МЛАДЕЖКИ СЕМИНАР ПО ГЕНЕТИКА

На 24.11.2017 г. в град София, в Биологическия факултет на СУ „Св. Климент Охридски” се проведе първият младежки семинар по генетика. Александра Иванова, Диана и Цветелина Михайлови от 11 е клас на ПГЧЕ „Васил Левски” имаха честта и удоволствието да посетят този семинар, да присъстват на лекция, да разгледат всички специалности във факултета, както и да обсъдят, заедно със студенти, учени и биолози, различни теми, засягащи генетиката. След дискусиите за проблемите и евентуални проекти за бъдещето на генетиката в България, момичетата успяха да навлязат в темата, въпреки че едва сега започват да я изучават,

„Останахме с много добри впечатление както от семинара, така и от отношението на всички. Радваме се, че имахме удоволствието да сме част от такова мероприятие и чакаме с нетърпение следващата година отново да бъдем поканени.“

„Освен че успяхме да посетим семинара и да научим нещо ново, както и да обсъдим различни въпроси с хора на академично ниво, имахме възможността и да се запознаем със студентския живот в София и въпреки че престоят ни беше кратък, успяхме да разгледаме много и да научим най-важното нови неща, за което всъщност и отидохме.“ – разказват те.

Пожелаваме успех по пътя на познанието на Александра, Диана и Цветелина!

ПЪРВИ МЛАДЕЖКИ СЕМИНАР ПО ГЕНЕТИКА

VARIANTS SHOWING PHARMACOGENETIC SUSCEPTIBILITY TO COMMON DRUGS AMONG PREDISPOSING SNPs TO FAMILIAL PAPILLARY THYROID CANCER

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Introduction:

Sporadic papillary thyroid cancer (PTC) is the most prevalent form of thyroid malignancy. Genetic predisposition to PTC has been widely studied however the genetic causes of familial cases are still unknown or controversial.

So far, FPTC usually presents as multifocal disease at a younger age and is associated with an increased incidence of nodal involvement and recurrence. The aggressive nature of FPTC suggests the existence of genetic aberrations that are yet to be identified.

The identification of new causative variants predisposing to FPTC and their relation to standard therapy tolerance will pave the way to the development of new targeted therapies for this kind of malignancy.

Here we report two SNPs defining sensitivity to opioids (MC1R_p.Arg151Cys) and to chemotherapeutics (cisplatin and cyclophasphamide) (MUTYH_p.Val22Met) identified by NGS analysis of four families with FPTC.

Materials and methods:

We extracted DNA from blood samples taken from 23 individuals belonging to four families with FPTC. 11 of the participants were affected by FPTC.

We performed NGS analysis using Illumina® sequencing platform and Trusight Cancer Panel®. Seventeen (17) predisposing variants have been selected among the members of the four families. Subsequently we checked each variant's relationship to commonly used drugs and/or chemotherapeutics using publicly available database PharmGKB (https://www.pharmgkb.org/).

Two SNPs have been identified (MUTYH_p.Val22Met and MC1R_p.Arg151Cys) which could impact patients' response to opioids and standard chemotherapeutics (cisplatin and cyclophosphamide). Such an approach could be used for drug response' predictions also in other common diseases.

Results:

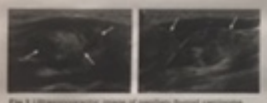

Fig.1 Ultrasonographic image of papillary thyroid carcinoma. A. Microlobulated nodule with microcalcifications and extrathyroidal extension. B. Metastatic lymph nodes.

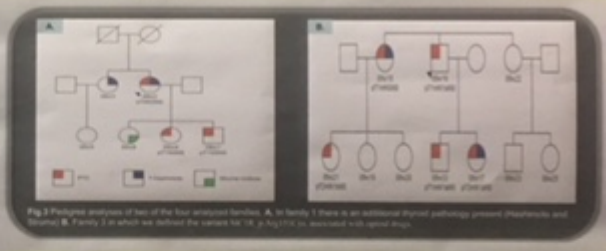

Fig.3 Pedigree analyses of two of the four analyzed families. **A.** In family 1 there is an additional thyroid pathology present (Hashimoto and Struma) **B.** Family 3 in which we defined the variant for 1R_p.Arg151Cys associated with opioid drugs.

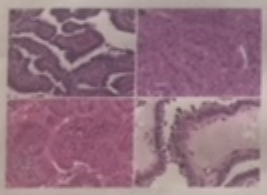

Fig. 2 – Papillary thyroid carcinoma.
A. Classical PTC.
B. Tall cell variant.
C. PTC with oncocytic changes of the epithelium.
D. Hobnail cell variant.

Common SNPs	rs	Polyphen-2 Score	PharmGKB result
MUTYH_p.Val22Met	rs3219484	benign (0.185)	Toxicity to cisplatin,cyclophosphamide
Specific SNPs	**rs**	**Polyphen-2 Score**	**PharmGKB result**
MC1R_p.Arg151Cys (specific for Family 3 – Fig.3)	rs1805007	probably_damaging (0.993)	Sensitivity to opioid drugs (Propoxyphene, nordextropropoxyphene)

Table 1 Single nucleotide polymorphisms (SNPs) among predisposing ones, associated with pharmacogenetic sensitivity to certain drugs. Last row representing the information taken from PharmGKB website.

Conclusion:

By NGS sequencing technology using cancer sequencing panel, individual mutation patterns of each family were found propably leading to th development of FPTC.

We identified two SNPs (MUTYH_p.Val22Met and MC1R_p.Arg151Cys) that could impact patients' response to opioids and standard chemotherapeutic (cisplatin and cyclophosphamide). Such an approach could be used for drug response' predictions also in other common diseases.

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