TETAM LAB 3

Genomics Research Lab of Epilepsy Genetics Research Group

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Overall Motivation

Epilepsy, affecting 1 % of world population is a complex disease with multiple dimensions. The most important contributor of the disease is genetic predisposition in a large spectrum. While some epilepsy types are pure genetic some other epilepsies arise from acquired defects like brain tumors or brain malformations. As epilepsy genetics research group we aim to discover the genetic or genomic variations underlying the epilepsy etiology, which later on supports patient diagnosis and identification of novel treatment strategies. For this purpose we apply main genetic research approaches including single gene and genomic analyses.

Genomic Research Lab

Over the last decade the implementation of high throughput technologies had a great impact on genetics research. Next Generation Sequencing technology allows sequencing of human genome in single run with specialized equipment. On the other hand, requirement of middle throughput data by diagnostic laboratories are met by massive parallel sequencing devices. While genome sequencing identifies point mutations and small scale indels, larger genomic abnormalities like copy number variations are detected by array comparative hybridization analysis, which shows genomic scale insertion and deletions in variable resolution.

Genomic Research Lab is equipped with a GS Junior Sequencer, which is a middle scale NGS device and Nimblegen MS200 microarray scanner which is used in array CGH analyses. Besides these devices, the laboratory also has an Agilent Bioanalyzer for on chip electrophoresis, Thermofischer Nanodrop for nanoscale spectrophotometry and all other equipment required for NGS and array-CGH analyses.

Current Research Projects:

- ***ARX* Gene Screening in Epileptic Encephalopathy patients**
  - MSc Study of Hande Özünlü
- ***SCN1A gene Screening in Dravet Syndrome and Epileptic Encephalopathy patients***

  Sunay Usluer and Aslı Gündoğdu

- ***KCNQ2 gene screening***
- **Whole Exome Analysis of Patients with Benign Familial Neonatal Seizures**
  - Postdoctoral Research by Sunay Usluer
- **Gene Identification in a Large Pedigree with Genetic Epilepsy with Febrile Seizures Plus Phenotype**
  - Postdoctoral Research by Sunay Usluer

Collaborations

Nationwide: Departments of Neurology and Pediatric Neurology in academic institutions and hospitals in Turkey.

International: EPICURE Consortium, EuroEPINOMICS/RES-CRP (Rare Epilepsy Research, Collaborative Research Project)

Selected Publications:

- **Sunay Usluer, Canan Aykut-Bingol, Berrin Aktekin, Kadriye Agan, N. Berfu Akbas, S. Hande Caglayan** "*Mir137* VNTR Expansion As A Risk Factor For GEFS+ Phenotype In A Large Kindred" (in preparation)
- **Seda Salar*, Sunay Usluer*, Özlem Yalçın Çapan, Bülent Kara, Cihan Meral, Uluç Yiş, Mutluay Arslan, Rıdvan Akın, Aslı Gündoğdu Eken, S. Hande Çağlayan** "Exome Sequencing Of The *SCN1A* Gene In 21 Turkish Patients" (in preperation. * Equal Contribution)
- **Sunay Usluer, Melek Asli Kayserili, Uluc Yis,** Costin Leu, Thomas Sander, **S. Hande Çağlayan** "Whole genome linkage and whole exome sequence analyses in a multiplex BFIS (Benign Familial Infantile Seizures) family reveal a synonymous change affecting splicing efficiency of *SCN1B* mRNA as the major causative variant" (Submitted to Epilepsy Research)

- Steffen Syrbe, ….**Hande S Caglayan**, **Mutluay Arslan**, …. **EuroEPINOMICS RES Consortium**, … Johannes R Lemke (2015) *De novo* loss-or gain-of-function mutations in *KCNA2* cause epileptic encephalopathy, ***Nature Genetics***, published online 9 March 2015; doi:10.1038/ng.3239.
- Julian Schubert,….. **EuroEPINOMICS RES consortium** (…**Hande Çağlayan**…), … Holger Lerche (2014), Mutations in *STX1B,* Encoding a Presynaptic Protein, Cause Fever-Associated Epilepsy Syndromes, **Nature Genetics,** published online 2 November 2014; doi:10.1038/ng.3130.
- **EuroEPINOMICS-RES Consortium** (S. Appenzeller, R. Balling, N. Barisic, S. Baulac, **Hande Çağlayan** et al); Epilepsy Phenome/Genome Project, and Epi4K Consortium (2014), De Novo Mutations in Synaptic Transmission Genes Including *DNM1* Cause Epileptic Encephalopathies, ***The American Journal of Human Genetics***, 95:1-11.
- Caroline Nava,…. **EuroEPINOMICS RES Consortium** (…**Hande Çağlayan**…), … Christel Depienne (2014), De novo mutations in *HCN1* cause infantile epileptic encephalopathy, ***Nature Genetics,*** 46 (6):640-645.
- A Suls, …. **C Meral, HS Çağlayan**, …I Helbig, the **EuroEPINOMICS RES** Consortium **(2013)** *De novo* loss of function mutations in *CHD2* cause a fever-sensitive myoclonic epileptic encephalopathy sharing features with Dravet syndrome, ***American Journal of Human Genetics***, 93:967-975.

- Epicure Consortium, EMINet Consortium, … **H. Çağlayan, Z. Yapıcı, D.A. Yalçın, B. Baykan, N. Bebek, U. Özbek,** … T. Sander **(2012),** Genome-wide association analysis of genetic generalized epilepsies implicates susceptibility loci at 1q43, 2p16.1, 2q22.3 and 17q21.32, ***Human Molecular genetics***, 1-14, 21 (24):5359-72.
- **Gökdemir Selim, Çağlayan Hande, Kızıltan Meral, Karaağaç Naci, Leblebici Cem, Yeni S.Naz (2012),** Presentation of an unusual patient with Lafora Disease, ***Epileptic Disorders***, 14(1):94-8.
- **Salar, S., Yeni, N., Gündüz, A., Güler, A., Gökçay, A., Velioğlu, S., Gündoğdu, A., Çağlayan, S.H. (2012),** Four novel and two recurrent *NHLRC1 (EPM2B)* and *EPM2A* gene mutations leading to Lafora Disease in six Turkish families, ***Epilepsy Research***, 98:273-276.
- **EPICURE Consortium,** Leu, C., … **Çağlayan, H., Türkdoğan, D., Baykan, B., Bebek, N., Özbek, U.,** … Sander, T. **(2012),** Genome-wide linkage meta-analysis identifies susceptibility loci at 2q34 and 13.31.3 for genetic generalized epilepsies, ***Epilepsia***, 53(2):308-318.
- **Yalçın, Ö., Baykan, B., Ağan, K., Yapıcı, Z., Yalçın, D., Dizdarer, G., Türkdoğan, D., Özkara, Ç., Ünalp, A., Uludüz, D., Gül, G., Kuşcu, D., Ayta, S., Tutkavul, K., Çomu, S., Tatlı, B., Meral, C., Bebek, N., Çağlayan, SH**. **(2011),** An association analysis at 2q36 reveals a new candidate susceptibility gene for juvenile absence epilepsy and/or absence seizures associated with genarilized tonic-clonic seizures, ***Epilepsia***, 52(5):975-983.
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- Yalçın, Ö., **Çağlayan, S.H.,** Saltık, S., Çokar, Ö., Ağan, K., Dervent, A. Ortrud K. Steinlein **(2007)** A novel missense mutation (N258S) in the *KCNQ2* gene in a Turkish Family Afflicted with Benign Familial Neonatal Convulsions (BFNC), ***Turkish Journal of Pediatrics*** , 49:385-389.