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NEUROSCIENCE  
INSTITUTE

# THE INSTITUTE

## THE WORLD HEALTH ORGANIZATION NEW INTERNATIONAL CLASSIFICATION OF THE DISEASES-11 REVISION: AUB'S LEADING ROLE IN THE COORDINATION OF THE REGIONAL STUDIES

The World Health Organization (WHO) is the primary health agency of the United Nations. Amongst its duties is to establish and regularly revise the International Classification of Diseases (ICD), a system applied worldwide by which diseases and disorders, including mental health conditions, are described and classified.

Currently, the WHO is in the process of revising the 10<sup>th</sup> edition of ICD that has been in use since the previous century with a view to publish the 11<sup>th</sup> edition (ICD-11) by 2018. The International Advisory Group for the mental and behavioral disorders section of the classification is a selection of mental health experts from across the globe and includes Dr. Brigitte Khoury, Associate Professor of Clinical Psychology in the Department of Psychiatry at the American University Beirut Medical Center (AUBMC). Its task is to advise the WHO on the proposed descriptions and guidelines based on the best evidence for their international reliability, cultural validity and clinically utility. The group collaborates with nine Field Study Centers established worldwide that combine academic research with clinical and advocacy interventions to reduce the mental health burden in their respective regions. These academic and clinical centers are found in Brazil, China, India, Japan, Mexico, Nigeria, Spain, and the United States. (continued on page 2)

## THE CURRENT SPECIALTIES AT AHNI

### Neurosurgery:

- Epilepsy surgery
- Brain tumors
- Brain mapping
- Spinal surgery
- Skull base surgery
- Functional neurosurgery

### Neurology:

- Epilepsy
- Sleep disorders
- Neuromuscular diseases
- Multiple sclerosis
- Movement disorders

### Pediatric Neurology:

- Neuro-genetics
- Epilepsy

### Psychiatry:

- Substance abuse
- Psychometric testing
- Individual, couple, family and group psychotherapy
- General psychiatry
- Mood disorders
- Child and adolescent psychiatry
- Neuromodulation
- Sleep disorders

# NEWS

## THE WORLD HEALTH ORGANIZATION NEW INTERNATIONAL CLASSIFICATION OF THE DISEASES-11 REVISION

In the Middle East, the American University of Beirut (AUB), through the Arab Regional Center for Research, Training and Policy Making in Mental Health, based within the Department of Psychiatry is the 9<sup>th</sup> field studies collaboration center. This collaboration was instrumental in coordinating internet based field studies in the Arab region through a large network of professionals who represented all the Arab countries. During the coming year, the clinical based field studies will start being conducted in all the centers, including the Arab regional one. As a result, clinicians from several countries in the region will be trained in a unified protocol to collect clinical data from patients regarding the new suggested classification and conform this data complies with the psychiatric presentation of an Arab patient population. Such emphasis on culture and its impact of diagnosis is unique in the ICD revision and invaluable to it being a true international classification tool.

Since 2009, regular meetings have taken place in South Africa, India, Brazil and Japan, among others. A regional event was held at the Columbia Global Center in Amman in April 2014. This event was jointly organized by the Arab Regional Center for Research, Training and Policy Making in Mental Health based at the Department of Psychiatry of AUBMC, Columbia University in New York

and the WHO in Geneva. The participants explored the situation of Mental Health in the Arab region and focused on the regional implementation of proposed field-testing studies based on the international protocols developed by the WHO. The meetings were attended by delegates and Arab regional experts from over 15 countries.

The last two years have witnessed the evolution of the draft versions of the ICD-11 in preparation for its submission for final approval by the WHO. In 2015, Dr. Joseph El-Khoury, who had recently joined the Department of Psychiatry at AUBMC, was appointed as a Global Mental Health Scholar for the Arab region, as part of the Columbia University Global mental Health program. Similar to colleagues from other world regions, his main role is to support the field studies aimed at establishing the validity, reliability, and clinical utility of the revised diagnostic criteria across socio-cultural and clinical settings. The team at AUB, in addition to Ms. Sariah Daouk, research assistant, will be in charge of coordinating studies to be carried out in five Arab countries (Lebanon, Egypt, UAE, Tunis, and Jordan). In Lebanon, a partnership was established between AUB and Hopital de la Croix (Cross Hospital), the largest psychiatric inpatient facility in the country and both will be the Lebanese medical centers where clinical field studies will be running.



## AUBMC LAUNCHES MULTIPLE SCLEROSIS AWARENESS CAMPAIGN IN NORTHERN LEBANON

The American University of Beirut Medical Center (AUBMC) in collaboration with the Nehme and Therese Tohme Multiple Sclerosis Center and Friends of MS at AUBMC, and Byblos Municipality launched the Multiple Sclerosis Awareness Campaign in Byblos.

