
NDAL

THE LIFE AND EVOLUTION OF A LEADING LABORATORY IN NEURODEGENERATIVE DISEASE RESEARCH

BOĞAZİÇİ UNIVERSITY
SUNA AND İNAN KIRAÇ FOUNDATION
NEURODEGENERATION
RESEARCH LABORATORY

SUNA AND İNAN
KIRAÇ FOUNDATION

BOĞAZİÇİ ÜNİVERSİTESİ
1863

NDAL

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SUNA KIRAÇ: OUR ROLE MODEL

"I am determined to live and put up a struggle in this country; I wish to be one of the criticized and not one of the critics. I have decided to take action, rather than talk. Economic crises will be overcome, political conflicts will be resolved; however, it is impossible to rebuild a society whose children have been wasted. Instead of expecting everything from the state or someone else, everybody should join hands in their own capacity to improve education. Keeping up with the times can only be possible with well-educated, brilliant minds. It also requires a well-defined, modern national education policy with precautions in place. This is the only way through which the young generations of Turkey can be well-educated and embrace the principles and reforms of the Republic. The effects of education are - by nature - persistent; therefore, the value of a modern system of education is priceless."

Suna Kıraç

FOREWORD

The human genome is a three-dimensional, dynamic structure; regulatory mechanisms on various levels of this structure control the expression of genes. Until recently, the majority of the genome was deemed to be non-functional, and by extension, obsolete, since only two percent coded for proteins. The genome does not have a static code and is of a depth and complexity that is beyond all expectations. The genome is also sensitive to environmental factors due to the epigenetic mechanisms that are transmitted from one generation to the next. As geneticists studying the human genome today, we hold an enviable position. From where we stand, we see a past full of achievements and a future that is even more promising. The accumulation of knowledge and new technologies that began to define genetic mutations causing hereditary diseases in the 1980s entirely changed the discipline of human genetics. After years of successfully understanding the etiology of hereditary diseases – particularly by using Mendel's rules – the discipline of human genetics entered a new phase with the completion of the Human Genome Project in the 2000s.

The Human Genome Project altered paradigms not only in biology, but in medicine as well, and taught us that not only Mendelian genetics (patterns of inheritance), but that the four major causes of death in humans, namely, cardio-vascular disease, cancer, stroke, and Alzheimer's, along with countless other common ailments such as adult onset diabetes, obesity, macular degeneration, etc., are also related to our genetic makeup. Geneticists were surprised; the genetics, in other words, the inheritance of these diseases were complex, the mechanisms of action were diverse and similarly complicated, and yet there were overlaps and similarities between the diseases. The technology and data available from the 1980s were insufficient to grasp all of this. These diseases were caused not only by rare and high-risk 'lethal' mutations, but also by rare/medium-risk and common/low-risk 'silent mutations' that make us what we are. So, starting in 2010, the field of biology underwent another major transformation and entered the age of systems biology and what is often dubbed "'omics" (genomics, transcriptomics, proteomics, and metabolomics) in the laboratory. The linear progress and success achieved in the genetics of complex diseases now entered a new stage in which discoveries could be made exponentially. Powerful new sequencing methods were completely changing the field of biology and having a radical impact on medicine. Biology was no longer confined to molecular biology and cellular science, but had evolved into systems biology. Through coupling with information technology and collaborations with mathematicians, computer scientists, and statisticians, biology became an interdisciplinary field in which it could be possible to decipher terabytes of data from the human genome, transcriptome and proteome. This revolution also influenced medicine and made it possible to study all common diseases on a systemic level.

Among diseases in which heredity plays a significant role, genetics has, without a doubt, been the most successfully applied to the study of neurological diseases, which affect our brain and nerves. In none of the other complex diseases are genetic mutations the direct cause of the disease, as they are in neurological or neurodegenerative diseases. Therefore, the young, highly complex and continuously-evolving discipline of neuroscience is the fastest rising star in science and medicine.

10 YEARS ON OUR WAY TO
A CENTER OF EXCELLENCE

THE FOUNDATION OF NDAL

Founded in 2005 with a mission to contribute to the progress of neuroscience, which is still in its infancy in Turkey, and to lead the way in the study of neurodegenerative diseases, the Neurodegeneration Research Laboratory (NDAL) is the first example of an academic collaboration between a leading state university and a prestigious foundation in Turkey. Founded at the Boğaziçi University's Department of Molecular Biology and Genetics with the support of the Suna and İnan Kıraç Foundation, NDAL conducts research on the molecular mechanisms of progressive brain diseases, such as Alzheimer's disease, Parkinson's disease, ALS, Huntington's disease, myotonic dystrophy, and ataxias, which cause rapid neuron death. As there is an insufficient knowledge base in this particular field at medical schools, NDAL has earned the trust of hospitals and clinics across the country. The center, with its experienced team, authority on the subject matter, and high-end laboratory infrastructure, has evolved into a center that can diagnose these diseases on a molecular level. The collected samples create a great potential for research and give NDAL a unique opportunity to conduct research on neurodegenerative diseases.

Having trained six post-doctoral researchers, eight PhD and twenty master students from 2005-2015, the center also employs two full-time administrative assistants, one lab specialist, and one technical assistant, and provides many undergraduate students with research experience. Prof. Robert Brown (UMass, USA) and Prof. Jeffrey Macklis (Harvard University, USA) who are among the most highly-respected specialists of ALS and motor neuron development in the world, have served as academic advisors to NDAL since its foundation and visit NDAL every year for conferences or to discuss joint projects.

İNAN KIRAÇ: NDAL INAUGURATION, JULY 2005

Our vision

In order to shed light on the complex structure of the central nervous system and to understand the mechanisms that trigger incurable neurodegenerative diseases, we strive to;

- Support and accelerate neuroscientific research,
- Bring new generation technologies to the laboratory,
- Train researchers that can apply these new methods,
- Transform research results into molecular treatments,
- Become a "Center of Excellence" in neuroscience.

Our mission

The objective of NDAL is to universally explore the mechanisms of neurodegenerative diseases with the latest technologies, a powerful and well-designed laboratory base, a dynamic team that promotes a rich scientific environment, and interdisciplinary and international collaboration.

Our values

- Leadership in the study of neurodegenerative diseases
- Professionalism, continuity, creativity, and innovation
- Teamwork and effective collaborations
- Making discoveries about neurodegenerative diseases and spreading knowledge
- Encouraging problem solving, creative thought and excellence

A PASSION FOR DNA

OUR AREA OF RESEARCH

The astounding progress made in the field of genetics in recent years has not only radically impacted the science and practice of medicine, but has also revealed that many prevalent diseases are directly linked to the structure of our DNA. This new information has changed all the paradigms in biology. The group of neurodegenerative brain diseases that we work on account for an important percentage of neurological diseases. Approximately 10% of these diseases are transmitted by Mendelian inheritance, whereas the remaining 90% are of a sporadic origin, meaning they are inherited in a complex manner. Our research aims to understand these diseases on a molecular level, to elucidate their genetic basis – which we now realize is far more complex than we had imagined – to shed light upon the cellular damage caused by these mutations, and to identify the affected molecular pathways. Only through an understanding of these can the long-awaited methods of treatment be developed.

Neurodegenerative Diseases

Neurons are the nerve cells in the brain and spine. Neurodegeneration refers to the destruction of the structure and function of neurons. The degeneration leads to the death of these cells, which initiates the process of the disease. Generally affecting people above middle-age, typically in developed societies where there is a high average age, the most important examples of neurodegenerative diseases today are Alzheimer's and Parkinson's, as well as ALS, ataxia, and Huntington's diseases. Disorders of the brain are devastating not only for affected patients, but also for their families, often robbing individuals of the qualities that we most strongly associate with being human. Moreover, since the mechanisms of action of these progressive diseases still remain unknown, treatments for these diseases are virtually non-existent. Therefore, along with cancer and cardiovascular disorders, neurodegenerative diseases constitute one of the main groups of illnesses that molecular science has been focusing on in the recent years.

The clinical features of neurodegenerative diseases are different; because in each disease, neuronal damage and death are observed in different parts of the brain. Selective vulnerability, which refers to the observation that a select group of neurons is vulnerable to degeneration, is a term that has emerged with the increasing prevalence of neurodegenerative diseases. Selective vulnerability aside, these diseases overlap in some ways in terms of cellular mechanisms at play and are thus categorized under the umbrella term of "neurodegenerative diseases." It is expected that understanding the mechanism of one, can help solve the mystery of other neurodegenerative diseases. Only a complete understanding of the disease mechanisms can lead to the development of effective treatments. Until recently, both clinicians and laboratory scientists felt a mixture of optimism and pessimism about the possibility of developing mechanism-based treatments. In order to develop mechanism-based treatments, it is necessary to first verify that the treatment works in a model system, test it on patients, and then optimize the treatment based on feedback from patients. This entails a long and expensive process, with no guarantee of success at the end. The circumstances have entirely changed in recent years, thanks to the progress made in cell and developmental biology, the ability to test experimental drugs in realistic animal models, and the powerful exome sequencing and bioinformatic analysis tools that have been developed in the past two years and which have made it possible to identify and explore all the coding regions of the genome. "Translational research", which brings genetics and medicine closer together than ever before and makes possible the rapid transmission of research lab results to the

bedside, requires not only teamwork between scientists and clinicians, but also interdisciplinary collaboration. At the forefront of what is leading translational research is the recent progress made in molecular genetics and cell biology, development of high-throughput genome technologies, the ability to read and study the human genome down to its finest details, and our ability to see -in high resolution- inside the cell, be it through chemical, physical, and visual methods.

The most common feature of neurodegenerative diseases is their late age of onset: in other words, age is an important factor. Another common feature is that in each of these diseases, about 5-10% of cases are inherited according to Mendelian rules, whereas in the remaining 90-95% of cases we see a complex inheritance pattern (the only exception is Huntington's disease, which always follows Mendelian inheritance). In complex inheritance, genetic, epigenetic, environmental and lifestyle-related factors play a part, in addition to a number of stochastic parameters. Nevertheless, the greatest risk factor is advanced age, in other words, the aging cell. Through our research, we strive to understand the more prevalent complex diseases of the nervous system from a genetic perspective.

Alzheimer's Disease

Especially prevalent in individuals aged 65 years or older, Alzheimer's is the most common neurodegenerative disease characterized by the limitation of daily activity and distortion of cognitive abilities, and is often accompanied by neuropsychiatric symptoms and changes in behavior. Although the cause of the disease remains largely unknown, it is observed that premature death of cells involved in cognition and memory in the cortex and hippocampus leads patients to experience short-term memory loss and inability to complete daily functions. As is the case in similar diseases, inheritance explains 10% of cases. The majority of the patients suffer from a sporadic version of the disease, which appears to have a more complex molecular basis.

Parkinson's Disease

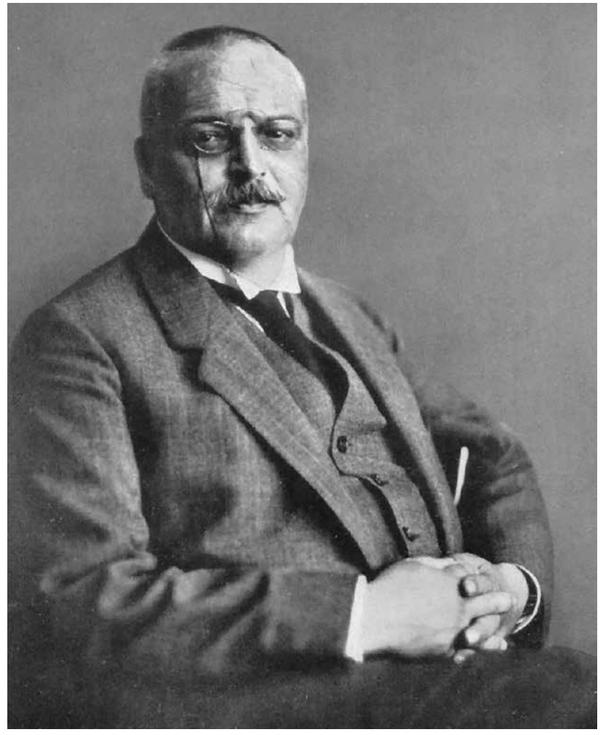
Parkinson's is a widespread neurological disease affecting more than four million people in the world. It is equally distributed between men and women; one out of a hundred people aged 65 years or older suffers from Parkinson's disease. Parkinson's is a disease with slow progression; it affects, but does not threaten life. It occurs due to a loss of the cells that synthesize dopamine in the brain. Parkinson's is not a disease of the elderly alone; although the average age at diagnosis is 60, one out of every twenty Parkinson's patients show the earliest symptoms before the age of 40. Patients between the ages of 21 and 40 are diagnosed with early onset Parkinson's disease.

