Investigation of *IFIT3* and *KCNS3* Gene Expression Patterns in the Peripheral Blood of Cryptogenic Epilepsy Patients

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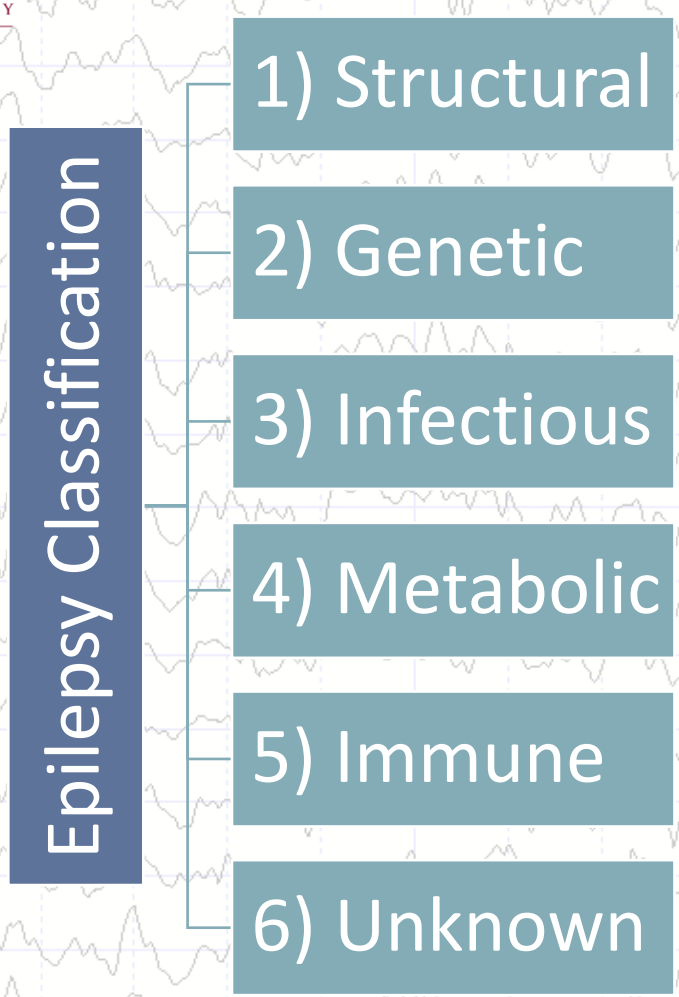
Epilepsy

- a chronic neurological disease
- mostly characterized by recurrent seizures
- still a great burden, effecting around 50 millions of people worldwide
- evaluation of patient's history, electroencephalography (EEG), neuroimaging studies, laboratory tests
- broad spectrum of manifestations



