate membrane filters. Appl Environ Microbiol. Jan;66(1):194-8.

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Activities

The main expertise of the Neurogenetics Department (ND) is in the fields of medical genetics and linkage mapping, focused on neurological diseases. The mission of ND is to excel in the fields of expertise for the benefit of the patient. ND objectives include: a) the performance of high quality research for: i) the identification of disease associated genes and risk factors, ii) understanding of the molecular mechanisms leading to pathogenesis and disease and iii) contributing towards the development of more effective therapies for the benefit of the patient, b) offering high quality molecular diagnostic services in the field of neurogenetic and other hereditary diseases for the Cypriot and other populations and, c) offering high quality educational programs for postgraduate (PhD, MSc) studies, BSc projects and internships. At present, ND fulfils its research objectives through participation in five current research studies on hereditary motor neuronopathy, spinal muscular atrophy, facioscapulohumeral muscular dystrophy, spinocerebellar ataxias and Charcot-Marie-Tooth disease. ND is offering diagnostic services for amyloidosis, Huntington disease, ataxias, Charcot-Marie-Tooth disease, spinal muscular atrophy, myotonic dystrophy, amyotrophic lateral sclerosis and other hereditary diseases and successfully participates in seven European external quality assessment schemes (EMQN-EQAs). ND currently hosts three PhD students and at least three additional students (MSc, BSc) each year.

Research Interests

- Expression studies in hereditary motor neuronopathy type Jerash in order to confirm or exclude a candidate gene mutation that we identified in a cluster of Jordanian patients.
- Identification of a novel axonal type Charcot-Marie-Tooth disease gene that we mapped to chromosome 9.
- Investigation of Cypriot patients and families with spinocerebellar ataxias that through our previous studies proved to be atypical as compared to other populations.
- Investigation of Type 2 Diabetes susceptibility loci in the Cypriot population.
- Investigation of Cypriot Parkinson disease patients at the known Parkinson disease genes.

Selected Publications

- Mintchev N, Zamba-Papanicolaou E, Kleopa K, Christodoulou K. A novel ALS2 splice-site mutation in a Cypriot juvenile-onset primary lateral sclerosis family. Neurology. 2009 Jan 6;72(1):28-32. PMID: 19122027.

- Kleanthous M, Patsalis PC, Drousiotou A, Motazacker M, Christodoulou K, Cariolou M, Baysal E, Khrizi K, Moghimi B, Pourfarzad F, van Baal S, Deltas C, Najmabadi H, Patrinos GP. The Cypriot and Iranian National Mutation Frequency databases, Human Mutation 2006 Jun;27(6): 598-599. PMID: 16705699.

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