Amyotrophic Lateral Sclerosis (ALS)

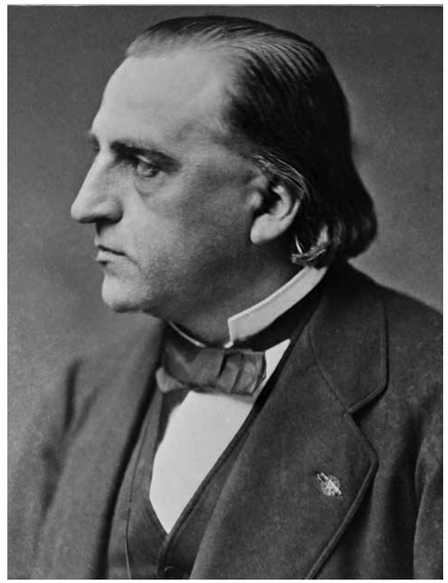
ALS is a progressive nerve/muscle disease caused by the rapid loss of motor neurons in the brain and spinal cord. In ALS, the degeneration and loss of upper and lower motor neurons lead to the paralysis of voluntary muscles. 5-10% of ALS cases are described as familial ALS (fALS), whereas the rest is categorized as sporadic ALS (sALS). Clinical findings of sALS and fALS are rather similar. The most recent discoveries also point to the similarities between sALS and fALS at genetic level. As in the case of all complex brain diseases, the understanding of the different mechanisms causing ALS is the most crucial factor in developing treatment methods.

Ataxia

The cerebellum is the part of the brain in charge of the coordination of complex functions such as walking, eye movements, speech, and swallowing. Ataxia (lack of coordination of muscles) can be caused by the premature death of brain



ALOIS ALZHEIMER



JEAN - MARTIN CHARCOT

cells or the dysfunction of the nerve pathways entering and exiting the cerebellum. Ataxia is the name given to the lack of voluntary co-ordination of muscle movements and has a number of subcategories, genetically the result of CAG (cytosine-adenine-guanine) repeat expansions as well as point mutations.

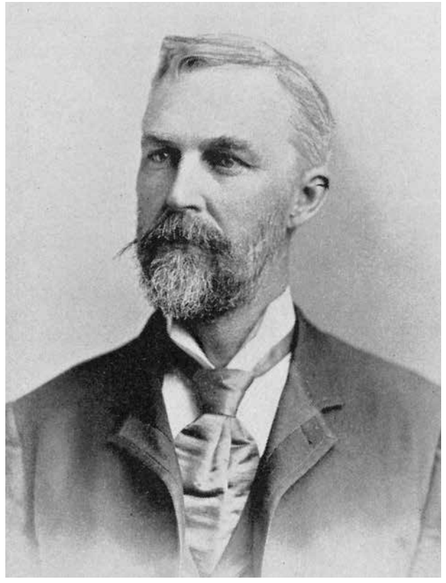
Patients suffering from the disease feel unsure when walking, experience dysfunction in fine motor skills such as writing, and may suffer from visual disorders. There are no medications that can cure the symptoms of ataxia. If ataxia is linked to reversible causes such as stroke, vitamin deficiency, or exposure to toxic drugs or chemicals, it is treated accordingly. However, in most cases, there is no effective cure available at the time.

Frontotemporal Dementia

Frontotemporal Dementia (FTD) is a type of dementia that affects the frontal and temporal lobes of the brain and leads to atrophy due to the death of neurons in these areas. FTD is the second most prevalent type of early onset dementia after Alzheimer's, and leads to changes in behavior, speech disorders, and difficulty in learning, decision-making, and feeling empathy. Since its clinical features are spread out across a wide spectrum, FTD is often confused with Alzheimer's or other psychiatric disorders such as bipolar disease, obsessive compulsive disorder, and schizophrenia. Clinical history, neuropsychiatric evaluation, and magnetic resonance imaging (MRI) play an important role in the diagnosis of FTD. Cases of FTD are categorized as sporadic or familial, the latter constituting more than 40% of all cases. Similar to all other neurodegenerative diseases, frontotemporal dementia still has no effective cure. The objective of genetic and cellular research is to understand the mechanisms of the disease so that suitable treatments can be developed.

Huntington's Disease

Huntington's is a late-onset and progressive neurodegenerative disease. The first symptoms emerge between the ages of 35 and 50. The clinical symptoms of Huntington's disease include involuntary writhing movements (chorea), decline in cognitive functions, and behavioral disorders. Unlike similar brain diseases, almost all cases of Huntington's disease are familial. The mutation that causes Huntington's disease is an expansion in the CAG repeat segment of the huntington gene. In healthy individuals, the number of repeats usually ranges from 15-25; in patients with Huntington's disease however, the number of CAG repeats exceeds 40. This number also determines the age of onset of the disease. Although Huntington's disease is exclusively familial and does not have complex patterns of inheritance, the mechanism of this disease has not yet been elucidated as well.



GEORGE HUNTINGTON

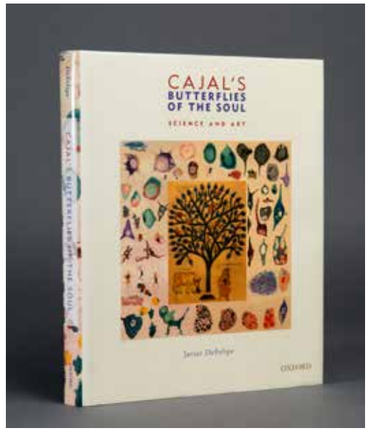
Myotonic Dystrophy

Myotonic Dystrophy (DM) is a slow-progressing disease that often begins in adulthood and causes muscle weakness and atrophy. Muscles of the face, jaw, hand, and neck are most affected in DM, whereas leg muscles are affected to a lesser degree. In addition to muscle weakness, other indications of the disease are cataracts, cardiac arrhythmia, and hormonal disorders that lead to hair loss, infertility, and diabetes in men, and menstrual irregularity in women. Familial DM is a rare type of myotonic dystrophy and appears in early childhood.

Molecular Diagnosis of Neurodegenerative Disease at NDAL

NDAL is the only laboratory in Turkey that performs the molecular diagnosis of complex neurodegenerative diseases. Therefore, it serves as a center that brings together scientists, clinical doctors, patients and their families from across the country. The number of genetic diagnoses made by NDAL until now is nearly 4500. The genetic diagnoses of these complex diseases require sophisticated experimental methods and is thus not routine clinical practice. The diagnoses fall under the category of research, as it is impossible for this type of work to be conducted at clinical laboratories, given the present conditions. The database of patient material at NDAL is an invaluable source for research. It is a "DNA bank" that can be used to advance neurodegeneration research. The research that is made possible through molecular diagnostics holds great promise in understanding the pathogenesis of disease, for each gene and each mutation have their own unique signatures. In other words, every gene and every mutation holds a key to unraveling a part of the disease mechanism.

EUROPEAN COST MEETING, 2007 NEURONAL REGENERATION AND PLASTICITY



CAJAL'S BUTTERFLIES OF THE SOUL

If a subject is not complicated or controversial, then it is probably not interesting.
Santiago Ramon y Cajal

SUNA KIRAÇ SCHOLARS AND İNAN KIRAÇ FELLOWS, 2011

EDUCATION AND RESEARCH AT NDAL

With its state-of-the-art laboratory facilities that are funded by the Kıraç Foundation, Boğaziçi University and TÜBİTAK, and its rich patient database, NDAL provides students with an academically up-to-date and internationally competitive environment in which they can also feel comfortable and happy. In addition, all graduate students at NDAL are given the opportunity to receive short-term training at specialized laboratories abroad. This opportunity is beneficial not only because it strengthens the knowledge base of the students, but also because it introduces them to the culture of research. From 2005-2015, a total of seven PhD and seventeen MSc theses have been completed at NDAL. One PhD thesis and three MSc theses are still in progress. Furthermore, the laboratory has trained five postdoctoral researchers.

NAZLI BAŞAK, PRESIDENTS SOYSAL AND SIMMONS

NDAL's first decade: Researchers / Graduate Students and areas of research

Serkan Alkan, PhD.

My main project at NDAL is the analysis and optimization of the experiments conducted as part of the MinE project that produce big data and require professional bioinformatic analysis. I am also in charge of updating our website *alsturkiye.org*.

Suna Lahut, PhD.

As part of my PhD research, I studied a large family, whose members suffer from Parkinson's disease. Apart from being the second largest family known to be afflicted with Parkinson's in the world, this family included many individuals who were not yet symptomatic, but carried the disease-causing mutation. They were all very open to cooperation. Very importantly, this family also represented sporadic PD cases, due to the unique feature of the mutation they carried. The objective of my research was to focus on this family to develop biomarkers that could help diagnose Parkinson's disease in its early phase. In addition to working on my PhD at NDAL, I also conducted some of my experiments at the Goethe University in Frankfurt. After studying some genes affected by the toxic gain-of-function mechanism in PD, I identified, for the first time, the CPLX1 gene as a possible biomarker for the disease. During the course of my PhD thesis, I published my research in peer-reviewed journals; four of them in international journals, and one in a Turkish journal.

Kadir Özkan, MSc.

During the course of my MSc and PhD education, I had four productive years at NDAL. Thanks to the opportunities made possible by the Suna and İnan Kıraç Foundation and Prof. Nazlı Başak, I completed my PhD thesis at Prof. Jeffrey Macklis' laboratory at Harvard University Department of Stem Cell and Regenerative Biology. As a part of my project, I explored if it is possible to obtain new functional neurons by altering the molecular characteristics of stem cells from the brain and whether these neurons could be used to replace the motor neurons that are damaged by ALS or spinal cord injury. I believe that my work will help pave the way for the development of stem cell-based therapies to such diseases in the future, and will be a source of hope for patients and their families.

Ceren İskender, MSc.

SOD1 is the first gene that was identified as having a role in ALS. Unlike most other genes implicated in ALS, SOD1 has not been associated with any other disease. As part of my MSc project, which was achieved through collaboration with the Reenan Laboratory at Brown University, I used the homologous recombination method to create a SOD1-based Drosophila model of ALS and characterized

the mutants to investigate the expression of genes implicated in the pathogenesis of ALS.

While continuing with my PhD at NDAL, I have had a leading role in establishing C9orf72-based molecular analysis of ALS. For my project, I am trying to understand the possible genetic causes underlying the phenotypical variations that exist between individuals with ALS. My analyses require exome sequencing, which today is the gold standard of genetic analysis; therefore, this new technique and bioinformatic evaluation are my areas of interest. During my time at NDAL, I took active roles as a researcher in several different projects and am a co-author in one nationally- and two internationally-published articles.

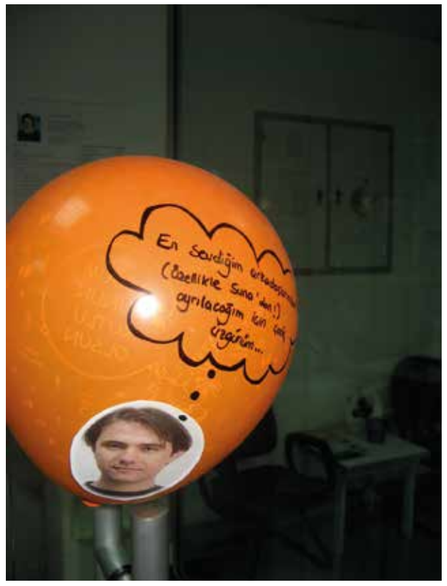
Ece Kartal, MSc.

