NDAL's Research Activities and Interaction Partners

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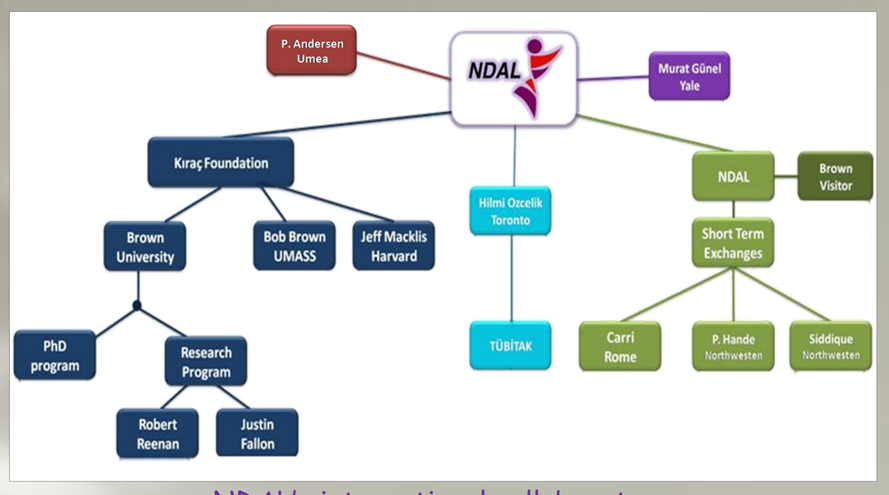
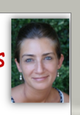
The Neurodegeneration Research Lab (NDAL), established at the MBG Department of Boğaziçi University (BU) in 2005 by the Suna and Inan Kıraç Foundation, is the first example of a collaborative initiative in the field of health sciences between a University and an NGO in Turkey. The prestigious Kıraç gift supports the lab in enhancing neurosciences in Turkey and contributes to its efforts in becoming a center of excellence on neurodegenerative disease biology. In addition to the Kıraç fund, NDAL is supported by BU Research Funds, The Scientific and Technological Research Council and The State Planning Department of Turkey. BU and NDAL are recognized as leading academic centers not only throughout Turkey, but also on international platforms for the establishment and successful application of molecular technologies in the analysis and diagnosis of genetic and complex disorders. The general theme of investigations currently underway is focused on biology relevant to motor neuron diseases (ALS centrally) and related disorders; it aims to understand the mechanisms leading to neurodegeneration, with the ultimate goal of developing therapies. NDAL is involved in several national and international collaborations, including two multi-centered European projects, that aim to unravel the cellular mechanisms underlying neuronal death, neuron regeneration and brain plasticity. Scientific collaboration protocols have been signed recently between BU, represented by NDAL, and the Neurosciences Department of Brown University. Other important collaboration partners of NDAL are Harvard University and University of Massachusetts Medical Schools. These collaborations aim to enhance neurobiological science in Turkey and specifically support research on neurodegenerative disease mechanisms.

Scientific Advisors of NDAL

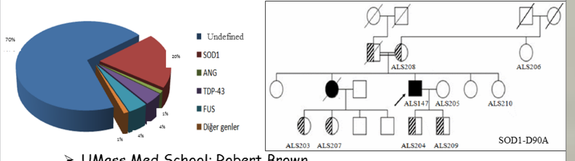


NDAL's international collaborators

Gaining Insights from Genetics/Genomics



- Familial ALS: Identifying new ALS genes
  - next generation genomic technologies
  - e.g. exomic and whole-genome sequencing



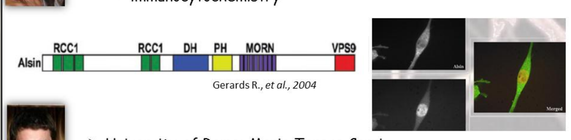
- UMass Med School: Robert Brown
- Yale Med School: Murat Gunel
- Umea Med School: Peter Andersen
- Montreal University : Guy Rouleau

Impact of New Genes and Loci on ALS Development

- Yeast orthologue of ataxin2, is shown to be a modulator of TDP-43 toxicity:
  - Expanded ATXN2 polyQ repeats and ALS risk?
  - Effect of ATXN2 on other ND than ALS?
  - Effect of other polyQ loci (SCA1, SCA3, HD etc) on ALS/ND?
- Mechanisms of Mutations:
  - Novel 18bp deletion in the FUS gene with incomplete penetrance
  - Novel SOD1-H71Y with incomplete penetrance
  - Recessive SOD1-D90A with 2 different haplotypes
  - Mutations in LAMA5: MND co-existing with mental retardation