Unknown

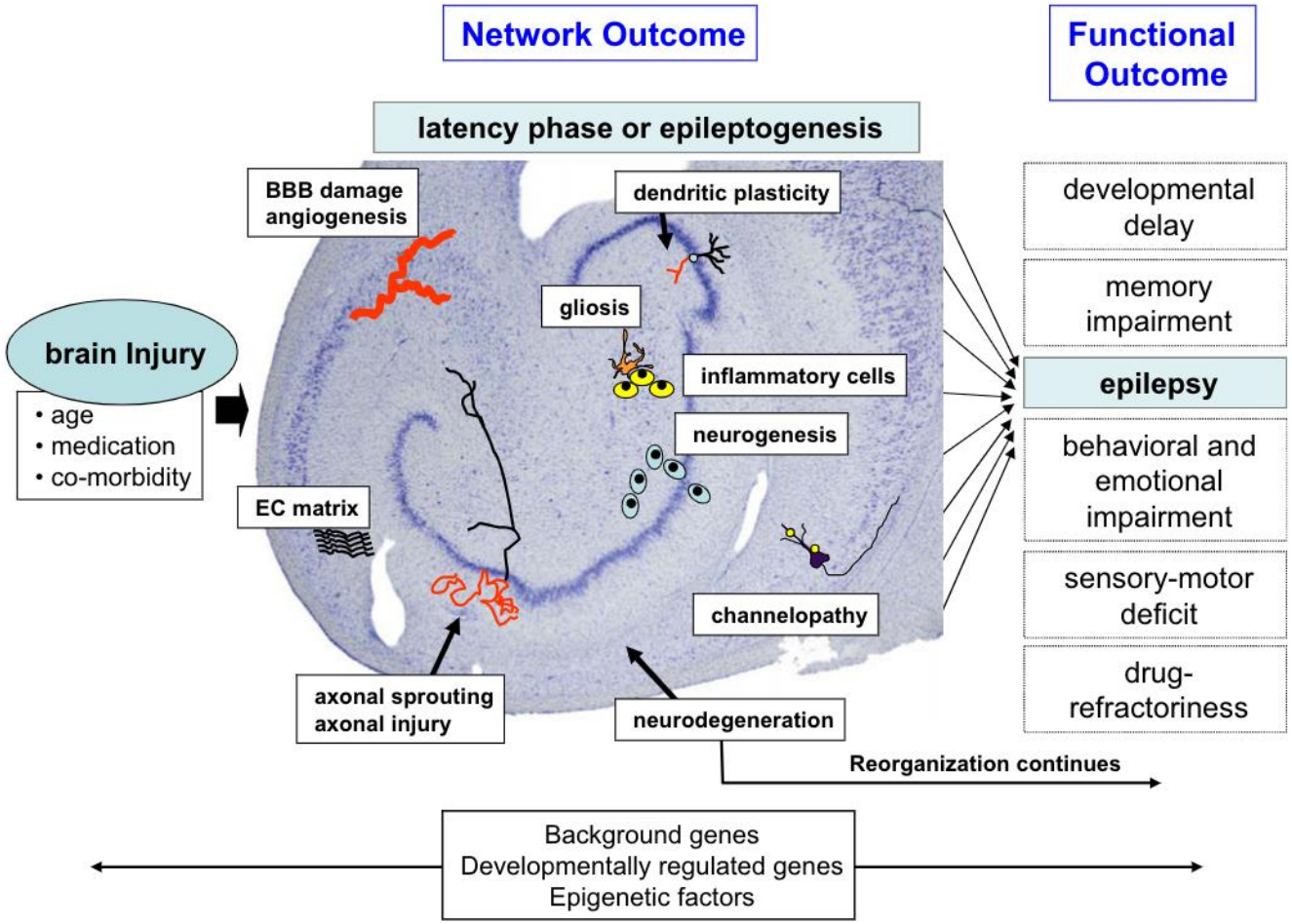
Cryptogenic Epilepsy:

Epilepsies with a lack of signs of previous brain damage and of obvious etiology

Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, Hirsch E et al. ILAE classification of the epilepsy: position paper of the ILAE commission for classification and terminology. Epilepsia. 2017;58(4):512-521.

Commission on classification and terminology of the international league against epilepsies and epileptic syndromes. Proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia. 1989;30(4):389-399.

Molecular Etiology



Molecular and cellular basis of epileptogenesis in symptomatic epilepsy Pitkänen, Asla et al. Epilepsy & Behavior, Volume 14, Issue 1, 16 - 25

Genetic Studies

- a better sight into mechanisms of the disease
- proper diagnosis
- prediction of risk factors
- prediction of prognosis

Mefford HC. Clinical genetic testing in epilepsy. Epilepsy Currents. 2015;15(4):197-201.

Aim of the Study

- Genetic expression profile differences in patients
- Molecular mechanisms of cryptogenic epilepsy
- Possible underlying etiology

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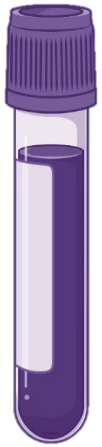
Screening of Patients

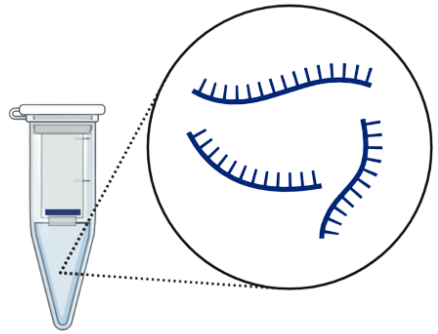
- Age
- Gender
- Onset of Seizures
- Types of Seizures
- Patient History & Neurological Examination
- Family History
- MRI Findings
- Number of Antiepileptics

Cryptogenic Epilepsy Patients (n=20)

Healthy Controls (n=20)