I recently completed my MSc at NDAL; because of the intellectual and friendly environment in the lab, I feel like I have been away from NDAL for much longer. Over the course of my three years at NDAL, I had a role in introducing the new technology of exome sequencing method to the lab. The goal of my thesis project was to use bioinformatics to evaluate exome sequencing data of complex pedigrees that could not be solved with traditional methods. In this way, I aimed to identify the mutations/genes that were implicated in the disease. Over the course of my project, I investigated 15 pedigrees and identified mutations that were linked to the disease. In addition to my thesis, my findings were reported in two international publications.

The experience I gained at NDAL, the opportunities that were made possible for me, the scientists I met, and the friends I made equipped me with a strong foundation from which I will benefit all my life. I will always be proud to have been part of the NDAL family.

Nesli Ece Şen, MSc.

Spinocerebellar ataxia type 2 (SCA2) is a movement disorder associated with a repeat mutation in the ATXN2 gene. Although the genetic basis of this disease was discovered 25 years ago, the lack of information about the function of the ataxin-2 protein makes it difficult to develop a cure for the disease. As part of my MSc project, I studied samples that we obtained from a large Turkish SCA2 family, as well as a rat model of the disease. My aim was to clarify the function of ataxin-2 and elucidate the downstream effects of the mutation in the ATXN2 gene. Furthermore, I tried to identify biomarkers that could help define and distinguish between the different stages of the disease. During this process, I contributed to the preparation of two international publications. I had the opportunity to conduct part of my research at one of our collaborating laborato-



ries, namely, the Experimental Neurology Laboratory at the Goethe University Frankfurt. In the future, my research will continue to focus on the function of Ataxin-2 and why only certain neurons are susceptible to the disease.

Cemile Koçoğlu, BSc.

Ataxias are caused by the degeneration of neurons in the cerebellum and typically present as lack of coordination, lack of control, loss of balance, and speech impediments. Ataxias comprise a group of neurodegenerative diseases in which a complex genetic interplay is implicated. In complex diseases, such as ataxias, constellation of many DNA variations, which would not lead to disease on their own, contribute to the disease mechanism. As part of the research I am conducting for my MSc at NDAL, I carry out bioinformatic analyses of data that is obtained using next-generation sequencing (i.e. whole exome sequencing). By analyzing exome data obtained from DNA samples of patients and their healthy relatives, I am trying to identify pathways that have a role in the development of ataxias.

Hamid Hamzeiy, BSc.

I was introduced to the field of complex neurodegenerative diseases for the first time during the early stages of my Master's education, while I was doing a rotation at NDAL. In 2014, I visited Professor Silani's neuroscience laboratory at our partner institution, Istituto Auxologico Italiano. While I was there, I mainly focused on ALS and the mutation that is most frequently linked to this disease, which is a repeat expansion in the C9orf72 gene. Cases of ALS that are linked to the repeat expansion in the C9orf72 gene can present with very different phenotypes; it is therefore clear that the mutations that have so far been linked to ALS do not paint the whole picture and that non-genetic factors also have a role in disease development. Examples of non-genetic

RECEIVING THE RESEARCH AWARD FOR EXCELLENCE IN SCIENCE, FROM YEŞİM ARAT, 2012

factors that might contribute to the disease mechanism are lifestyle and environmental conditions, which can cause epigenetic changes, which in turn, influence gene expression. Therefore, it is very important to understand the basis of epigenetic differences and how epigenetics can contribute to the disease. As part of my master thesis, I am studying whole genome DNA methylation, a common type of epigenetic modification, in ALS and in a number of other neurodegenerative diseases. After investigating the status of whole genome methylation of patients and healthy control groups, I will use next-generation technologies to analyze the differences between the two groups. This way, I aim to shed light on the still unexplained causes and mechanisms of various neurodegenerative diseases, in particular, ALS.

Fulya Akçimen, BSc.

ALS is a complex neurodegenerative disease which is the result of more than one mutation and one mechanism. Today, it is known that mutations in more than 33 different genes can cause ALS. The focus of my research at NDAL, is the use of bioinformatic methods to assess data obtained from next-generation sequencing (NGS). NGS yields data that can reveal variations between affected and healthy individuals at the level of DNA. The objective of my Master's thesis is to use such data to pinpoint the genes and mutations associated with ALS. The next stage of my research will involve elucidating the biological pathways underlying disease mechanism and thinking about how these altered pathways can be restored.

Aslı Gündoğdu Eken, MSc

Since I became a part of NDAL in 2005, my responsibilities at the lab include managing the patients, conducting genetic analyses, and developing new methods. Along with Irmak Şahbaz, who joined us in 2009, I am also responsible for keeping track of the laboratory inventory and ordering supplies. Considering the increasing workload at NDAL, I am thankful to be working with Irmak. I feel privileged to have these responsibilities in a lab where such extraordinary research is taking place.

Opportunities for Collaboration and Education Abroad

Among the laboratories in which NDAL students have the opportunity to receive short-term training are the labs of Robert Brown (UMass, Worcester), Jeffrey Macklis (Harvard University, Cambridge), Maria Teresa Carri (European Brain Research Institute in Rome), Teepu Siddique (Northwestern University, Chicago), Justin Fallon and Robert Reenan (Brown University, Providence), Murat Günel (Yale University, New Haven), Georg Auburger (Goethe University, Frankfurt), Peter Andersen (Umea University, Umea), Vincenzo Silani (University of Milan, Milan) and Jan Veldink (University Medicak Center, Utrecht). These scientists also act as co-advisors for some of the student theses at NDAL.

PhD Program at Brown University

With the funds that were allocated as part of the "Memorandum of Understanding" signed with Brown University in 2008, an agreement was made for collaboration between NDAL and the departments of neuroscience and molecular biology and genetics at Brown University. This collaboration entails education and research. In terms of education, every year, the Kıraç Foundation provides a scholarship to a student that graduates from the Boğaziçi University Department of MBG with a high GPA and who is admitted to the graduate program at Brown University. Initiated in October 2009, the program has so far offered scholarships to five students, the first two of whom successfully completed their PhDs in 2015. The collaboration between NDAL and Brown also makes possible the Suna Kıraç Neurodegenerative Diseases Workshops in Istanbul, which are organized biennially at Boğaziçi University with Brown University faculty, whom we have established close ties with. In addition to the students who are doing their doctoral work as part of the structured PhD program, five students from NDAL (each did three month-long internships at Brown) and an undergraduate student from Brown did a summer internship at NDAL. Again, as part of the collaboration between NDAL and Brown, Prof. Nazlı Başak was invited as keynote speaker to the official opening of the Brain Research Institute in November 2013.

Alumni Testimonials

Gizem Tanrıver, 2014 BSc, Boğaziçi University, PhD candidate, Cambridge University, England

Being part of NDAL means advancing cutting-edge research by working with a great team at one of the leading laboratories in Turkey and in the world, while also being able to enjoy the most pleasant conversations at coffee breaks. It means comparing each lab you visit with NDAL and feeling that something is missing. This is why being part of the team at NDAL fills me with pride that will last a lifetime.

Sena Agım, 2012 MSc, NDAL
PhD candidate, Purdue University, USA

The three years I spent at NDAL during my Master's studies laid the foundations for my career. Collaboration with foreign institutions, the organization of international conferences, interaction with experienced researchers, and

the encouragement of students to participate in all of this does not exist in any other laboratory in Turkey. My training at NDAL greatly contributed to my ability to adapt to the research culture in the United States without experiencing much difficulty. As I continue on my path with this strong foundation, I think of NDAL with much appreciation and longing.

Özgür Ömür, 2013 MSc, NDAL, Product specialist, Medtronic Medikal, Istanbul

NDAL is among the few organizations in Turkey that provides a prestigious graduate education that goes beyond the traditional understanding. With its innovation and internationally competitive environment, NDAL trains its students to easily adapt to both the aca-

demic and work life, and guides them towards success and productivity. As an MSc graduate, I stand out professionally due to my goal-oriented attitude, determination, work discipline, and many other attributes that I acquired and developed at NDAL. For the high-quality education and training that we received at NDAL, I am eternally grateful to Prof. Nazlı Başak and the Suna and İnan Kıraç Foundation, which supported the establishment of the lab and never ceased to support our research.

Özgün Uyan, 2012 MSc, NDAL, PhD candidate, University of Massachusetts, USA

I consider NDAL to be the place where I began my academic career and laid the foundations of my scientific background. Throughout my studies as a Master's student, the opportunities provided by NDAL, including working on intellectually-rewarding projects and being part of collaborations in Turkey and abroad, allowed me to conduct scientific research at the level of international standards. My experience at NDAL helped me adapt to my current PhD program in the United States. Also, by organizing the biennial Suna Kıraç Conferences and the Suna Kıraç Workshops, NDAL gives students and young researchers the amazing opportunity to listen to and interact with leading researchers. In addition, the friendships I made throughout my education will always remind me of NDAL's importance in my life.

Gönenç Çobanoglu, 2012 MSc, NDAL Clinical studies assistant specialist, Nova Nordisk, Istanbul

I have always felt lucky and privileged to have completed my Master's at NDAL, for NDAL gives students the opportunity to develop themselves not only academically, but also socially. By presenting at and helping with the organization of international conferences, meeting academics who are leaders in their fields, participating in short and long-term exchange programs, and planning activities outside of the lab, we all graduated from NDAL as well-rounded individuals. Every day at work, I recognize the advantage of having received

this kind of an education. I would like to extend my infinite thanks to the Suna and İnan Kıraç Foundation for providing us with these opportunities, which changed our lives, and to Prof. Nazlı Başak for training and mentoring us in the most excellent way.

B. Arman Aksoy, 2010 BSc, Boğaziçi University, 2015 PhD, Memorial Sloan-Kettering Cancer Institute, USA

Since my second year as an undergraduate student at Boğaziçi University, NDAL has been like a second home for me and my colleagues at NDAL have become my second family. As a member of the NDAL family, I learned so much – both academically and culturally – from the research projects I worked on and our collaborations with leading academicians abroad. Thanks to everything I have learned and the unique research experience I had under the mentorship of my dear professor Nazlı Başak, I became qualified enough to continue my academic career as a PhD student. It has been five years since I graduated from NDAL, but I will forever be proud to have been part of the NDAL family.

Pınar Deniz, 2011 MSc, NDAL
PhD candidate, Fordham University, USA

Although it has been four years since I graduated, I cannot help but smile every time I think back to my time as a student at NDAL. It was at NDAL that I learned that real success is not achieved simply by being a good scientist, but that it is also necessary to live with awareness in every aspect of life and always try to improve oneself to be a better person. Our dear professor Nazlı Başak was not only our guide to the field of science, but also a much-admired role model, who helped us grow in every aspect of life and always supported our progress. The three years I spent at NDAL were invaluable for me. I would like to infinitely thank everyone who played part in bringing NDAL to life.

Aslıhan Özoguz, 2010 PhD, NDAL
2010-2014, Postdoc, NDAL

In 2001, during my Master's work at the Boğaziçi University Department of Molecular Biology and Genetics, we began working on the genetic analysis of ALS for the first time in Turkey. At this time, our capabilities were rather limited. During my PhD work, however, NDAL was established with the support of the Suna and İnan Kıraç Foundation. The expanded research facilities and reputation of the institution made it possible to increase our collaboration, first with medical doctors in Turkey and later with research teams abroad. Through opportunities provided by NDAL, I had the chance to gain experience at research laboratories of prestigious universities, such as Northwestern, Harvard, and Yale. At each laboratory, I gained a new perspective. In addition, being actively involved in the organization of the Suna Kıraç Conferences contributed to my education, academically, socially and culturally. During the eight years that I spent at NDAL, first as a graduate student and then as postdoctoral researcher, it was a great privilege to have been part of a team that is dedicated to understanding neurodegenerative diseases on a molecular level and improving the quality of life of patients and their families.

