UNDERSTANDING THE GENETIC CHARACTERISTICS OF MOLDOVAN MULTIPLEX EPILEPSY FAMILIES USING WHOLE EXOME SEQUENCING

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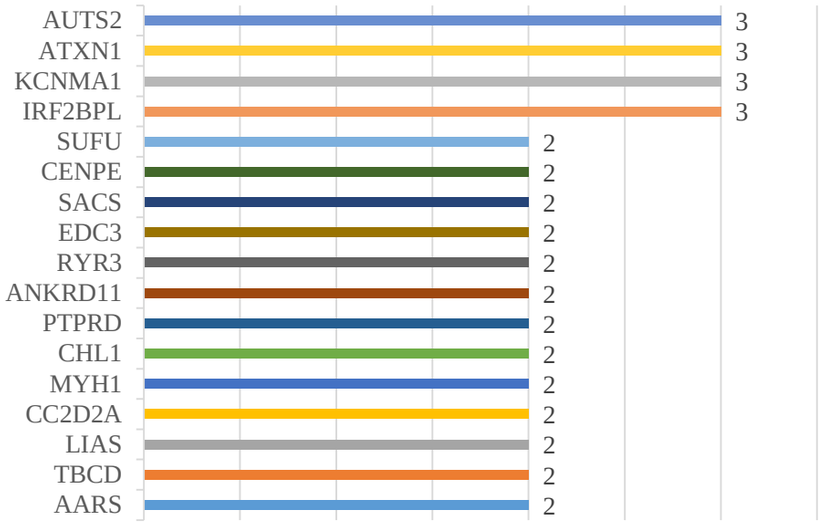
Background:

- Although several theories have been proposed to explain the origin of epilepsy, its cause is still **unknown in about half of cases**.
- In most cases, the link between a gene and the condition is not yet clear and studying **multiple affected members of a family** is needed..

Purpose of the study:

- To estimate the **genetic biomarkers** of multiplex epilepsy families from the Republic of Moldova and their role in epileptogenesis.

Fig. 3 Most involved genes



Conclusions:

- The preliminary results of our studies are truly revolutionary, as they represent an absolute novelty for the country and the eastern **"genetically virgin" territories..**

Material and methods:

- **Whole Exome Sequencing (WES)** was performed on the first 11 epilepsy families from a newly started National Epilepsy Registry (Fig. 2, 3).
- It was followed by a descriptive analysis of the data.

Fig. 1 Distribution by age groups

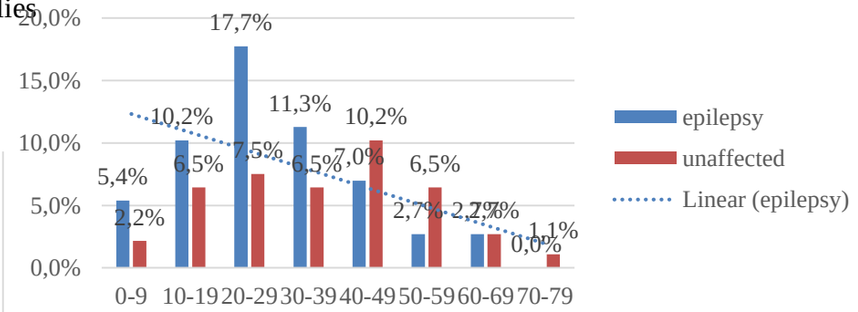
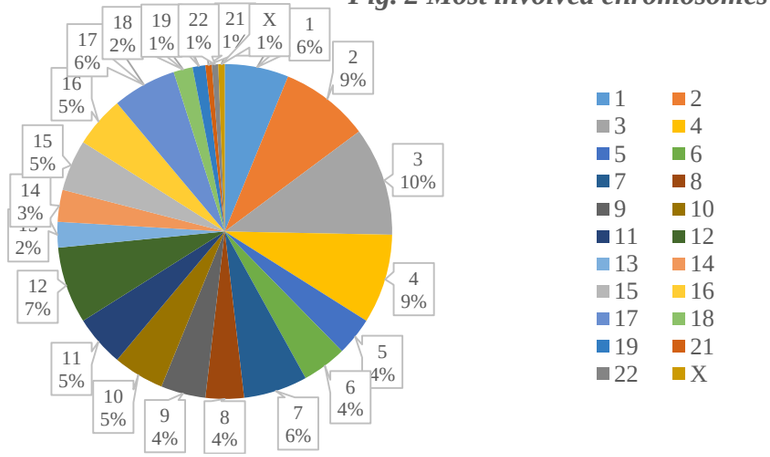


Fig. 2 Most involved chromosomes



Results:

- Our National registry counts now **74 families including 186 members**: subjects with epilepsy (106) and the control group (80 healthy relatives). (Fig.1)
- We identified **potential biomarkers for familial epilepsy**, via *Whole Exome Sequencing*, as summarized bellow.
- Subjects will continue to be recruited and the Registry updated.

CATEGORY	POTENTIAL BIOMARKER
Proband's sex	Female (39%)
Seizure onset	Generalized (63,6 %)
Seizure type	Motor variants (55%)
Awareness	Impaired (75.5 %)
Most involved chromosomes	1, 2, 3, 4, 7, 12, and 17 (Fig.2)
Most involved genes (Fig. 3)	AUTS2, ATXN1, KCNMA1, IRF2BPL, SUFU, CENPE, SACS, EDC3, RYR2, ANKRD11, PTPRD, CHL1, MYH1, CC2D2A, LIAS, TBCD and AARS
Seizure onset age correlated with WES	• 1-5 years – the chromosomes 3, 4, 7, 9 and RYR3, DUSP6, EFHC1, CC2D2A genes; • 6-10 years – the chromosomes 2, 3, 4, 16 and KIF1A, PTPRD, RECQL4, MACF1, APOB, BCAT1, EML1, PREPL, GMPPB, LRPPRC, AARS, CENPE, WDR19, MEGF10, WFS1, CKAP2L, XYLT1 genes. • 11-15 years – chromosomes 12, 15, 17 and ARNT2, CCND2, CNTN4, CTNNA2, EDC3, MUT, MYH1, PTPN11, SLC12A6, SLC25A19, SUFU genes.

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20 22 octombrie 2021