Results: Publicly available guidelines were reviewed and compared to reach a consensus in terms of the investigated gene-drug pairs, their different level and classification of evidence, which are rated through a scoring system, the recommended therapeutic strategy and the clinical impact of pre-emptive PGx test. Information on the strength of the recommendation (classification of recommendation, level of evidence and clinical impact) were considered necessary to be integrated in the prescribing system along with the therapeutic recommendation. A prototype of a decision-support system is being developed through the partnership with two high-tech companies in Italy, which are actively working on the healthcare system computerization.

Conclusions: Scientific and clinical expertise in the oncologic pharmacogenomic field were put together, thanks to the coordinated efforts of an established partnership. The pre-emptive pharmacogenomic approach in the clinical practice in Italy was implemented and demonstrated its benefit in both patients' clinical outcome and quality of life, with an economic advantage for the healthcare system.

Exploring the Gut-Thyroid Axis in Paediatric Coeliac Disease Patients of Hellenic Origin Reveals Selected Genomic Variants in *CTLA4*, *BACH2*, and *IL23R* Genes That May Account for Overlapping Susceptibility Between Graves' Disease and Paediatric Coeliac Disease

A. Balasopoulou[a], *D. Kampolis*[a], *M. Krini*[b], *K. Spanou*[c], *A. John*[d], *B.R. Ali*[d], *M. Kanariou*[c], *N. Constantinidou*[c], *G. Chrousos*[b], *E. Roma*[b], *G.P. Patrinos*[a,d], *T. Katsila*[a]

[a]Department of Pharmacy, School of Health Sciences, University of Patras, Patras, Greece, [b]First Department of Pediatrics, University of Athens Medical School, Athens, Greece, [c]Department of Immunology and Histocompatibility, "Aghia Sophia" Children's Hospital, Athens, Greece; [d]Department of Pathology, United Arab Emirates University, College of Medicine and Health Sciences, Al-Ain, UAE

Objectives and Study: Differential diagnosis and theranostics of a series of autoimmune inflammatory disorders remain challenging as we still need to dissect the molecular determinants and cross-talk in the cell signaling of the gut-thyroid axis. Several genetic, epidemiological, clinical, serological, and pathophysiological data indicate that coeliac disease is associated with autoimmune thyroid disorders and in particular, Graves' disease. Today, no clear nomogram is effective to allow for optimum disease management and patient stratification. Herein, we explore the role of selected genomic variants for overlapping susceptibility between Graves' disease and paediatric coeliac disease aiming for an immunogenetic model towards the identification of coeliac disease patients with an increased risk of developing Graves' disease.

Methods: Extensive data mining, pathway analysis and literature review resulted in the selection of *CTLA4, BACH2* and *IL23R* variants. For data validation, coeliac paediatric patients of Hellenic origin (n = 109) and their ethnically matched counterparts (n = 111) were genotyped by PCR and Sanger sequencing. Hardy-Weinberg equilibrium was determined by Pearson's goodness-of-fit chi-square, log-likelihood ratio chi-square and Exact tests. Genotype and allele frequencies were evaluated by the Fisher's Exact test. A two-tailed p-value of <0.05 was considered statistically significant. The R project for statistical computing (R i386 3.2.1) was used.

Results: Selected *CTLA4, BACH2* and *IL23R* variants may account for the overlapping susceptibility between Graves' disease and paediatric coeliac disease in patients of Hellenic origin.

Conclusion: *CTLA4, BACH2* and *IL23R* variants may serve as the building block of a nomogram to optimize Graves' and Coeliac disease management and patient stratification.

Application of Next-Generation Sequencing Technology and Establishment of Biobanks

K. Klaassen, M. Stojiljkovic, N. Tosic, B. Zukic, S. Pavlovic

Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Belgrade, Serbia

Institute of Molecular Genetics and Genetic Engineering has become widely recognized as an expert centre for rare diseases (RD). It is the first institution is Serbia that applied NGS methodology in research and diagnostics of RD. We are also the institution with RD biobank collections containing DNA, RNA, mononuclear cells and tissue samples from over 2000 of patients affected with 50 different diseases.

An accurate diagnosis was provided to over than 100 RD patients who were undiagnosed for years. We used Clinical-Exome Sequencing TruSightOne Gene Panel (4813 clinicaly-relevant genes), Illumina MiSeq instrument and Illumina VariantStudio. For monogenic diseases, filtration and prioritization of variants were performed according to "in-house" pipeline, using virtual gene panels. Variants were analyzed by various *in silico* softwares and classified according to ACMG guidelines. Variants selected by these criteria were confirmed by conventional Sanger sequencing and parents' samples were analyzed whenever available.

Furthermore, novel variants in *DNAI1*, *MUT*, *PAH*, *PCCB*, *SLC37A4*, *SPAG16* and *SPAG17* genes were functionally characterized in adequate in vitro systems such as immortalized patients' fibroblasts or CRISPR /Cas9 edited commercial cell lines.

Clinical-exome sequencing enabled diagnosis of more than 50 different diagnosis (hematological, metabolic, endocrinological, pulmonary, immunological, orthopedic, dermatological, ophthalmological, cardiological, epileptic encephalopathies etc.). It was particularly important for genetically heterogeneous diseases, such as glycogen storage diseases, branched-chain organic acidurias, primary ciliary dyskinesia, MODY or mitochondriopathies. Moreover, different diseases with overlapping clinical manifestations were accurately diagnosed.

Also, we used TruSeq-Amplicon Cancer Panel to analyse different childhood and adult rare hematological malignancies. Besides studying diagnostic and prognostic malignancy markers, we designed "in-house" virtual pharamocogenomic panel, and performed association studies of pharmacogenomic markers and the course and outcome of rare hematological malignancies, resulting in recommendations for therapeutic modalities in accordance with genomic profile of the patient.

This work has been funded by MESTD, Republic of Serbia (III41004).