Caroline Pirkevi, 2009 PhD, NDAL
Embryologist, Quality Manager, Memorial Hospital, Istanbul

Dear Professor Başak and the NDAL Family,

Ten years have passed since the inauguration of this great laboratory. I remember it as if it were only yesterday; the celebration we had in the space which used to be the terrace, how we had excitedly placed bookmarks with NDAL logos inside the copies of "Tuesdays with Morrie", and how we came up with the NDAL logo in the first place. That's how long I have been around. Back then, I couldn't quite understand how things would change by moving the laboratory to a new space, but it did indeed impact many things. In a well-established and leading institution like Boğaziçi University, NDAL gave graduate students a sense of belonging and an opportunity to feel like they were members of a large family. I considered it a great privilege to be able to work in a laboratory where we had vast bench spaces, our own desks, pipette sets, electrophoresis devices and PCR machines we could use without having to wait in line. In addition, the Suna and İnan Kıraç Foundation scholarship that I received during my endless wait for a position as a research fellow gave me the opportunity to focus on my research and continue my PhD work. It has been five years since I left NDAL, but I actually do not feel like I have left; for, with her sincerity, kindness, love, and grace, Nazlı Başak turned NDAL, which initially just seemed to be a laboratory that was detached because it was on a separate floor, into a large family. She listened to each and every one of us whom she trained. Even after we left NDAL, she tried to understand the paths we hoped to follow, and supported us.

ROBERT HORVITZ (NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE, 2002)

Her dedication to each of us was reciprocated with great love and loyalty. Happy 10th anniversary to all of us!

Altar Sorkaç, 2009 BSc, Boğaziçi University
2015 PhD, Brown University, USA
Suna and İnan Kıraç Foundation Scholar

Last year, I completed my PhD at the Brown University Department of Neuroscience and I am currently working as a postdoctoral researcher at the laboratory of Dr. Gilad Barnea in the same department. NDAL had a huge role in getting me to where I am today. I began working at NDAL when I was in my third year of undergraduate studies at Boğaziçi University and I learned many important skills there, ranging from molecular biology research techniques to conducting database research. In addition, I realized for the first time what it meant to have colleagues. I met many people at NDAL and formed important friendships, which became stronger with the different places we went to as NDAL, the events we organized together, and our collaborative work in the laboratory. One of the most important things NDAL gave me was the realization that as a scientist, I do not have to limit myself to only doing research. I also came to see how important the communication and collaboration between scientists is. The 2nd Suna Kıraç Neurodegeneration Conference, which we organized in 2009, for example, was not only so much fun, but also extremely instructive. I will forever be indebted and thankful to everyone who made these experiences possible for me, and will always recall the days I spent at NDAL with much longing.

Aslı Şahin, 2009 BSc, Boğaziçi University
2015 PhD, Brown University, USA
Suna and İnan Kıraç Foundation Scholar

In 2015, I completed my PhD on ALS at the Brown University Department of Molecular Biology, Cell Biology, and Biochemistry with Dr. Robert Reenan as my advisor. In 2016, I will continue my postdoctoral research in Dr. Mark Albers' laboratory at Harvard Medical School and Massachusetts General Hospital. As an undergraduate at Boğaziçi University, I had my first research experience at NDAL, under the supervision of Dr. Nazlı Başak. While at NDAL, I learned the basic techniques of molecular biology research through working on cell cultures. Most importantly, I realized what it meant to work together as a team in a laboratory and decided that this was the career path I wanted to follow. During the 2nd Suna Kıraç Neurodegeneration Conference in 2009, I met Dr. Robert Reenan, who would later become my PhD thesis advisor. In fact, it was during this conference that Dr. Reenan, who had never worked on ALS before, noticed a huge gap in the field. Eventually, my thesis was born out of this gap. During my doctoral work, I continued to collaborate with NDAL. I would like to thank everyone who made it possible for me to have the opportunities that have brought me to where I am right now.

Selen Şenocak, Brown University, USA
Undergraduate Student

Dear Professor Başak,
Happy Teacher's Day to you! I wish I could have been at NDAL and given you flowers today; as a mentor, scientist, and humanist, you had a great impact on me and become a role model for me in every respect. I feel very lucky to have been your student, and I am certain that all the students you have trained and mentored feel the same way. With my love, respect, and eternal thanks.

What a lovely letter from Selen Şenocak.
It must be so heart-warming and a validation of your great efforts to receive such a letter. I have never doubted that you are one of those very special teachers who opens doors and changes lives for the better.
Ann Nevans (a friend of NDAL)

JUSTIN FALLON, ÜMİT TAFTALI, KADRİ ÖZÇALDIRAN

ÖZALP BİROL

NDAL LINES OF RESEARCH

Gaining Insights in ALS Genetics / Genomics

- The distinct genetics of ALS in Turkey: Identification of new ALS genes using next generation methods
- Investigation of repeat expansions in Turkish ALS patients
    - ATXN2
    - C9ORF72
- Global methylation levels in ALS and related disorders

Collaboration: Robert Brown, UMass, USA; Peter Andersen, Umea University, Sweden; Leonard van den Berg and Jan Veldink, UMC Utrecht, The Netherlands and clinicians from medical schools/hospitals throughout Turkey

Aslıhan Özoğuz, PhD
Ceren İskender, MSc
Hamid Hamzeiy
Altar Sorkaç
Güneş Birdal

Analysis of Novel Disease Genes and Mechanisms

- Bioinformatic analysis
    - GWAS and CNV analyses
    - Whole exome analysis
    - Pathway analysis
    - Whole genome analysis
- Project MinE

Collaboration: Toronto University, Canada; Istituto Auxologico Italiano, Italy; UMC Utrecht, The Netherlands; Genomize, Turkey; Acıbadem University, Turkey; UMass, USA; Yale University, USA; TÜBİTAK, Turkey

Zeynep Sena Ağım, MSc
Özgün Uyan, MSc
Alireza Khodadadi, MSc
Ece Kartal, MSc
Cemile Koçoğlu
Fulya Akçimen

Molecular Basis of Neurodegenerative Diseases

- Huntington's disease
- Dominant and recessive cerebellar ataxias
- Myotonic dystrophy
- Friedreich ataxia, spinobulbar muscular atrophy, dentato-rubral pallidoluysian atrophy
- Alzheimer's disease and frontotemporal dementia

Collaboration: Tübingen University, Germany; Manchester University, England and Edinburgh University, Scotland

Caroline Pirkevi, PhD
Pınar Gencer, MSc
Nazan Saner, MSc
Sinem Hocaoğlu, MSc
Mine Güzel, MSc
Ayşe Latif, MSc
Didem Erbahar, MSc
Begüm Erdoğan, MSc

Understanding Disease Mechanisms: Parkinson's Disease

- Impact of alpha-synuclein in Parkinson's disease
- Developing molecular biomarkers for predictive diagnosis
    - Large Turkish PARK4 pedigree
    - Sporadic PD
    - Presymptomatic PD

Collaboration: Alexis Brice, Pitié-Salpêtrière Hospital, France; Georg Auburger, Goethe University, Germany

Caroline Pirkevi, PhD
Suna Lahut, PhD
Özgür Ömür, MSc

Understanding Disease Mechanisms: Spinocerebellar Ataxia type 2

- Understanding general mechanisms of
  - ATXN2 function
  - ATXN2 KO mice
- Developing blood biomarkers for SCA2
  - An extended Turkish SCA2 pedigree

Collaboration: Georg Auburger, Goethe University, Germany

Nesli Ece Şen, MSc

Molecular Development of Corticostriatal Projection Neurons

- Induced Neurogenesis of Upper Motor Neurons from Cortical Progenitors
  - Replacement of degenerating upper motor neurons with new neurons in ALS
- Development of Corticostriatal Neurons
  - Dysgenesis of cortical neurons that degenerate in Huntington's disease and in related cortico-basal ganglionic degenerations

Collaboration: Jeffrey D. Macklis, Harvard University, USA

Kadir Özkan, MSc

Accurate ALS Animal and Cell Models

- Introducing human SOD-1 mutations into Drosophila using homologous recombination
  - Behavioral analyses
  - Life span analyses

Collaboration: Robert Reenan, Brown University, USA

- Yeast-two-hybrid system
- Transient and stable transfections of neuronal cell lines
  - Expression analyses in RNA and protein levels

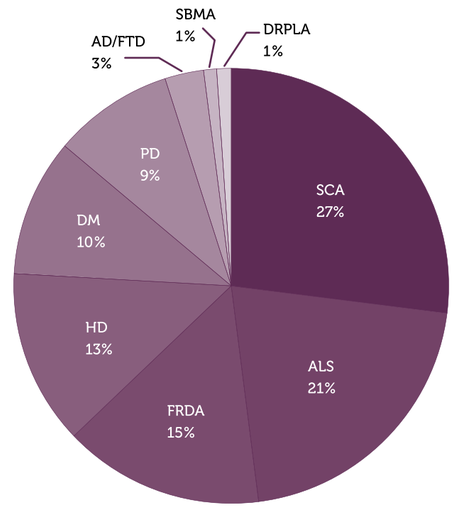
İzzet Enünlü, PhD
Mehmet Ozansoy, PhD
Suna Lahut, PhD
Gönenç Çobanoğlu, MSc
Pınar Deniz, MSc
Ceren İskender, MSc
Arman Aksoy
Aslı Şahin

Center of Excellence as a Diagnostic Reference Laboratory

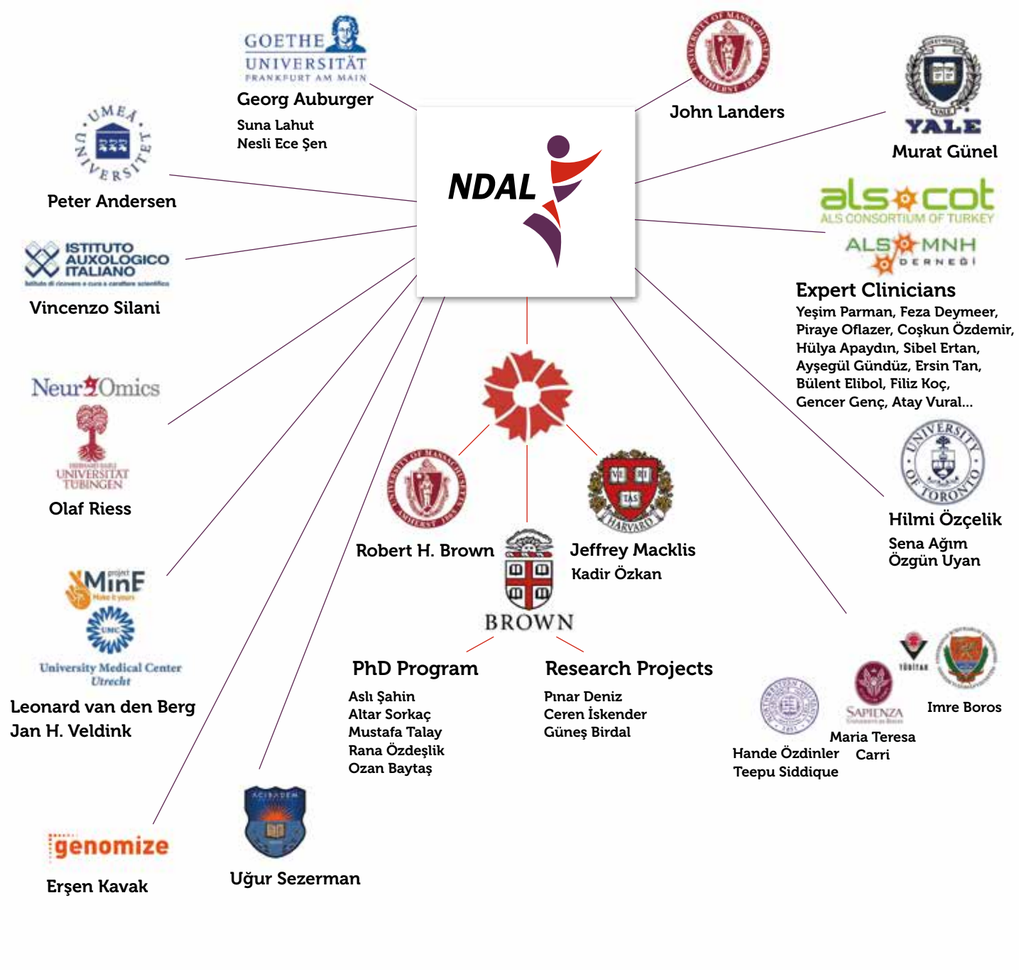
- Molecular diagnosis in several neurodegenerative diseases
  - PCR-based techniques and NGS
  - Nationwide referral of samples
  - Rich repository on patient material

Collaboration: Expert neurologists

Aslı Gündoğdu Eken
Irmak Şahbaz
Güneş Birdal



NDAL COLLABORATIONS



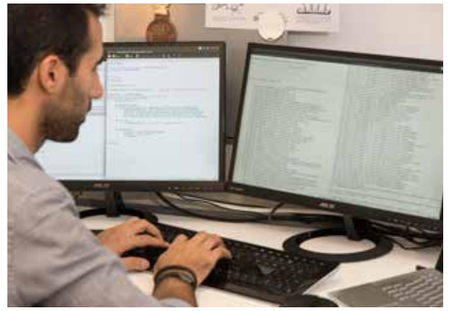
MBG-BRIDGE, GENETIC MEETING, 2010

3RD SUNA KIRAÇ NEURODEGENERATION CONFERENCE, 2011

WE WILL UNDERSTAND AND CURE ALS TOGETHER WITH OUR PATIENTS.