Held on Saturday, January 30, 2016 at the Centre Culturel de Byblos, the press conference aimed at raising awareness about Multiple Sclerosis among the Byblos community and the surrounding region. The event was attended by Mr. Ziad Hawat, president of Byblos municipality, Dr. Samia Khoury, Director of the Nehme and Therese Tohme Multiple Sclerosis Center and Abou Haidar Neuroscience Institute - Associate Dean for Clinical and Translational Research at AUBMC, Mrs. Roula Douaidy representing friends of MS, and representatives of local NGOs and universities.

In his opening note, Mr. Hawat stressed on the importance of such campaigns and the role of municipalities in maintaining a healthy community in their own villages and cities.

Multiple Sclerosis (MS) is an autoimmune disease where the body's immune system attacks myelin, the protective covering of nerves in the central nervous system. MS affects women twice as often as men. While MS is not hereditary, scientists believe the disease is triggered by environmental factors in a person who is genetically predisposed to respond.

Defining MS and highlighting its signs and symptoms, Dr. Samia Khoury covered the latest progress achieved in research and treatment. Dr. Khoury also highlighted the importance of the Lebanese Ministry of Public Health and the NSSF especially when it comes to dispensing medications and patient coverage. She also stressed the need for awareness about the disease in all Lebanese

regions, since this will have tremendous positive outcomes on its treatment. Professor Khoury emphasized that raising awareness and supporting patients cannot be done without the help and back up of "Friends of MS" at AUBMC.

Mrs. Roula Douaidy explained the pivotal role Friends of MS is playing, their mission in supporting needy MS patients at the Center, raising awareness about the disease and providing financial aid in MS ongoing research. In her note, Mrs. Douaidy highlighted the achievements fulfilled over the years and the future awareness activities they have lined up in Byblos.

The Nehme and Therese Tohme Multiple Sclerosis Center at AUBMC will work closely with the local community. A future collaboration with Byblos universities, schools and NGOs will include the organization of a bigger awareness conference for NGOs, universities and schools in the area.

"It is with knowledge we can protect ourselves and assist others, and that is the right way to fight any disease. Community outreach is at the core of AUBMC's values, we have a mission to equip people with the right knowledge to be and stay healthy in order to build a healthy community. This comes hand in hand with our promise to offer the best medical and patient care to our community and beyond," concluded Dr. Khoury.





# FRIENDS OF MS AT AUBMC

## FUNDRAISING EVENT

On Saturday, February 6, 2016, Friends of MS at AUBMC organized a fundraising event for the 4<sup>th</sup> consecutive year at the Four Seasons Hotel, Beirut under the patronage and in the attendance of Mrs. Lama Tammam Salam to support needy patients diagnosed with multiple sclerosis.

Mrs. Salam expressed her pride in supporting the Multiple Sclerosis Center at AUBMC, reflecting on the center's extended commitment to delivering the highest quality of care to this community. "It is our duty to support and help this center, being the only center in Lebanon dedicated to MS patients and their families, in fulfilling its promise to deliver the best patient care to patients with multiple sclerosis. Since its inception, the center, led by a highly dedicated and specialized team, has supported more than 150 patients both psychologically and financially," she added.

Dr. Samia Houry, professor of neurology and Director of AUBMC's Abou Haidar Neuroscience Institute (AHNI) and Multiple Sclerosis (MS) Center, explained the symptoms, although unpredictable, for the disease which is more common among women than men. She also emphasized the support and contribution of the Ministry of Public Health in the treatment of patients as well as the extensive research conducted by the center in an effort to further advance the treatment of the disease.

In his note, Dr. Bassem Yamout, Director of Clinical Research at Nehme and Therese Tohme Multiple Sclerosis Center at AUBMC, stressed on the efforts initiated towards accelerating research to understand the local etiology of the disease and find appropriate treatments to hinder its progress.

Mrs. Hind Khodr Saab, member and representative of Friends of MS at AUBMC, shed light on the latest achievements accomplished over the past three years. She presented an overview of the plan of action that has been set to kick off in 2016 through organizing several awareness campaigns and providing sufficient funds to support patients with MS.

It's worth mentioning that along with Mr. Wissam Breidy, the Master of the Ceremony, Junaid Zeineddine and Rojo Del Libano, were also in attendance. They offered the attendees amazing performances and a memorable event.



