CA 15129, DiMoPEx
Diagnosis, **Mo**nitoring, **P**revention of **Ex**posure Related Non-Communicable Diseases

COST is supported by the EU Framework Programme Horizon 2020

WG1-WG2-WG3-WG5-WG6

Complex diseases as a model system for phenotype modulation- structural and functional analysis of molecular biomarkers

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Introduction

Our research is in the field of molecular genetics and its application in molecular diagnostics. This applied research has led to accumulation of fundamental results related to the regulation of the expression of the selected genes and identification of new biomarkers. We are also active in spreading knowledge regarding the potential of this scientific discipline, as in informing physicians about the possibilities and advantages of molecular diagnostics of rare and multifactorial diseases.

Methods

The role of various genetic and non-genetic factors in studied diseases is investigated by analysis of biological samples and clinical data using methods of molecular genetics, molecular biology, biochemistry and biostatistics, and different model systems: permanent and primary cell lines and zebrafish (*Danio rerio*) as an animal model, confocal microscopy with live imiging system.

Exposed individuals/patients

The repository of biological samples has been established for different diseases: thrombosis, cardiomyopathy, chronic obstructive pulmonary disease, asthma and solid tumors (pancreatic, colorectal, thyroid).

Project aims

Research interests of our group are mostly oriented towards the molecular basis of selected cardiovascular, respiratory and malignant diseases, with the focus on genetic and non-genetic factors that contribute to the disease onset and/or modulation of clinical phenotype. Genes, which we choose through associative studies as potential modulators of phenotype, have been further analyzed on posttranscriptional and/or posttranslational levels.

Results

We analyzed selected genes in their involvement in regulation of hemostasis, inflammatory processes, tissue remodeling, protection from oxidative stress, cell proliferation and cell death:

- Montelukast, drug used in combination with inhaled corticosteroids for the management of persistent asthma, show tendency to reduce mRNA level of Transforming growth factor beta 1 gene expression in induced sputum cells.
- We observed significant association between -889T>G variant in promoter region of hepatic *CYP2C19* gene and bleeding events in patients taking clopidogrel (drug exerting antiplatelet function).
- We concluded that prothrombotic mutations (FV Leiden and FII G20210A) do not determine the age of the onset of first thrombotic manifestation.
- In patients with hypertrophic cardiomyopathy, besides variants in 16 in sarcomeric genes, we identified additional 4 pathogenic or likely pathogenic variants in nonsarcomeric genes, using targeted next generation sequencing (NGS) analyses
- In oxidative stress treatment, zebrafish embryos treated either with great mullein (*Verbascum thapsus)* or coltsfoot *(Tussilago farfara)* water extracts, used for treatment of numerous diseases, showed production of reactive species.
- We first established gender-related reference intervals for urinary biomarker of oxidative stress (8-oxodG/creatinine), one of the dominant form of oxidative modifications of DNA.

Discussion/Conclussions

Our research contributes to the explanation of the molecular pathology of the studied diseases, and results in specific protocols and biomarkers with potential to improve disease prevention, diagnosis and treatment.

References

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