SCIENTIFIC MEETINGS

International Suna Kıraç Conferences on Neurodegeneration, Istanbul organized biennially under the guidance of NDAL advisors Dr. Robert Brown and Dr. Jeffrey Macklis, and hosted by the Pera Museum and the Suna and İnan Kıraç Foundation, the Suna Kıraç Neurodegeneration Conferences have become a series of prestigious international conferences in which leading scientists in the field of neurodegenerative disease biology take part. The objective of the Suna Kıraç Neurodegeneration Conferences is to bring together world-renowned specialists in brain science, neurodegeneration, and neurodegenerative diseases in Istanbul and give them the opportunity to discuss and share their most recent discoveries, brainstorm together, and interact with Turkish scientists, clinicians, and importantly, students. This direct contact not only promotes collaborations between laboratories, but also creates an unprecedented academic atmosphere in Turkey and an invaluable opportunity for students. We now know that the brain and its diseases are far more complicated than ever imagined and cannot be understood through the expertise of and data collected by a single laboratory, no matter how advanced the facilities of this laboratory may be.



Today, science can only advance through collaboration between laboratories, the creation of large consortiums, and the mutual sharing of data. By supporting such collaborations, the Suna Kıraç Neurodegeneration Conferences aim to accelerate the cure of neurodegenerative diseases by advancing our understanding of the mechanisms at the root of neurodegenerative diseases. The 5th conference will be held in 2016 and will mark the 10th anniversary of NDAL.

Four Suna Kıraç Conferences have taken place from 2005-2015:

- 2007: New Frontiers in Understanding and Treating ALS
- 2009: Stem Cells, RNAi and Neurodegeneration
- 2011: Recent Themes in Motor Neuron Biology and Neurodegeneration
- 2014:The Motor System: From Development to Neurodegeneration
    - Keynote speaker: Nobel laureate H. Robert Horvitz

Words on the Suna Kıraç Conferences from previous speakers and participants

Jeffrey Macklis, Max and Anne Wien Professor of Life Sciences, Harvard University

Every one of the Suna Kıraç Conferences on Neurodegeneration has been world-class, in terms of their state-of-the-art topics covered, speaker lists, opportunities for personal and collegial interactions, and organizational aspects. Bringing top-level science from multiple fields to bear on understanding and potentially treating neurodegenerative disease, ALS in particular, has been outstanding and rather unique– having the opportunity to do this in the magnificent city of Istanbul has been exceptional.

Robert Brown, Neurology Department, UMass

The Suna and İnan Kıraç Conferences on Neurodegeneration have been outstanding. They have provided an extraordinary venue for first-rank scientists from diverse backgrounds (Europe, Asia, U.S.) to explore cutting-edge concepts in ALS and neurodegeneration. Flawlessly organized, these symposia have addressed a wide range of multi-disciplinary concepts and technologies in the vanguard of neurobiology and neurogenetics. Situated in the elegant Pera Museum, the meetings have fostered in-depth, often catalytic but relaxed discussions, as well as an unparalleled opportunity for junior scientists to meet leaders in the field. A collaborative tone prevails through the sessions, emanating from the warm, energetic leadership of Nazlı Başak. Beyond the stimulating dynamics of the meetings, the Kıraç conferences have also been memorable because of the stunning beauty of Istanbul and the remarkable hospitality of the Kıraç family. Over the last decade, it has been a privilege to be associated with the Kıraç Conferences and the NDAL. I look forward to continued close association with Nazlı and her team, the Kıraç Conference and the Kıraç family as we continue our combined efforts to find a treatment for ALS.

Martha Constantine-Paton, Department of Biology, Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology

The Suna Kıraç Conference on Neurodegeneration in Istanbul was exceptionally informative and a very important conference for bringing together an international group of investigators focused on ALS and motor systems. There was more than enough time to talk informally with other investigators and particularly to the very bright and involved students working on this disease in Turkey. The conference was the optimal size and the venue was wonderful for allowing considerable informative discussions and important information exchange. Also Professor Başak was a wonderful host and expedited many of the interactions I had with many of the individuals I had not met before.

Guy Rouleau, Montreal Neurological Institute and Hospital, Department of Neurology and Neurosurgery, McGill University

An exceptional meeting with respect to the quality of the speakers and discussion, the razor-sharp focus on the disease, and the excellent organization of the event. However, what impressed me the most was the devotion of

GUY ROULEAU, ROBERT BROWN

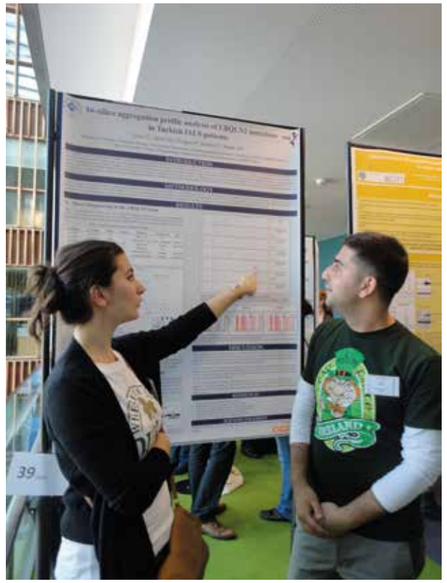
ROBERT BROWN, JEAN PIERRE JULIEN

Proud to be on the same boat with you:

ROBERT BROWN AND JEFFREY MACKLIS

AFTER SUNA KIRAÇ CONFERENCE ON NEURODEGENERATION, 2014 ON NESIME:

WITH ROBERT HORVITZ, MARTHA CONSTANTINE-PATON AND JEFFREY MACKLIS



ENCALS MEETING 2012, DUBLIN, IRELAND

the family and the staff to the cause – for me it was inspirational.

Kevin Talbot Nuffield, Department of Clinical Neurosciences, University of Oxford

The Suna Kıraç meeting was one of the most enjoyable, stimulating and enriching ALS meetings I have ever attended. The exceptional hospitality of our hosts, the matchless atmosphere of Istanbul and the quality of the participants all made for a unique experience. The most distinctive feature for me was the relaxed atmosphere which fostered a spirit of intellectual exchange about some of the most profound aspects of ALS. The Suna Kıraç Foundation should feel justly proud of its achievements in facilitating these meetings, which will have a lasting impact in fostering collaboration between Turkish ALS researchers and colleagues throughout the world.

Jonathan D. Glass, Department of Neurology and Pathology, Emory University

My visit to Turkey and participation in the Suna Kıraç Conference on Neurodegeneration was truly inspirational, both scientifically and culturally. The science presented at this meeting is top-notch and cutting-edge, my interactions with scientific colleagues, old friends and new, continues to influence my thinking and approach to my own work. This was my first visit to Turkey – a beautiful country with warm and friendly people and a rich history of art and science. I hope to return soon.

Justin Fallon, Brown University

The Suna Kıraç Conference on Neurodegeneration was an absolute delight and success. The quality of the science and the warmth and generosity of our hosts were beautifully complemented by the grandeur of Istanbul.

Suna Kıraç Workshops on Neurodegenerative Diseases, Istanbul

In addition to the Suna Kıraç Conferences, the Workshops on Neurodegenerative Diseases are coordinated biennially at Boğaziçi University, in collaboration with Brown University. During the workshops, professors from the Brown University Department of Neuroscience and Department of Molecular Biology, Cell Biology, and Biochemistry lecture graduate students over the course of two-and-a-half days on the animal and cell culture models used in neurodegenerative disease research and on the current avenues being explored for therapy development. About 100 graduate students attend the workshops, which consist of lectures and a practical course. The practical courses are organized and led by the Kıraç scholarship PhD students at Brown and the NDAL assistants. Most recently, the third workshop took place in January 2015:

- From Genetic Models of Neurodegenerative Disease to Therapies, Boğaziçi University, January 2011, January 2013, and January 2015.

Other International Meetings

In addition to the Suna Kıraç Conferences, NDAL has also hosted a series of other international meetings:

- Annual meeting of COST European Coope ration in Science and Technology (Splendid Hotel, Büyükada, September 2007).
- "Innovations in Neuroscience", organized in collaboration with University of Göttingen and Max Planck Institutes. The aim of this meeting was to establish a neuroscience PhD program at the newly-founded Turkish-German University (Splendid Hotel, Büyükada, September 2011 and 2012).
- DNA Day Talk: Professor James D. Watson (Boğaziçi University, April 2011).

4TH SUNA KIRAÇ CONFERENCE, JUNE 2014: JUSTIN FALLON

SUNA KIRAÇ NEURODEGENERATIVE DISEASE WORKSHOP, 2015

3RD SUNA KIRAÇ CONFERENCE, 2011

FUNDAMENTALLY HUMAN: CONTEMPORARY ART AND NEUROSCIENCE

ACADEMIC AND SOCIAL ACTIVITIES

James D. Watson Exhibition

Brought to life through the collaboration of NDAL and the Suna and İnan Kıraç Foundation, James D. Watson's exhibition, "Journey to the World of DNA", was displayed at Boğaziçi University's Özger Arnas Hall, January-February 2007.

Suna Kıraç Honorary Doctorate Degree Award

Upon the recommendation of the School of Arts and Sciences, the Boğaziçi University Senate decided to confer an honorary degree on Suna Kıraç in July 2008, for her work to provide equal opportunity in education.

"Fundamentally Human" Exhibition

"Fundamentally Human: Contemporary Art and Neuroscience" was exhibited at the Pera Museum from April-July 2011 as part of the 3rd Suna Kıraç International Neurodegeneration Conference.

LET US CHALLENGE ALS: LET US SAVE LIVES IN ORDER TO LIVE!

The Ice Bucket Challenge

Please support us in the Turkey campaign of the Ice Bucket Challenge that has spread across the globe in August 2014, so that we can find a cure for ALS and give hope to the >7,000 ALS patients suffering from this disease in Turkey. Even the smallest contribution makes a difference!

As NDAL, we have been conducting research on ALS for many years and trying to find a way to fight this disease, which so far does not have a cure. We are confident that research will lead to a treatment. Those helping us in our quest to learn more about ALS and develop therapies are our invaluable clinicians, who make the diagnosis of the disease, the Suna and İnan Kıraç Foundation, which has established a fully-equipped laboratory at Boğaziçi University to study ALS and other neurodegenerative diseases, and Boğaziçi University, which has fully supported us in our endeavors. However, equally important are our patients and their families, who provide us with samples for our research. Today, we are here to show our patients our loyalty to them. Please join hands with us to accelerate the development of a cure for this disease. Since there is no cure yet, let us at least improve the quality of life of our patients, by helping them develop the home care units they need and building an ALS Care Clinic.