# NEWS FROM THE BENCH

## BASIC NEUROSCIENCE: FEATURED RESEARCH

### Neural Stem Cells

*Dr. Wassim Abou Kheir*

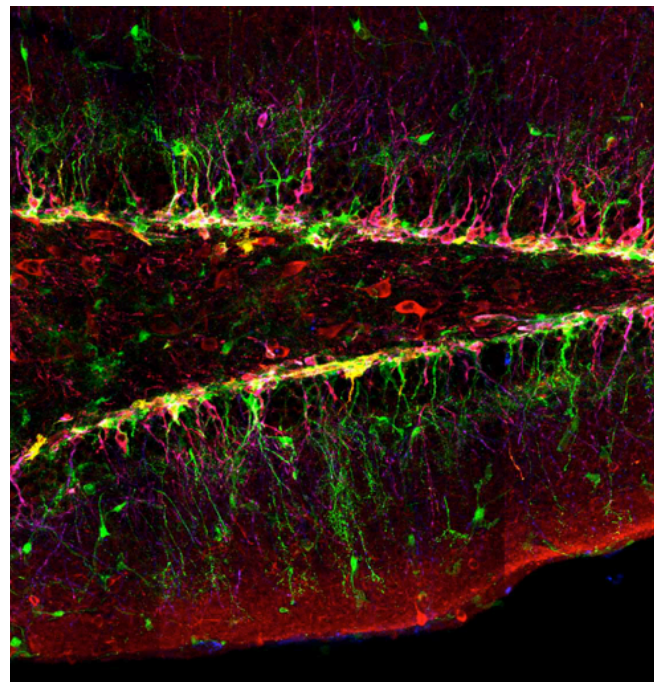
The approaches to understand neuroscience and investigate the underlying aspects of neural cell biology have been revolutionized by the concept of stem cells. An important leap in neuroscience was marked by neural stem cells and how they convey a consistent supply and a renewable stream of cells which are, in a controlled environment, physiologically functional. The applicability of these cells is in how they hold the promise to treat a range of neurological diseases as well as an understanding of the etiology of different disorders. There exist different types of stem cells ranging from Embryonic Stem cells (ES) to induced Pluripotent Stem Cells (iPSCs) and neural stem cells. In the lab at the Department of Anatomy, Cell Biology, and Physiology, we are interested in all the different types of stem cells, as each is eminent for exploring and elucidating the molecular mechanisms controlling the fate of neuronal cells during development and adulthood. Moreover, they all serve to help in modeling diseases, understanding the underlying mechanisms, and achieving potential therapeutic treatments.

There are a number of therapeutic techniques that are being used in clinics regardless of the scarce knowledge of their mechanism of action. Deep Brain Stimulation, for example, is considered effective when used to alleviate the symptoms of a number of neurological and psychiatric disorders, yet its therapeutic mechanism of action is still unknown. We, in our lab, are trying to explore

the involvement of stem cells in partially conveying the therapeutic improvements. We are mainly looking into the increase in proliferation of stem cells, also referred to as adult neurogenesis in specific brain zones, following deep brain stimulation, and we are trying to map out the fate of these dividing cells. Moreover, we want to correlate this increase to the behavioral improvements of animals when challenged into different tasks.

The hippocampus is highly prone to inflammatory insults and therefore adult neurogenesis could be altered by different pathological factors that might tip-off the balance in the stem cells niche. This might impede memory and learning, two main hippocampus-related functions. In our lab, we are investigating the relationship between neural inflammation induced by Lipopolysaccharide inoculation in the brain and neurogenesis. We expect that systemic infections with toxins would depress adult neurogenesis and that would be correlated with a decline in the behavioral assessments.

In Lebanon and abroad, neuropsychiatric disorders exert a large burden on the population and healthcare centers. Although the causes of mental illnesses remain largely illusive, genetic factors play an important role in the etiology of the different illnesses.





# NEWS FROM PSYCHIATRY

Studying mental illnesses like schizophrenia and bipolar disorders pose a challenge in that animal models are not really suitable for faithfully recapitulating the disease and it is very hard to culture primary neuronal cells. Therefore, in our lab we are trying to model different neuropsychiatric illnesses using iPS cells technology. By examining the genetic information from patients who suffer from psychiatric illnesses, we will be able to explore the relationship between genes, environmental factors, and disease risk and accordingly discover the explanations for how and why mental illnesses may occur.

The lab at the Department of Anatomy, Cell Biology and Physiology is also interested in cancer and cancer stem cells in particular. We are targeting cancer stem cells in brain tumor models, mainly glioblastomas and neuroblastomas, with different treatments. Both gliomas and neuroblastomas pose a great health burden worldwide with a poor and moderate prognosis, respectively. We are investigating the anti-tumor effects of the famous anti-diabetes drug Metformin and the effects of many well-established drugs like rapamycin in targeting the cancer stem cell population in brain tumors.

As I am not a neuroscientist by training, the neuro-research in my lab couldn't have been achieved without the help and guidance of prominent neuroscientists in the field. I am lucky in having such mentors and collaborators like Dr. Nayef Saade, Dr. Ziad Nahas, and Dr. Elie Al-Chaer to carry on with the different projects in the lab. It goes without saying that without talented and dedicated students and staff, nothing could be achieved. In conclusion, you are only worth the people you are working with.