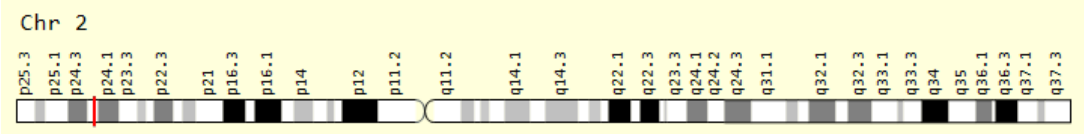


10 mL of peripheral blood collected into EDTA tubes



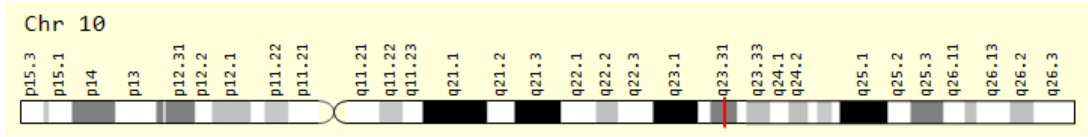
Total RNA Isolation

KCNS3



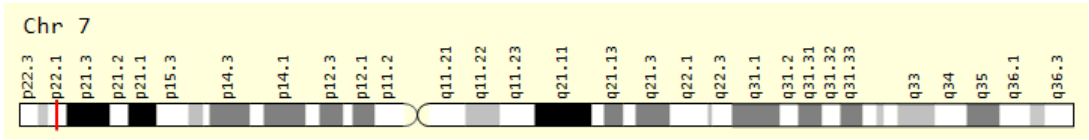
Potassium Voltage-Gated Channel, Modifier Subfamily S, Member 3