Relationship with the ALS Association

It is estimated that there are about more than 7,000 ALS patients in Turkey. Founded as a non-profit organization in 2001 to support patients and relatives and let them know they are not alone, the ALS-MNH Association maintains close ties with NDAL. Last year, the association opened a branch office in Izmir. The co-directors of the association, Mr. İsmail Gökçek and Dr. Alper Kaya, ALS patients themselves, are both good friends and colleagues of ours who successfully run the association. In order to support the research at NDAL, the association has shared samples from many ALS patients with us in the recent years. The majority of these samples will be analyzed with next-generation DNA sequencing as part of Project MinE, which is discussed in the later pages of this book. The neurologists in Turkey whom we collaborate with, the ALS Association of Turkey, our patients, and their relatives have greatly contributed to our research and success. Today, research is possible only through collaborative work. We challenge ALS and other neurodegenerative diseases not on our own, but together with all those who are mentioned above. We strive – with all our hearts and strength – to spread awareness about neurodegenerative diseases in Turkey, so that these diseases can be openly discussed without prejudice. Prepared and printed with support from the Suna and

İnan Kıraç Foundation in order to help ALS and Huntington's disease patients and their families, the booklets "Living with ALS" and "Huntington's Disease" are a compilation of information about these disorders and patient care. The booklets have been distributed all across Turkey with the help of the ALS Association and clinicians specializing in ALS and other movement disabilities.

3RD SUNA KIRAÇ CONFERENCE, JUNE 2011
TURKISH ALS ASSOCIATION MEMBERS

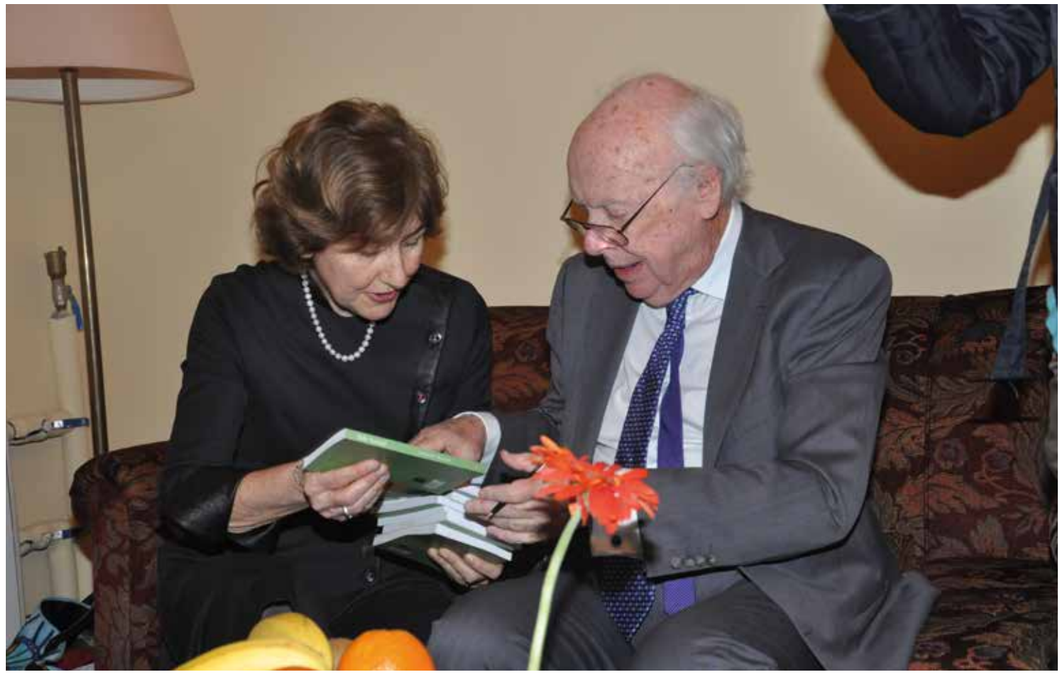
3RD SUNA KIRAÇ CONFERENCE, JUNE 2011: JOHN DONOGHUE

DNA Day Conference: April 18th 2011

James Watson's Visit to Boğaziçi University

"Science seldom proceeds in the straightforward logical manner imagined by outsiders. Instead, its steps forward (and sometimes backward) are often very human events in which personalities and cultural traditions play major roles."

The Double Helix



VARIABILITY IS THE LAW OF LIFE, AND AS NO TWO FACES ARE THE SAME, SO NO TWO BODIES ARE ALIKE, AND NO TWO INDIVIDUALS REACT ALIKE AND BEHAVE ALIKE UNDER THE ABNORMAL CONDITIONS WHICH WE KNOW AS DISEASE

SIR WILLIAM OSLER

SUNA KIRAÇ HONORARY DEGREE AWARD CEREMONY

Nazlı Başak, 2008

Dear Presidents, esteemed members of the Kıraç and Koç families, guests, members of the press, colleagues, and students: Welcome to our honorary degree award ceremony. Thank you all for sharing our joy on this special occasion!

Today, we are gathered here to present to Ms. Suna Kıraç an honorary doctorate upon the recommendation of Boğaziçi University's Department of Molecular Biology and Genetics and the School of Arts and Sciences, and the approval of the University Senate. Most of us know Suna Kıraç as an industrialist and businesswoman; however, today she is being awarded an honorary doctorate from Boğaziçi University for her extraordinary commitment to education. She is, therefore, given this award for the outstanding and continuing contributions she has been making to education across the nation. Underlining the importance of education and, in particular, emphasizing the significance of making contributions to education, in an institution of learning, especially in one of the leading universities of Turkey, such as Boğaziçi University, is quite a rewarding and honoring duty; right now, in your presence, I am pleased to have been given this duty.

At the heart of education lies teaching and investing in the growth of an individual. Education is transmitted from one generation to the next; as a result, it shapes the soul of society. Suna Kıraç has always believed that education was one of the most important tools through which Turkey could develop and prosper, and thus dedicated a considerable amount of time to the subject of education. She undertook important responsibilities for ensuring quality of and equal opportunity in education, brought many innovating ideas to life, and personally worked on these projects.

Education is expensive, but there is something more costly than education, and that is a lack of education. In a country like Turkey, where half of the population is under the age of 25 and birth rates are high, the most important problem to overcome is lack of education. In Ms. Kıraç's words, "Economic crises will be overcome, political conflicts will be resolved; however, it is impossible to rebuild a society whose children have been wasted. Instead of expecting everything from the state or someone else, everybody should join hands in their own capacity to improve education. Education is too important for society to simply be left to the responsibility of the state."

A better education for the next generation

As early as the 1980s, Suna Kıraç realized that lack of education was the most urgent problem of this country. For her, education was the sole key with which the potential of the future could be unlocked. Education meant broader horizons, broader visions, self-confidence, productivity, and quality.

One of the structural problems in Turkey was the lack of a trained workforce. Suna Kıraç always believed that this problem could only be overcome by modern and high-quality education, but one had to fight for that. By saying, "I am determined to live and put up a struggle in this country. I wish to be one of the criticized and not one of the critics. I have decided to take action, rather than talk", she faced the problems in education with the resolve and discipline that she had acquired in her professional life.

For Suna Kıraç, the first requirement of a modern and high-quality education system was the implementation of a curriculum that would prepare students at the international level. She developed the plans of Koç High School as part of that vision. The mission statement of Koç High School describes the ideal citizen, rather than the ideal student: "to develop the intellectual and humanitarian qualities of students and work towards educating them as self-confident, ethical young people with leadership qualities and a strong sense of responsibility." Initiating the Koç High School was an invaluable experience for Suna

Kıraç, through which she saw the weaknesses and shortcomings of the Turkish education system. These experiences had an important role in planting the seeds of Koç University and the Educational Volunteers Foundation of Turkey (TEGV).

"Keeping up with the times can only be possible with well-educated, brilliant minds. It also requires a well-defined, modern national education policy with precautions in place. This is the only way the young generations of Turkey can be well-educated and embrace the principles and reforms of the Republic. Both the state and the private sector must allocate funds to education. The effects of education – by nature – are persistent; therefore, the value of a modern system of education is priceless." For Suna Kıraç, supporting education should have no limits; the riches of this land should be invested in the people of this country.

"Real education consists in drawing the best out of yourself." (M. Gandhi)

Sincerely believing that increased social awareness in Turkey can only be made possible through education, and foreseeing that financial support alone is not enough to bring the level of education in Turkey to a level that is acceptable in today's world, Suna Kıraç fought with all her power in the front ranks. Her next colossal project after Koç High School and Koç University became the Educational Volunteers Foundation of Turkey (TEGV).

In order to eliminate inequality in education, Suna Kıraç, along with 15 like-minded businesspeople and academicians, established TEGV, Turkey's largest volunteer "army" for education, in 1995. With TEGV, improving the extracurricular education of children aged 7-16 at 82 places in Turkey became a major social project. Today, TEGV has more than 200,000 donors. For the first time in Turkey, a foundation has been able to get support from this number of donors. In addition, the number of volunteers working directly with TEGV has exceeded 10,000. With Suna Kıraç as their honorary chair, the volunteers of TEGV have so far provided educational services to more than one million children.

Suna Kıraç continues to develop her ideals for the education system in Turkey. In addition to her contributions to Koç University and Galatasaray University, she also extends her support to the research laboratory, NDAL, that she helped establish in 2005 at the Boğaziçi University Department of Molecular Biology and Genetics, so that NDAL can gain internationally-recognized success in the field of healthcare research.

A life dedicated to education

Suna Kıraç is a leader, a trailblazer, a wise person and an exemplary individual for society, not only because she is knowledgeable, but also because of her actions, values, diligence, sense of duty, strong sense of principle, and tolerance.

Suna Kıraç was awarded an honorary medal from the Galatasaray Education Foundation in 1995 and the Order of Merit was conferred upon her by the Turkish State in 1997. In addition, she is the recipient of many other awards. Today, we are proud to present to her an honorary doctorate from Boğaziçi University.

Suna Kıraç believes that the key to Turkey's bright future is education. She trusts the next generation and knows that the education given to the young people of this country will be the most important factor in determining Turkey's future.

We salute, with utmost respect, Ms. Suna Kıraç as the leading "Educational Volunteer" of

Turkey, as the "Mother", not only of İpek Kıraç, but also of hundreds of thousands of Turkish children, and as the role model of young people from all regions and backgrounds in Turkey. We thank Ms. Kıraç infinitely for being here with us today.

Dear Ms. Kıraç, we believe in your ideals with all our hearts and we are here today to show you our support. We hope you will accept this award as proof of our commitment to your ideals.

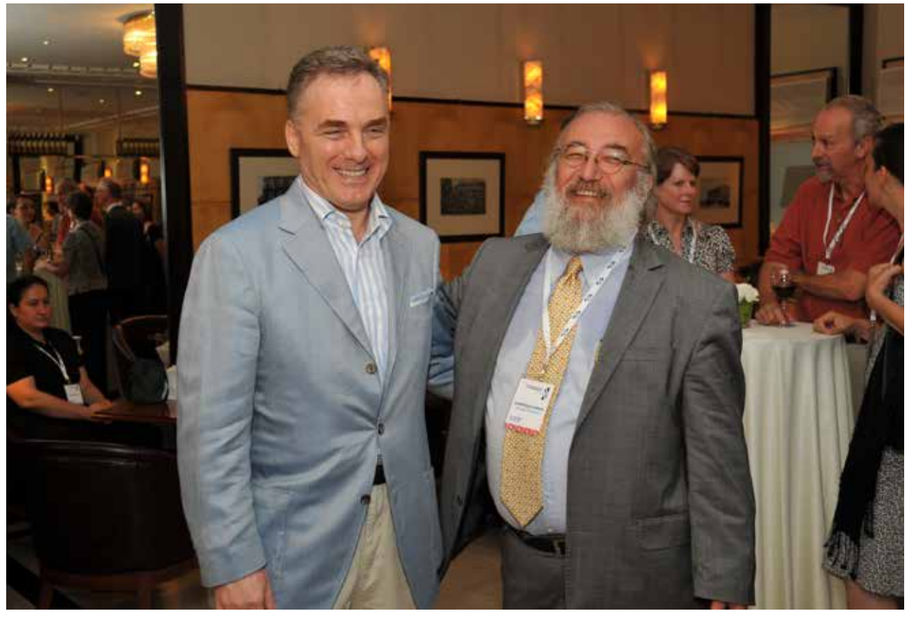
BRILLIANCE: IT'S IN OUR DNA...