## AUBMC LAUNCHES FOCUS FUND AT THE 3<sup>RD</sup> ANNUAL CONFERENCE OF THE CHILD AND ADOLESCENT PSYCHIATRY PROGRAM AND THE ABUHaidAR NEUROSCIENCE INSTITUTE

**First child mental health fund in Lebanon and the Arab region**

Under the title of "School Mental and Behavioral Health: ADHD, Learning Disorders and Comorbidities" the Child and Adolescent Psychiatry Program at the Department of Psychiatry at the American University of Beirut Medical Center (AUBMC), in collaboration with Abu-Haidar Neuroscience Institute (AHNI), organized their third annual conference on Friday, February 12, 2016 at AUB Hostler Auditorium. The conference marked the launching of the 'Focus Fund', a newly established child mental health fund at AUBMC to empower and effectively care for children with emotional, behavioral, and learning disorders. This endeavor will be the first endowed mental health fund in Lebanon and the Arab region dedicated to improving children's mental wellbeing, emotional resilience, and quality learning by focusing on the child, family, professionals, schools and community.

The event was attended by Dr. Ziad Nahas, chairman of the Department of Psychiatry at AUBMC, Dr. Fadi Maalouf, chairman of the organizing committee of the conference and director of the Child and Adolescent Psychiatry Program, Dr. Samia Khoury, Associate Dean for Clinical and Translational Research and Director of the Abu-Haidar Neuroscience Institute

(AHNI) and the Nehme and Therese Tohme Multiple Sclerosis Center, representing Dr. Mohamed H. Sayegh, Executive Vice President, Raja N. Khuri Dean, Faculty of Medicine at the American University of Beirut (AUB), Mrs. Ghina Smadi, president of Focus Fund.

National, regional, and prominent international speakers from the UK and the Netherlands and professionals who work with children with emotional, behavioral and learning difficulties including psychiatrists, psychologists, and other members of a multidisciplinary team joined the conference. In addition, school counselors and concerned parents were in attendance.

In his opening speech, Dr. Fadi Maalouf welcomed the audience and stressed on the importance of such conferences to secure the right approach and treatment for children with ADHD, learning disorder, and their comorbidities, "We are proud of the achievements the Child and Adolescent Psychiatry Program has accomplished over the past three years. This wouldn't have been possible without the support of so many, and the foremost the support of AUBMC leadership for believing in our work."

Several topics were covered during the event ranging from neurobiology to non-medical treatments, cultural challenges and practical tips that can be used in the classroom. In that sense, the annual conference was relevant to various professionals who work with children and adolescents within and outside the school setting. The conference also highlighted the importance of a multidisciplinary approach to clinical problems, focusing on the most recent evidence-based assessments and interventions for Attention Deficit Hyperactivity Disorder (ADHD) and learning disorders.

In her speech, Mrs. Smadi highlighted the importance of Focus Fund in supporting parents and children in their journey with mental health issues and added, "Mental health problems can lead young people to become disruptive, difficult, withdrawn and disturbed, and it's vital they are supported and not just ignored or told off. Our children need support; without doubt, creating more programs of this sort will result in emotionally resilient and happier children."



Launching the Focus Fund, Dr. Samia Khoury said, "I am honored to be here to witness the launch of a fund whose mission is to improve the emotional resilience, mental health and learning experiences of children throughout Lebanon." She added, "I am confident that AUBMC will build on the fundamental role the fund will significantly play in laying the foundations for other similar funds that would make the care for children with diagnosable social, emotional, behavioral, and learning problems available, affordable, and accessible."

'Focus' is a group of volunteers dedicated to improving the emotional resilience, mental health and learning experiences of children throughout Lebanon by actively engaging with parents, teachers, professionals, and policymakers to deliver comprehensive and adequate care for those in need while making treatment available, affordable, and accessible. The program featured an awareness video clip indicating that up to 25% of adolescents living in Beirut suffer from an emotional,

behavioral, or learning disorder while only 6% of those needing treatment receive it.

The fund will help train primary care professionals and pediatricians identify mental health problems in children and provide general mental health education to parents, in an effort to make cases accessible to all. It will also educate teachers by promoting the teaching of life skills and building emotional resilience in schools, supporting projects that aim to develop and adapt these programs, enhancing positive parenting, introducing the needed skills to parents of children with difficulties, and supporting families of children in need of seeking mental health and/or special educational interventions at AUBMC in order to ensure mental healthcare is affordable for all.

Following the core of their commitment to child mental health, Child and Adolescent Psychiatry Program (CAPP) and Focus Fund will organize three annual awareness events, targeting professionals, teachers, and parents in the course of 2016.

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## UPDATES ON THE AGNES VARIS PROGRAM FOR SUBSTANCE USE DISORDERS (LAUNCHED IN 2015)

The Agnes Varis Substance Use Disorders Program has added a new psychologist to the team, Ms. Mona Chebaro.

In addition, a one-day workshop for physicians and nurses from Ain Wa Zain hospital was conducted earlier this year. A second seminar was also conducted in May.2016. And a substance abuse awareness lecture was delivered at IC in April 2016.

The program continues to expand and is going to start clinical research activities soon.

