DEVELOPMENT OF NGS PANEL FOR EVALUATION OF PHARMACOKINETICS OF IMMUNOSUPPRESSIVE DRUGS USED IN RENAL TRANSPLANTATION

Tsvetelin Lukanov[1,2], Milena Ivanova-Shivarova[1,2], Petya Yankova[1,2], Bushra Nabil Al Hadra[2], Valentina Atanasova[1], Spaska Lesichkova[1,2], Daniela Marinova[1], Marianka Petrova-Yanachkova[3,4], Dobrin Svinarov[3,4], Anastasia Mihaylova[1], Elisaveta Naumova[1,2]

[1]*Clinic of Clinical Immunology with Stem Cell Bank, University Hospital „Alexandrovska“, Sofia, Bulgaria*

[2]*Department of Clinical Immunology, Faculty of Medicine, Medical University, Sofia, Bulgaria*

[3]*Clinical Laboratory and Clinical Pharmacology, University Hospital „Alexandrovska“, Sofia, Bulgaria*

[2]*Department of Clinical Laboratory, Faculty of Medicine, Medical University, Sofia, Bulgaria*

Although routine therapeutic drug monitoring is performed in organ transplantation, it is still difficult to predict the effectiveness of immunosuppression (IS).

The aim of the study was to evaluate the applicability of the NGS panel for personalized monitoring of immunosuppressive therapy in kidney transplant patients.

Materials and methods: We have designed a custom panel for targeted re-sequencing of genes associated with response to the immunosuppressive therapy using AmpliSeq designer. Our panel includes 22 genes with 442 primer pairs divided in 2 pools and covering 99,46% of the exonic regions of the genes. The sequencing was performed on Ion S5 platform with 540 Chip, and variant annotation was performed on Ion Reporter. To validate the clinical applicability of the panel, we examined 71 kidney transplant patients routinely monitored for cyclosporine (n = 33) or tacrolimus (n = 38) concentrations.

Results: In the analyzed 11 genes, >1000 polymorphisms were identified - synonymous (65%), missense (30%), frameshift (3%), nonsense (>1%), %), including 5 unknown frameshift mutations and 12 unknown nonsynonymous SNPs. The highest polymorphism is observed in the group of ATP binding proteins – 547, compared to 344 in the group of cytochrome P450 genes. Several SNPs that correlate with the metabolism of the administered immunosuppressive drugs have been identified.

Conclusion: Preliminary results show that the developed panel allows successful genotyping of enzymes involved in the metabolism of IS drugs. The panel may find application for pharmacogenetic evaluation of the response to therapy to contribute to a personalized approach in kidney transplant patients.

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