LIFE AT NDAL

NDAL provides students with an academically challenging, fully equipped educational environment, as well as a workspace and lab setting that prepares them for conducting research on an international level. This said, NDAL is more than just a center for education and research; it has also become a place that fosters strong and long-lasting friendships that extend beyond the work environment. Today, NDAL has become a family.

SUNA AND İNAN KIRAÇ FOUNDATION

NDAL'S 10TH ANNIVERSARY



ÖZALP BİROL, KADRİ ÖZÇALDIRAN

4TH SUNA KIRAÇ CONFERENCE OPENING CEREMONY, JUNE 2014

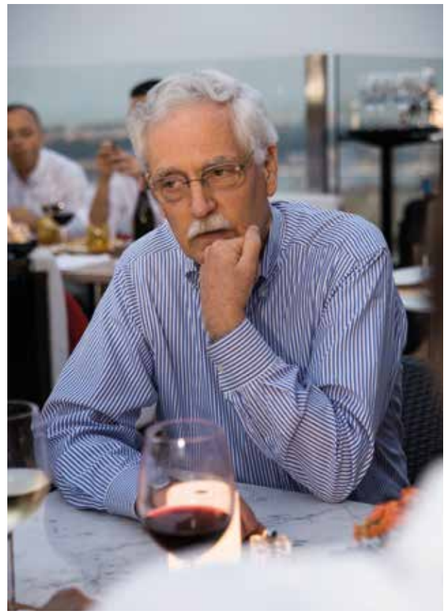
SCIENCE AND ART BELONG TO THE WHOLE WORLD,
AND BEFORE THEM VANISH THE BARRIERS OF NATIONALITY.
J.W.v.GOETHE

WORDS FROM OUR SCIENTIFIC ADVISORS

Robert Brown, Neurology Department, UMass Medical School

It has been a privilege to be associated with NDAL. Since its inaugural ceremony ten years ago, NDAL has made remarkable progress; what was then an architectural drawing in a sparsely-equipped open space is now a thriving laboratory with more than 20 members. Over this decade, NDAL has been recognized internationally as one of the premier laboratories for molecular diagnostics in Turkey and indeed Europe. Under the visionary leadership of Prof. Nazlı Başak, NDAL has studied cases from across all of Turkey, providing the first nationwide surveys of genetic defects in disorders like ALS. In this process, NDAL has trained numerous doctoral and post-doctoral fellows, establishing research opportunities not only within NDAL but also in a collaborative network of laboratories in the U.S. and Europe. Dr. Başak has also established superb working relationships with leading Turkish neurologists in Istanbul, Ankara and elsewhere, adding an all-important clinical dimension to the laboratory investigations.

This has facilitated detailed correlations of genotypes with their corresponding clinical phenotypes; moreover, this consortium of the NDAL with its clinical partners should provide a perfect venue for the development of an ALS clinical trials network in Turkey. The success of the NDAL is a tribute not only to the exemplary leadership of Dr. Başak but also the vision of the Kıraç family and its associates. Looking forward, I welcome an extended affiliation with the NDAL and will be honored to assist in any way possible in its research and clinical programs. There is no doubt that the NDAL will continue to play a pivotal role in the quest for a treatment for ALS.



Jeffrey Macklis, Max and Anne Wien Professor of Life Sciences,

Harvard University

Over the course of this first decade of NDAL, we have witnessed it emerge from a seedling onto the world stage of neurodegenerative disease research– through a set of powerful and distinctive Turkish opportunities in ALS and related research. Prof. Nazlı Başak, the inaugural NDAL director, wisely led her talented students and postdocs to take unique advantage of the large population of Turkey, and its somewhat contained genetics, to identify new families, new phenotypes, and new genetics of ALS. These, in turn, will offer the field new vantage points from which to better understand what contributes to ALS, by what mechanisms, and how best to intercede therapeutically. Rather than simply adding another laboratory to the world, the founding and building of NDAL has broadened the world's ALS and related neurodegenerative disease research to include the Turkish population, its partially unique genetics, and its network of highly-trained clinical neurologists and ALS specialists. Importantly, NDAL has brought the international ALS community to patients and families of Turkey who are struggling with ALS, and it has joined these patients and families with the wider ALS community worldwide.

GUY ROULEAU, JEFFREY MACKLIS

4TH SUNA KIRAÇ CONFERENCE OPENING CEREMONY, JUNE 2014

PHD DEFENSE ASLIHAN ÖZOĞUZ

TEAM SPIRIT EVERYWHERE

THE FUTURE IS HERE: THE MONUMENTAL PROJECT OF ALS, MINE

Initiated on the ALS/MND Global Day 2013 by two young and entrepreneurial ALS patients in collaboration with the Netherlands ALS Center at University Medical Center Utrecht and the ALS Foundation Netherlands, Project MinE aims to understand the mechanisms that contribute to ALS. Currently, only half of the genes associated with ALS have been mapped. In addition, significant genetic variations exist between individuals from different ethnic groups. On a molecular and mechanistic level, the disease is far more heterogeneous than what was initially estimated. Through publications released in the recent years, students that were trained, and presence at international conventions, NDAL has gained a reputation among the scientific community working on ALS and neurodegenerative disease biology. In 2014, NDAL was invited to be the Turkish partner of Project MinE, the largest ALS project to date. The invitation of partnership alone is an indication of the reputation that NDAL has in the world of ALS research.

Project MinE is the most extensive and ambitious project launched to understand ALS. It is a colossal initiative, bringing together ALS research laboratories from 16 different countries.

Such an approach to elucidate the genetic roots of a disease is unprecedented, not only in ALS research, but overall in neurodegenerative disease research as well. The project aims to sequence the genomes of 15,000 patients and 7,500 healthy controls. Our participation in Project MinE will earn NDAL respect and increase visibility. More importantly, we expect that the samples and data from NDAL will add richness to Project MinE, due to the ethnic diversity in Turkey, especially given that the majority of samples being analyzed for the project are from Caucasian patients of Western European, Central European and North American background due to the racial makeup of the currently participating countries. Above all, however, the project's goal of making revolutionary breakthroughs in the understanding of and therapeutic approaches to ALS is putting this neurodegenerative disease under the microscope in a radical way that is supported by international collaboration, and laboratory and bioinformatics technologies that have been developed for the purposes of this project.

BIOINFORMATICS AND BIG DATA ARE THE NEW BIOLOGY

KICK-OFF MEETING, PROJECT MINE, 2014

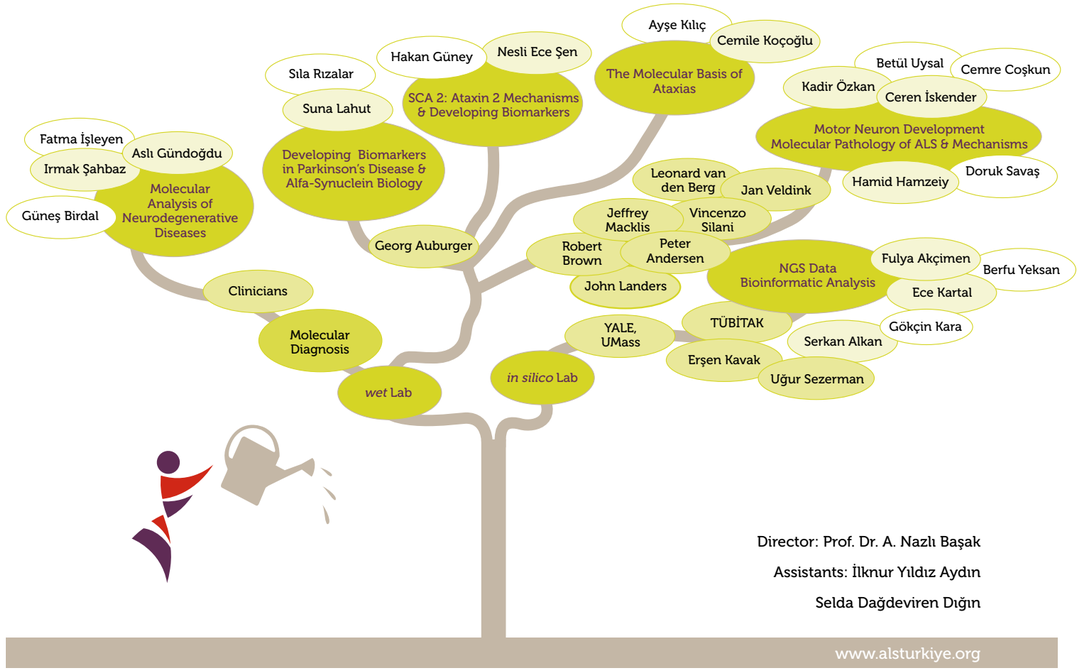
NO MATTER HOW COUNTERINTUITIVE IT MAY SEEM, BASIC RESEARCH HAS PROVEN OVER AND OVER TO BE THE LIFELINE OF PRACTICAL ADVANCES IN MEDICINE. WITHOUT ADVANCES, MEDICINE REGRESSES AND REVERTS TO WITCHCRAFT.

A. KORNBERG

(NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE, 1959)

NDAL TREE OF HOPE

Strategies and Projects



Director: Prof. Dr. A. Nazlı Başak

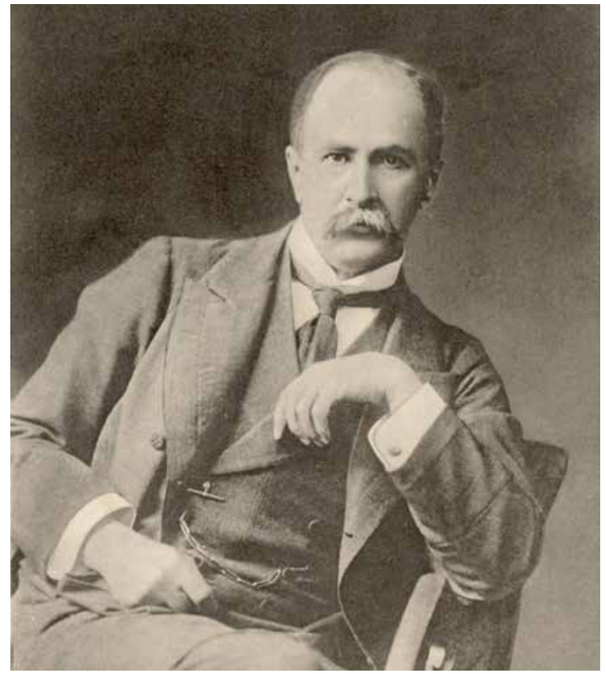
Assistants: İlknur Yıldız Aydın

Selda Dağdeviren Dığın

www.alsturkiye.org

If it were not for the great variability among individuals, medicine might as well be a science and not an art

Sir William Osler



ON NESIME WITH GEORG AUBURGER AND SUZANA GISPERT

BOĞAZİÇİ UNIVERSITY FOUNDATION: BEHZAT AZERİ, CANAN ÖZDEMİR

BEGÜM ERDOĞAN, MSC THESIS DEFENSE, 2008

CAROLINE PİRKEVİ, PHD THESIS DEFENSE, 2008

ASLIHAN ÖZOĞUZ, PHD THESIS DEFENSE, 2010

NDAL PUBLICATIONS

Theses

PhD Theses (2005-2016)

Kadir Özkan
Molecular and Cellular Development of Cortical Projection Neurons: Specification, Diversity and Directed Differentiation from Endogenous Progenitors for Functional Circuit Repair, 2016.

Suna Lahut
Parkinson's Disease in a Large Turkish Pedigree with SNCA Duplication (PARK4): Developing Molecular Biomarkers for Predictive Diagnosis, 2015.

Aslıhan Özoğuz
Amyotrophic Lateral Sclerosis in Turkey: Studies on Familial and Sporadic ALS using High-throughput Genomic Technologies, 2010.