As for the service at the inpatient psychiatry, it keeps on expanding and the team is working diligently to enhance the therapeutic environment with a current focus on expanding and enhancing psychological and social services on the unit in addition to constantly improving all psychiatric services.

# FRIENDS OF MS AT AUBMC

Established by a group of committed volunteers in February 2012, the Friends of MS is engaging in various activities to increase awareness and raise funds to support needy MS patients and MS-related research at AUBMC.

### Friends of MS supporting needy MS patients

Since 2012, more than 150 needy patients are being financially supported at the center.

Coverage included:

- More than: 200 MRI, 50 admissions including full coverage of hospitalization bill to covering NSSF difference related hospitalizations and tests bills, 30 Lumber Puncture with the needed tests, many blood studies, evoked potentials, EEGs, etc. procedures for pain management.
- Collaboration with the Ministry of Social Affairs to facilitate the process of securing/ providing the handicapped card.

### Friends of MS Supporting MS awareness activities

Many awareness activities were planned and organized jointly by the Friends of MS at AUBMC and the Nehme and Therese Tohme Multiple Sclerosis Center.

### 2012-2015

- The first national MS awareness campaign was launched in collaboration with the Ministry of Public Health.
- Educational brochures and pamphlets were created to be used during awareness campaigns.
- Patient educational days took place.
- Yearly participation in the marathon was intended to help in raising awareness about the disease.
- Creating an MS awareness ad that was broadcasted on TVs during May (MS Awareness month). It was also played as intro ad during December 2015 in movie theaters (Cinema City Down Town and City Mall).
- Bike for charity was organized in collaboration with Beirut by bike.
- MS educational days took place in many



# NEWS FROM NEUROLOGY

Lebanese regions, targeting communities, NGOs, schools and universities: Bekaa, Kisserwan and now Byblos, Jamhour, Saint Coeur, AUB campus, NDU etc.

- In May 2015, an MS day took place in Zeytouna Bay where yoga activities were provided to patients and their families.
- In June 2015, a Porsche/Goldwing ride was organized in collaboration with Porsche Club Lebanon and Goldwing Lebanon. The ride supported tremendously in spreading awareness about the disease among young generation.
- On yearly basis, a fundraising brunch is being organized to help collect funds and support our needy patients.
- Ongoing TV, radio, and magazine interviews

## 2016

- We organized for an Avant premiere of "Bil Nisbi La Bokra Chou" where more than 1500 people attended to support our cause.
- Friends of MS at AUBMC and Nehme and Therese Tohme Multiple Sclerosis Center have collaborated with the Municipality of Byblos to launch an awareness campaign about MS. The awareness plan for the upcoming year will be as follows:

### - Phase I:

Press conference to launch the awareness campaign

Date: Saturday, January 30, 2016

Time: 10:30 am – 12 noon

Venue: Centre Culturel de Byblos

### - Phase II:

Collaboration with Byblos Universities to present a 2-3h awareness day to all high school, university students of the region, hospitals, NGOs etc.

Date: May-June 2016

### - Phase III:

Social activity including entertainment (TBA)

Date: May-June 2016

Venue: Byblos (TBA)

## Friends of MS supporting in MS research

Friends of MS always support MS research conducted at the center by raising awareness about the importance of these studies for the patients as well as their significance in the science of treating MS. On the other hand, Friends of MS try to financially support ongoing research whenever need be.

The Department of Neurology proudly held its annual graduation dinner on Saturday, June 4, 2016 in Le Bristol.

Our graduate residents for this academic year 2015-2016 were: Dr. Sahar Farhat, Dr. Zainab Abdallah, and Dr. May Fakhredin in addition to our graduate fellows: Dr. Wissam Yamak and Dr. Nour Estaitieh.

The graduating residents and fellows honored Dr. Riad Khalifeh who was presented with the distinguished teacher award.



# MEET THE NEUROLOGIST



DR. JOHNNY SALAMEH

## 1. Tell us a about your education and work: AUB, after AUB, and back to AUB.

### Education

Following high school at College des Freres, I joined AUB where I finished my undergraduate studies in biology followed by medicine. After one year of internship at AUBMC, I completed a neurology residency at the University of Nebraska Medical Center / Creighton University Medical School in Omaha, followed by a fellowship in Neuromuscular Medicine and Electromyography at the Massachusetts General Hospital/Brigham and Women's Hospital/Harvard Medical School in Boston, MA.

### Work

In 2009, I joined the Department of Neurology at the University of Massachusetts Medical

School in Worcester, MA as Assistant Professor and rose to the rank of Associate Professor in 2013. At the University of Massachusetts Medical School, I served as program director of neurology residency, co-director of Neuropsychiatry residency, Director of the Neuromuscular division and EMG lab, and co-director of Neurology Clinical Trials Unit.

### Return home

Throughout this journey returning to Lebanon and AUB was always on my mind.