IFIT3

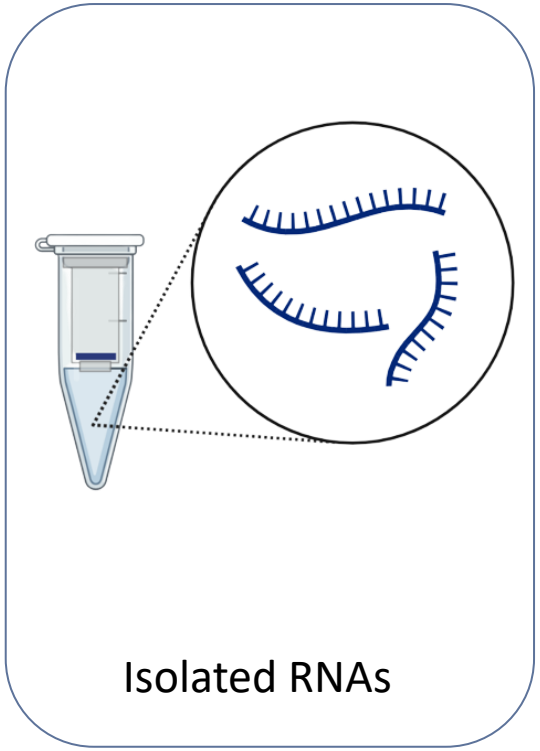


Interferon Induced Protein With Tetratricopeptide Repeats 3

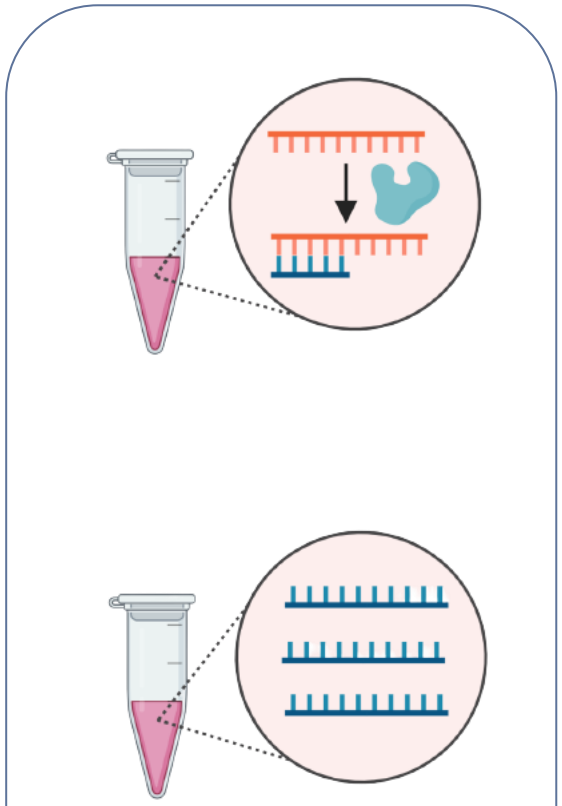
ACTB



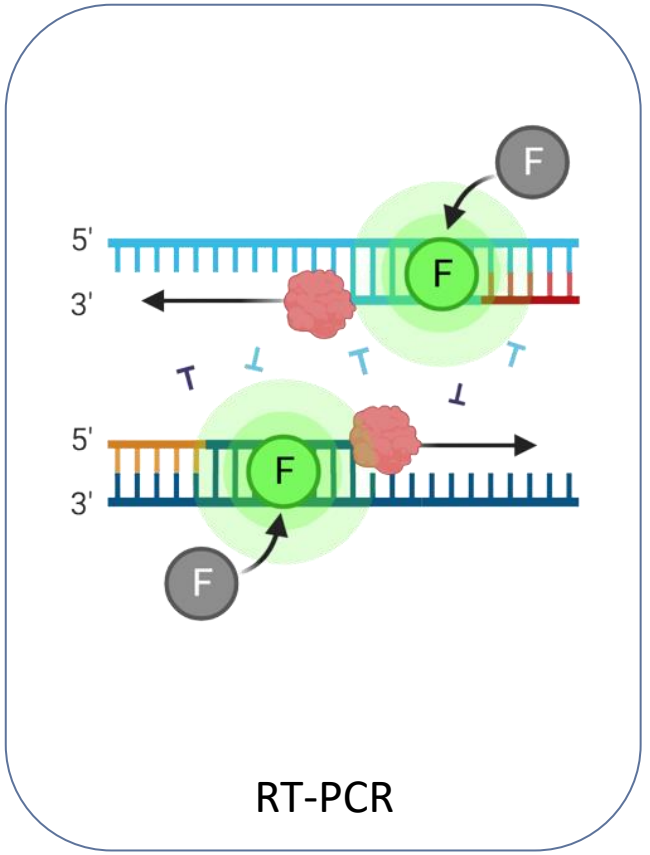
Beta-Actin



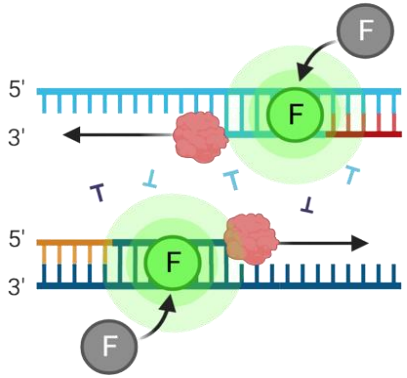
Isolated RNAs



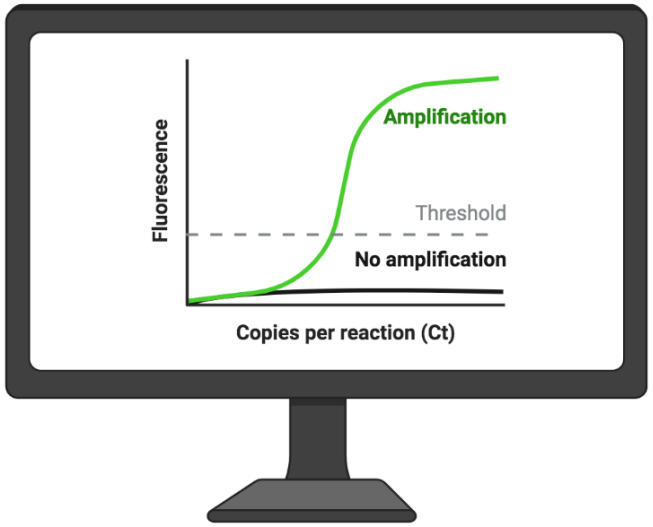
Reverse Transcription



RT-PCR



RT-PCR



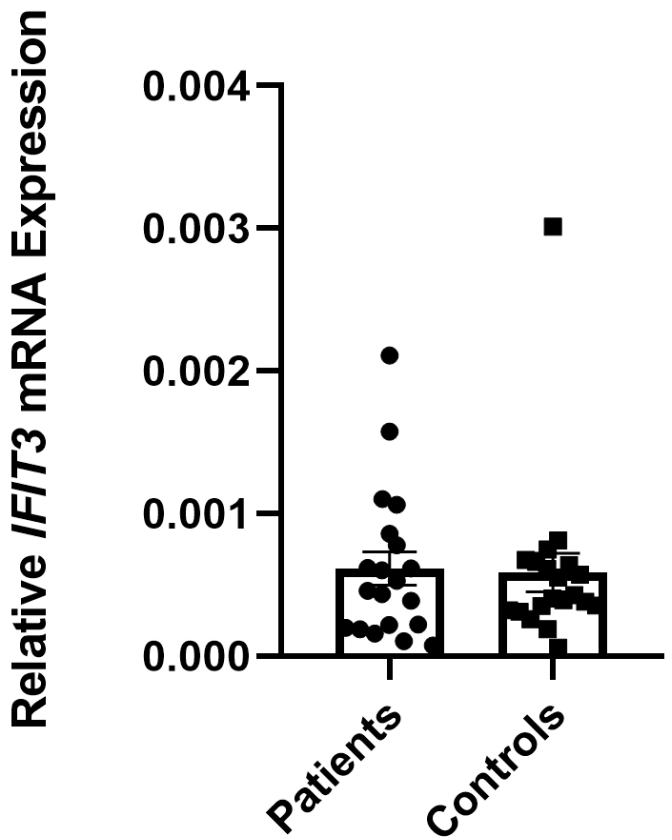
Cycle of threshold (Ct) data

Delta-Delta Ct
Student t-test

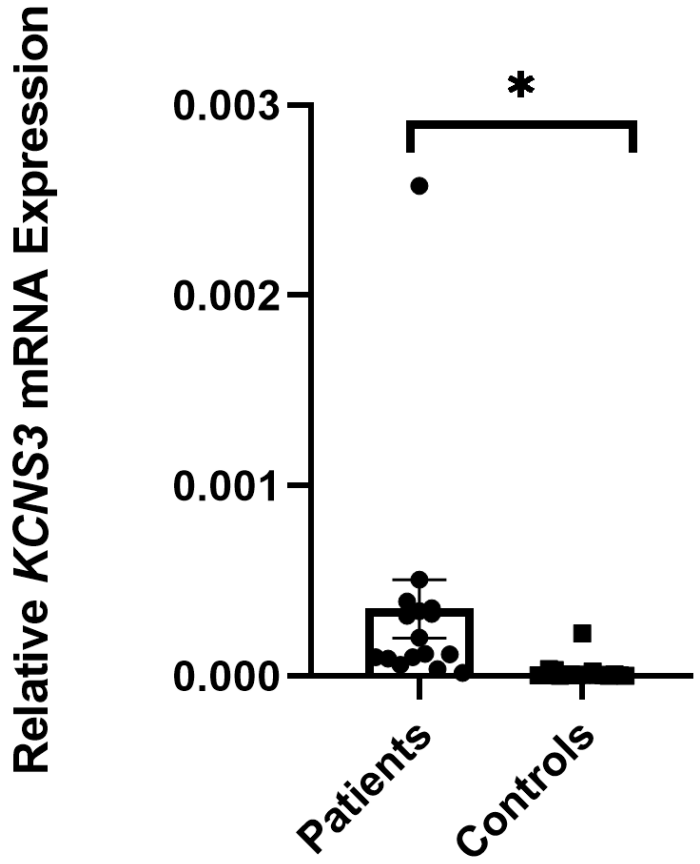
Age	• 29.2 ± 10.14 (19-62)
Gender	• 11 males 9 females
Onset of Seizures	• 18.25 ± 10.45 (2-40)
Types of Seizures	• 15 with focal seizures • 2 with generalized tonic-clonic seizures • 3 unclassified

Patient History & Neurological Examination	• No findings in birth history • No findings in neurodevelopmental history • No findings in neurological examination
Family History	• 2 patients with related parents • None have a relative with an epilepsy history
MRI Findings	• None
Number of Antiepileptics	• 14 were on monotherapy

Results



p= 0.8778



p= 0.0284

Conclusions

- Channelopathy is a more likely molecular mechanism underlying cryptogenic epilepsy.
- *KCNS3* gene might have a role in the pathophysiology
- *KCNS3* gene might be a possible candidate for a biomarker in cryptogenic epilepsy.

Discussion

- IFIT3 ⟶ a possible gene in differentiating the types of epilepsy (symptomatic, idiopathic, cryptogenic) [1]
- K channel subunits [2]
- A possible biomarker ⟶ studies with larger groups

[1]Wang J, Lin ZJ, Liu L, et al. Epilepsy-associated genes. *Seizure*. 2017;44:11-20. doi:10.1016/j.seizure.2016.11.030
[2]Rawat C, Kushwaha S, Srivastava AK, Kukreti R. Peripheral blood gene expression signatures associated with epilepsy and its etiologic classification. *Genomics*. 2020;112(1):218-224. doi:10.1016/j.ygeno.2019.01.017

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Thank you for listening!