Caroline Pirkevi
Parkinson's Disease in Turkish Patients: Molecular Defects in Familial and Isolated Cases, 2009.

Mehmet Ozansoy
Effects of Extremely Low Frequency Electromagnetic Fields on Caspase Activities, 2006.

Nagehan Ersoy
Molecular Analysis of Polyglutamine Diseases and Investigation of the Interaction between Huntington and n=Nuclear Receptor Corepressor, 2005.

Mehmet Baki Yokeş
Molecular Genetics of Alzheimer's Disease in the Turkish Population, 2005.

Completed MSc Theses (2005-2015)

Nesli Ece Şen
Spinocerebeller Ataxia Type 2 in a Large Turkish Pedigree: Mechanisms and Biomarker Development, 2015.

Ece Kartal
Application of Next Generation Sequencing and Bioinformatics to Neurodegenerative Disorders, 2015.

Özgür Ömür
Genetic Factors Contributing to ALS in Turkey: ATXN2 PolyQ Repeat Expansions and Associations SNP/CNV, 2013.

Ceren İskender
Genetically Accurate Models of SOD1-based Amyotrophic Lateral Sclerosis in Drosophila: Validation and Characterization, 2013.

Zeynep Sena Ağım
Schizophrenia: another Emphasis of ERBB4 and NRG1 Impact on Disease Development using GWA Datasets and Bioinformatic tools, 2012.

Özgün Uyan
The Genetics of Sporadic ALS: The First Turkish GWAS and Novel SNP and GNV Association, 2012.

Gönenç Çobanoğlu
Possible Interactors of Alsin and Effects of its Expression, 2012.

Suna Lahut
The Impact of Mutant Alsin Protein on Motor Neuron Models and The Effects of Alsin Gene Knock-Down on Motor Protein Genes, 2011.

Pınar Deniz
Genetically Accurate Models of SOD1-Based ALS in Drosophila Melanogaster, 2011.

Abdülkadir Özkan
Temporal and Comparative Analysis of Genes that Play a Role in Brain Vascular Development, 2009.

Didem Eruslu
Myotonic Dystrophy: Application of a Novel Triplet-Repeat-Primed-PCR approach to Turkish DM Patients and Molecular Analysis of a Large Turkish Kindred with Von Hippel-Lindau Disease, 2008.

Begüm Erdoğan
Huntington's Disease in Turkey: Possible Effects of Glutamate Receptor Gene Polymorphisms on Age of Disease Onset, 2008.

Refika Mine Güzel
Analysis of the Vascular Endothelial Growth Factor and Angiogenin Genes as Risk Factors for Amyotrophic Lateral Sclerosis in the Turkish Population; Identification of a Possible Novel Mutation, 2006.

Fatma Sinem Hocaoğlu
Molecular Analysis of Alzheimer's Disease and Frontotemporal Dementia: a Novel Mutation in the Presenilin 1 Gene of a Turkish Patient with Early Onset Familial Alzheimer's Disease, 2006.

Ayşe Latif
Molecular Analysis of Hemoglobinopathies and Construction of a Database; Identification of a Novel IVS-II-2 (T-A) Mutation, 2006.

Nazan Saner
Spinocerebellar Ataxias 8, 12 and 14 in Turkey: Molecular Bases and Genetic Analyses, 2006.

Caroline Selma Pirkevi
The Molecular Pathology of Friedreich Ataxia: DNA Analysis and Diagnosis in Turkish Patients, 2005.

Theses in progress, 2015

Ceren İskender (PhD)
Molecular Basis of ALS in Turkey: the C9Orf72 Expansion Mutation and Disease Modifiers.

Cemile Koçoğlu (MSc)
Bioinformatic Evaluation and Pathway Analysis of NGS Data of Ataxia Patients.

Hamid Hamzeiy (MSc)
DNA Methylomic Profiling of Amyotrophic Lateral Sclerosis.

Fulya Akçimen (MSc)
Evaluation of NGS Data and Pathway Analysis in Neurodegenerative Diseases.

Articles 2005-2015

International Journals

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10 YEARS AGO...

TODAY...

To live, like a tree alone and independent,
To live, like a forest in brotherhood...
Nazım Hikmet


Sevdiğiniz ile ALS'yi Yaşamak
Huntington Hastalığı


2nd Suna Kıraç Workshop on Neurodegenerative Disease İstanbul
3rd Suna Kıraç Workshop on Neurodegenerative Disease İstanbul


New Frontiers in Understanding and Treating ALS April 5-8, 2007
Stem Cells, RNAi and Neurodegeneration July 19-21, 2009
Recent Themes in Motor Neuron Biology and Neurodegeneration June 23-26, 2011
Suna Kıraç Conferences on Neurodegeneration İstanbul
The Motor System: From Development to Neurodegeneration June 12-14, 2014

NDAL'S ACADEMIC GENEAOLOGY

An "academic genealogy" is an inheritance tree that shows how scholars succeed their teachers; in particular, the PhD advisor is shown to be the person's "mother" or "father". As a scientist, your academic family tree is an important part of your heritage that links you to your "ancestors" and future "descendants", and which extends into the past and into the indefinite future. Graduate studies hold a significant place in the life of a young person; this period of time is instructive, not only scientifically, but also academically and socially. The academic advisor and the academic environment of a young person have a significant impact on his or her behavior, zeal for research, and professional development. We strive to underline the importance of the period of graduate studies through NDAL's 10th anniversary book. We are proud to be the academic descendants of the monumental founders of biochemistry, such as Justus von Liebig, August Kekule, Adolf von Baeyer, Emil Fischer, Johann Freudenberg, and of Friedrich Cramer, who translated biochemistry to the field of molecular biology. We promise to continue their centuries-long legacy of science and live up to our academic heritage.

Johann Heinrich Schulze

Ernst Anton Nicolai

Ernst Gottfried Baldinger
Jena University, 1760

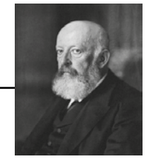
Johann Christian Wiegleb

Johann Friedrich August Göttling
Göttingen University, 1789

Karl Wilhelm Gottlob Kastner
Jena University, 1805

Justus von Liebig
Erlangen University, 1823

Friedrich August Kekulé
Giessen University, 1852



Adolf von Baeyer
Berlin University, 1858
Nobel Prize in Chemistry, 1905

Hermann Emil Fischer
Strasburg University, 1874
Nobel Prize in Chemistry, 1902

Karl Johann Freudenberg
Berlin University, 1910

Friedrich Cramer
Heidelberg University, 1949

A. Nazlı Başak
Max Planck Institute, Göttingen, 1977

Hilmi, Ayşe, Şükrü, Ghazi, Hamdi
Boğaziçi University
1990 - 2000

Onur, Nagehan, Baki, Mehmet, Caroline
Boğaziçi University
2000 - 2010

Aslıhan, Suna, Kadir, Ceren
Boğaziçi University
2010 -

FINAL WORDS OF GRATITUDE

NAZLI BAŞAK, 1st Suna Kıraç Conference, APRIL 2007

Dear Ms. Kıraç, dear Mr. Kıraç,

You are not alone in your journey to achieve your dreams. We are with you, we are accompanying you. The young people sitting in the audience are working hard to make your dreams come true. On their journey to achieve your dreams, and on their journey to achieve their own dreams, these bright young individuals need role models. Since they held your book in their hands this morning, you have become their role model. They are so privileged to have you as their role model, Ms. Kıraç: you will inspire them to set goals for themselves and raise the bar.

We all have dreams, but we also live with the awareness that dreams cannot always be fulfilled; this is in the nature of dreams. However, with this conference today, with all the wonderful people who have come from faraway places to share their knowledge and experiences with us, and the bright young people filling this room to learn from them, we have taken a major step in achieving one of our greatest dreams. We have all the reason to be optimistic and hopeful. I think I can speak for every single person sitting in this room when I say that I sincerely believe and hope with all my heart that this conference, the 1st Suna Kıraç Conference on Neurodegeneration, will open new frontiers in understanding and treating ALS, and will contribute to research efforts to develop effective therapies. It will mark a milestone in ALS research. Thank you for making this conference possible, Ms. Suna Kıraç and Mr. İnan Kıraç!

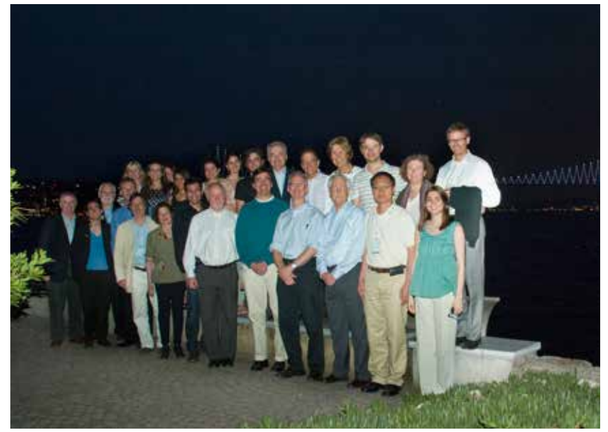
Two roads diverged in a wood and I-
I took the one less traveled by,
And that has made all the difference.
Robert Frost

January 2016

Dear Ms. Suna Kıraç, Mr. İnan Kıraç and Ms. İpek Kıraç,

It has been nine years since I delivered the speech above and ten years since NDAL was inaugurated. These fulfilling years we spent at NDAL seem to have passed in the blink of an eye. What have we achieved over this past decade? Well, that is exactly what this book was intended to present to you and our supporters. It was not easy to fit into these pages the last ten years, during which we spent nearly as much time at NDAL as we did at home. Yes, over the past decade, we have achieved many "firsts" and have become a prestigious, leading laboratory in Turkey, thanks to the findings of our research projects, our publications, advisors, the Suna Kıraç Conferences on Neurodegeneration, our collaborations, and gifted students. I am certain, however, that as you flip through the pages of this book, many of you will be looking for the answer to one question in particular: when will there be a cure for ALS? In light of all that we know now, it is still difficult to answer this question. There is no doubt that we know substantially more about ALS today, as compared to what we knew ten years, five years or even one year ago. Every day, we witness new discoveries and significant developments in the technologies available for ALS researchers. Not tens, but hundreds of top-notch laboratories worldwide are conducting research on ALS, made possible with significant financial support, the establishment of large consortia and multi-center trials. As a result, ALS research is gaining incredible momentum.

Today, NDAL is part of all these developments and is an active member of this force. There are many reasons to be optimistic; however, we still refrain from saying that a cure for diseases afflicting this complex system will be available in the immediate future. We are still feeling our way in the dark; we can tell that it is about to be dawn, but we don't know exactly when we will see the sun. Our dreams are no longer just dreams, however; we are rapidly and more consciously



Trust me, children, we will see beautiful days,
we will see days filled with sunshine.
Nazım Hikmet

heading towards a clear target. And we want our patients and their families to know that ultimately, there is one goal we are all working towards, and that goal is to develop a cure for these diseases as soon as possible.

Dear Ms. Suna Kıraç, Mr. İnan Kıraç and İpek; I thank you and our distinguished teammates for the trust you have placed in me and the NDAL team, the great responsibility you have given us, and your invaluable support. It is an honor to have been given this challenging, important and exciting duty. At the end of this past decade, I clearly see how broad an impact NDAL has had on our lives. I also see to what extent our young laboratory has grown and evolved to be an esteemed and active center of research that is respected in Turkey and abroad.

Dear Ms. Kıraç, Mr. Kıraç and İpek; through your support, and with your "magic wand" you have touched not only my life, but the lives of all ALS patients and their families across the world as well. On behalf of NDAL, our ALS patients and their families, I would like to thank you from the bottom of my heart for giving me this duty and opportunity. With the hope that our knowledge, creativity, passion and dedication will make it possible for our dreams to take flight, and that through this we will contribute to humanity, I wish NDAL a happy 10th anniversary!

BRAINSTORMING: JEFFREY MACKLIS, ROBERT BROWN, İNAN KIRAÇ, ÖZALP BİROL