## 2. What triggered your interest in the field of Neurology and ALS disease in particular?

During Medical School, I was fascinated by neuroscience. My love to the field increased significantly during my internship and early clinical years as I started taking care of patients with neurological diseases. Later on during my neuro-muscular fellowship, I met and worked closely with Dr. Bob Brown, a world leader and expert in ALS and was involved in taking care of many patients with ALS. I attended many events to raise awareness about ALS as well as to support patients and their families during the initial stage of diagnosis and later as the disease progressed. I quickly realized how devastating this disease is and the urgent need to find treatment as well as better supportive care. As such, I was involved in many ALS research projects both at the basic and clinical levels.

## 3. Who was the most significant influence on your development as a neurologist?

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#### **4. How do you see your area over the next ten years at AUBMC?**

Since I joined, we opened the Amyotrophic Lateral Sclerosis (ALS) Neurology Clinic at Ahmad and Jamila Bizri Neuro-outpatient Center here at AUBMC. We were also recently selected to join The Northeast Amyotrophic Lateral Sclerosis (NEALS) Consortium as the first clinical research site in the Middle East. The announcement was made in an annual meeting held in Florida on November 4-6, 2015. As a NEALS member, AUBMC will have the privilege to access many valuable resources, most importantly a supportive network of experienced and knowledgeable ALS research sites and researchers who are committed to the collaborative, free-flow of information and ideas to improve ALS patient care and disease understanding. I am hoping that this clinic will become a major referral for patients with neuromuscular diseases, particularly ALS, in Lebanon and the region.

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#### **5. Tell us more about your involvement in research, and how do you intend to promote that at AUBMC?**

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Center here at AUBMC. We were also recently selected to join The Northeast Amyotrophic Lateral Sclerosis (NEALS) Consortium as the first clinical research site in the Middle East. The announcement was made in an annual meeting held in Florida on November 4-6, 2015. As a NEALS member, AUBMC will have the privilege to access many valuable resources, most importantly a supportive network of experienced and knowledgeable ALS research sites and researchers who are committed to the collaborative, free-flow of information and ideas to improve ALS patient care and disease understanding. I am hoping that this clinic will become a major referral for patients with neuromuscular diseases, particularly ALS, in Lebanon and the region.

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#### **6. What fascinates you the most about neuroscience?**

The complexity and uniqueness of the human nervous system fascinates me.

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#### **7. What are the factors that make you excited about practicing neurology every day?**

In neurology, you get to play a detective role on daily basis. All cases we encounter are challenging and I enjoy dwelling into all the details to get to the correct diagnosis so I can provide the appropriate treatment and counseling for our patients. There is no single boring moment in neurology!

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#### **8. What were some of the most rewarding moments of your career?**

I am blessed with many rewarding moments while taking care of patients thought to have serious untreatable illnesses and comforting



them by finding out that, on the contrary, they can be treated. Another rewarding moment that I remember is in research when we found a particular drug that works in treating a previously untreatable disease.

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## 9. Outside work, what do you enjoy doing the most?

I enjoy spending time with my family. I also enjoy biking and running.

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## 10. If you were to address a group of medical students interested in neurology, what would be the message you'd like them to know that will impact their future careers?

Neurology is one of the most dynamic areas of medicine, with advances on many fronts. This is reflected in the ever increasing research opportunities to develop therapeutic interventions to delay, or hopefully prevent neurodegenerative diseases. The new breeds of neurologists will play a major role in developing as well as providing these interventions which most likely will include novel drugs, stem cell technology, gene therapies, and new immunosuppressant modalities. There will also be an increased role for neurologists in interventional fields such as vascular/stroke medicine, neurocritical care, pain, and neurostimulation.

# MEET THE RESEARCHER



DR. RIYAD KHOURY

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## 1. Tell us a about your education and work background.

In 2002, I graduated with a Bachelor's degree in Biology from the Lebanese University. After that, in 2003, I joined Paris XI University where I completed a Master of Science (MS) in Genetics under the supervision of Pr. Annie Sainsard-Chanet, a proficient geneticist. During my third Master's internship that I performed in her laboratory, "Mitochondria and Senescence lab", I developed an interest in mitochondrial biology that motivated me to pursue a PhD degree in the same field. By the end of my third internship, my application for a PhD scholarship funded by the European community was accepted. This gave me the opportunity to embark on a PhD and therefore complete the research work that I initiated during my Master's program in the "Mitochondria and

Senescence lab". My doctoral studies focused on the use of a filamentous fungus model to decipher the molecular mechanism(s) behind the pathogenicity of the Mitochondrial ATP/ADP transporter mutations, which in humans are responsible for autosomal dominant forms of progressive external ophthalmoplegia (adPEO). We clearly demonstrated that these mutations are responsible for large-scale mitochondrial DNA deletions and a significant loss in energy metabolism. During my PhD, I was also able to develop, and for the first time, a new genetic tool allowing easy gene replacement with 100% efficiency. This tool is extremely useful for the scientific community working on filamentous fungi.