Functional Studies on Alsin

- Investigation of alsin-interacting proteins:
  - mutations of alsin give rise to juvenile ALS as well as other neuromuscular diseases
    - yeast-two-hybrid system
    - co-immunoprecipitation /Western blot
    - immunocytochemistry

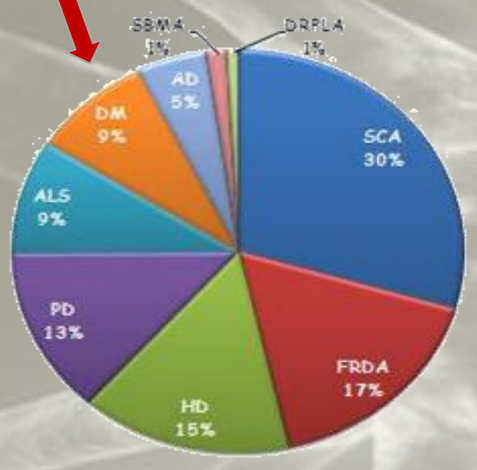


- University of Rome: Maria Teresa Carri
- Northwestern Med School: Teepu Siddique

NDAL: Center of Excellence as a Diagnostic Reference Lab

- NDAL is the only center in Turkey which offers routine molecular diagnosis in several neurological disorders.
- Samples from all over Turkey are being referred to NDAL for molecular analysis.
- NDAL has a very rich repository on patient samples.

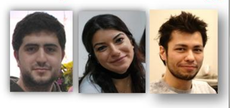
- Medical schools and hospitals throughout Turkey



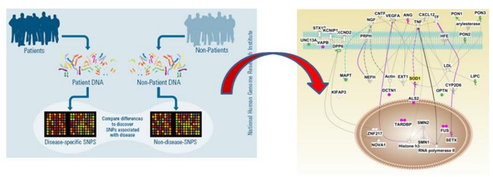
Neurodegenerative diseases studied at NDAL

Lines of Research

Application of Bioinformatics andSystems Biology to Human Disease



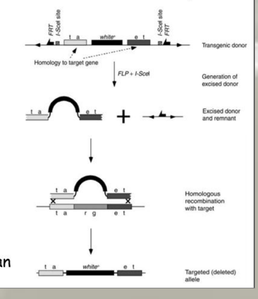
- Polymorphisms, mutations and pathways in neurodegenerative and mental disorders
  - GWAS: SNP genotyping in sporadic ALS



- University of Toronto: Hilmi Ozcelik

Accurate Animal Models of Neurodegenerative Disease

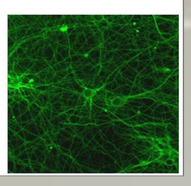
- Introducing human ALS mutations to Drosophila
  - homologous recombination



- Brown University: Robert Reenan

Corticospinal Motor Neuron (CSMN) Development and Repair

- Molecular mechanisms effective in motor neuron development, differentiation and repair
  - candidate genes playing a role in the development of CSMN
- Functional studies
  - temporal analysis of the expression of cand genes in tissue
  - knock-out mice models of cand genes
  - in vivo cell labelling
  - fluorescent cell isolation
- PhD project:
  - activation of progenitors in the adult cortex to develop into CSMNs (controlled neurogenesis)



- Harvard University: Jeffrey Macklis

A. Nazlı Basak is the PI and the director of NDAL. The lab currently consists of three post-docs, 2 PhD students , 6 MSc students, 2 technical lab assistants and 2 lab managers , who all report to the PI. The lab also harbors several undergraduate students, who assist on a voluntary basis in different projects. Opportunities for further catalytic development of the research program in the next 3 years include:

•Establishing in-house colonies of useful lines of mice, including ALS mice ($SOD1^{G93A}$, alsin (-/-), FUS^{mutant} (Robert Brown collaboration), lines of HSP mice, and perhaps new lines relevant to study of corticospinal motor neurons (Jeffrey Macklis collaboration).

•In parallel, an appropriate next step is to extend the already considerable tissue repository that the lab has developed. Specifically, a library of hundreds and eventually thousands of DNA samples from cases and controls that are carefully phenotyped would be a resource of considerable impact, not only within Turkey but for investigators everywhere. This should undoubtedly be predicated on DNA collection but might powerfully be extended to other tissues including autopsy specimens.

•The entire process of discovery and therapy development in neurologic disorders would be well served by the establishment of a network of clinicians, both for acquisition of tissue samples but also hopefully as a clinical investigation network.