Over time, my addiction to research and mitochondrial biology became manifest. This undoubtedly led me to a giant in the field of mitochondrial biology, Dr. Pierre Rustin, a skillful biochemist whose name is tantamount to excellence in mitochondrial research. Therefore, after completing my PhD in Genetics in 2009, I was lucky enough to join Dr. Rustin's team at Robert Debre Hospital (INSERM U676) in Paris, as a postdoctoral fellow.

During that period, which extended till 2013, we developed new gene therapy strategies, in mice as well as in human cell culture, in order to compensate for mitochondrial respiratory chain deficiencies that are implicated in a wide range of human diseases including mainly, metabolic, neurodegenerative and neuromuscular disorders. We were able to create the first mouse model expressing a non-human gene, the alternative oxidase (AOX), which confers a bypass to the respiratory chain, enabling therefore these mice to survive in the presence of different respiratory chain lethal inhibitors, namely cyanide. Currently, the AOX expressing mice are being crossed to mouse models for neurodegenerative and mitochondrial diseases to test their capacity to compensate the underlying respiratory chain deficiencies.

In 2014, I was appointed as an assistant professor in the PLM department with a joint appointment in the neurology department. Since then, and with the precious support of Dr. Mamdouha-Ahdab Barmada, I established a new laboratory to diagnose accurately

mitochondrial related disorders using kinetic analyses, protein profiling and molecular investigations. Concurrently, I pursue my research in the mitochondrial field by studying, in a cellular model, the link between mitochondrial bioenergetics and amyloid-beta plaques accumulation, a hallmark of Alzheimer's disease.

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## 2. What was the most significant influence on your development as a scientist?

In one word "Research". For more than a decade, I was implicated in authentic research experiences that allowed me to develop questions, plan experiments, and collect, analyze, and interpret data. This considerably helped me develop the ability to tackle relevant, real-life problems by asking rigorous questions and developing strategies for their solutions. It also promoted my analytical and critical reasoning and improved my communication skills.

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## 3. What triggered your interest in the Mitochondrial Biology field and Mitochondrial-related disorders in particular?

All began during my Master's program where I started to gain deeper insight into the fundamentals of these tiny entities, called the mitochondria, both at the theoretical and practical level. In addition, during that period, I was lucky enough to be part of the French mitochondrial community "MeetOchondrie" where I had the chance to meet renowned scientists working on different mitochondrial aspects, which considerably contributed to my increasing interest in this field of science. This was further amplified during my PhD when I saw for the first time live videos showing mitochondria traveling over long distances in neuronal axons to sites of high energy demands and discovered how the disruption

of this process leads to neurological diseases. This occurred in one of the annual meetings of the European Consortium of Mitochondria and Ageing (MiMage), which I was part of. Finally, additional and fundamental incentive to pursue research in the mitochondrial medicine field originated from the simple and saddening fact associated with the complete lack of treatment for the broad range of mitochondrial-related human disorders which cover all medical specialties.

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#### **4. Many do not see the link between Mitochondrial Biology and Neuroscience. What would be your message to a group of students in the neuroscience field to highlight this link?**

Mitochondria are important organelles in all cell types, but they are particularly important in the nervous system. They are the main ATP producers needed for normal electrical activities of neurons and synaptic transmission. For instance, the overall ATP in neuron-rich grey matter of the brain has been estimated to be similar to that in the leg muscle during a marathon, which explains why a tissue with a contribution of only 2% to bodyweight can make more than 20% of resting whole-body metabolism.

Additionally, mitochondria have a central role in neurotransmitter synthesis, production and regulation of reactive oxygen species, calcium homeostasis, cellular signaling, and neuronal death. Therefore, it is not surprising to know that mitochondrial dysfunctions are implicated in a big set of Neurologic disorders, which exhibit a diverse range of age of onset, symptoms, and outcomes—from isolated childhood onset vision or hearing loss to a multisystem neurodegenerative disorders with strokes, neuropathy, ophthalmoparesis, and epilepsy occurring at any age. Thus, an understanding of the reciprocal relation between mitochondrial dysfunction and neurological disorders is fundamental to choosing a suitable treatment,

and it has the potential to open up new therapeutic approaches.

View all this, it is essential for students interested in the Neuroscience field to be aware of the vital link between mitochondria and the nervous system. It is therefore important to look also at neuroscience from a different angle and in an unconventional manner. This will unquestionably provide new opportunities for students and will open new horizons in unexplored areas whether in their medical or scientific careers.

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#### **5. How do you see your area over the next ten years at AUBMC?**

Currently, the importance of defining and analyzing mitochondrial biology stems from the fact that it is one of the fastest growing areas of study in genetics and medicine, connecting diverse scientific disciplines ranging from embryology to cancer, to infectious and degenerative diseases. Indeed, disturbances in mitochondrial activities are now known to play a role not only in the so-called “rare” childhood diseases, but in many common diseases related to aging, including heart disease, diabetes, Parkinson disease, and dementia, as well as cancer occurrence, progression and therapy, in addition to demyelinating diseases.

Therefore, the mitochondrial biology field will undoubtedly gain exponential interest among peers at AUBMC. Furthermore, when we consider the increasing number (1/5000) of mitochondrial-associated human diseases, which cover all medical specialties, it is surprising that no mitochondrial diagnosis center exists in the Middle East. Actually, and despite the growing number of samples (muscle biopsies, etc...) referred to be tested for mitochondrial dysfunction, only a few can be sent to Europe and USA because of the major cost implicated with cryopreservation and special insurance required in mailing such frozen tissues. Thus, creating a mitochondrial diagnostic laboratory, which is currently in its final stages, will be of a great benefit for



AUBMC and will further help implement a “Mitochondrial Medicine” Field.

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## 6. Tell us more about your involvement in research and how do you intend to promote that at AUBMC?

I always tell my students that nothing can be as rewarding as the satisfaction of knowing that something you discovered or developed is making a difference in people’s lives or is improving our understanding of natural or other phenomena. Through my own experience in research, I always try to show them how exciting it is to be part of an adventure that will change what will happen next year or in 10 or 15 years’ time. Having said that, I deeply believe that only practical experiences represent successful strategies to foster research among students in our institute. For that, students must be encouraged to get involved in research and join as soon as possible one of AUB’s basic or translational research centers.

In that regard, we have currently developed two research projects that we expect to be potentially engaging and inspiring for more students to join in research.

The first project aims to better understand mitochondrial involvement in neuromuscular diseases. Two lines of analysis, patient-derived and cell-based, will be set to outline respiratory chain lesions, whether genetically or environmentally induced, and define their consequence on mitochondrial activity and the secondary cellular responses they induce. The second project was initiated at the end of my postdoctoral fellowship at Dr. Pierre Rustin’s laboratory in Paris. This project aims at deciphering the link between mitochondrial dysfunction and amyloid-beta plaques accumulation –hallmark of Alzheimer’s disease– in cellular models.

Interesting results obtained from this project were published this month in “Free Radical Biology and Medicine” Journal where we have shown a direct link between mitochondrial respiratory chain dysfunction and accumulation of amyloid beta plaques (El-Khoury et al., 2016).

## 7. What were some of the most rewarding moments of your career?

As I mentioned earlier, during my postdoctoral fellowship we were developing new gene therapy approach to compensate for mitochondrial respiratory chain deficiencies, which are responsible for a broad range of non-curable human disorders such as neurodegenerative and neuromuscular diseases. This approach relied on the creation of a transgenic mouse expressing the alternative oxidase AOX gene that is absent in mammals. The AOX is a mitochondrial protein that is widespread in plants, fungi and lower animals. In plants, it was called the cyanide resistant pathway due to its ability to maintain respiration and thus oxygen consumption in the presence of cyanide –a lethal inhibitor of the respiratory chain and thus respiration. The capacity of the AOX to overcome a respiratory chain blockade was an incentive for multiple research labs to try, over a decade, to create transgenic mice expressing the AOX.

However, for an unknown reason, all the attempts were unsuccessful. Knowing that, accepting this challenging project has put me directly under pressure. In addition and for long, I thought that expressing the AOX in mice would be lethal. However, after two years of trials, the rewarding moment arrived when I first observed that potential AOX-expressing mice expressed the AOX protein in the brain. Excitement was further amplified when I showed that this expression was extended to 15 other organs and that the mice expressed a functional AOX. This led us to the ultimate moment where we have shown that the whole mice resisted to Gaseous cyanide. This was the first AOX-expressing (cyanide-resistant) mouse that is currently used to introduce the AOX in mice models of neurodegenerative diseases with an underlying mitochondrial respiratory chain deficiency.

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## 8. Outside work, what do you enjoy doing the most?

I dedicate a significant amount of time to my work since it is my hobby which I like to practice every day. So, when I am not engaged in a professional activity or spending time with my lovely family, I enjoy being physically active. I therefore regularly practice basketball and frequently participate in outdoor activities mainly rock climbing and skiing. This is extremely revitalizing and helps me keep my brain fit.

After being an anti-reader nearly all my life, I discovered lately, during my postdoctoral fellowship, the pleasure of reading. Pierre-Henry Gouyon –my “Population and Evolutionary Genetics” professor during my PhD– and Richard Dawkins, both renowned scientists in the “Evolutionary Biology” field were the main incentive for this recently discovered avocation. So, in my free time, I like to read non-fiction books, mostly those related to science and more precisely to “Evolutionary Biology” written by these two scientists. Indeed, their topics, whether it is Lenski’s bacteria, our own ancestors or the physical laws that govern our universe, are all laid out with that combination of clarity, style and verve that is hallmark and will not leave you indifferent.

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