E. faecium, in the gut microbiota content. The data of the clinical trial (63 parameters of each patient) was used for the development of a new methodology for the detection of personalized treatment process biomarkers. These biomarkers are essential for the development of new machine learning models, which could predict the success of a patient's personalized treatment.

3PM related conclusion and outlook

The CVD are subject to prevention by correction of the individual profile including each person's unique microbiome dependent on individual lifestyle, nutrition and behaviour. To recommend prognostic treatment for the patients with a diagnosed stage of "metabolic disorder", IT tools (IS) need to be applied in order to calculate the complex individual biomarkers in the context of individual variations.

The algorithm under testing is a potential tool to estimate (in addition to the detected genetic) lifestyle-dependent, epigenetic, environmental and nutritional factors in an individual to provide the level of recommendations and adequate prognostication that is crucial to implement 3PM [5].

To prove and suggest a provisional role of individual nutrition or pharmabiotics treatment in 3PM, the cohort studies with precise individual measurements of the biomarkers, prioritized with correlation analysis of the initial data, analysis of the main components, cluster analysis and a well-known machine learning procedure "feature selection", need to be performed. The strong demands for the improving of the design of cohort studies are highly recommended by 3PM experts [6].

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Creation of lactobacilli based pharmabiotics for individual prevention and treatment of infectious-inflammatory diseases of the human urogenital system

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The principles for individual immunobiotics developments and testing of their efficacy on the urogenital tract infectious-inflammation diseases

Personalized use of immunobiotics is a promising direction in the prevention of various infectious and inflammatory diseases associated with microbiome changes of the genitourinary system in humans.

Recently, the strain-dependent properties (adhesive ability, resistance to antibiotics, and gut biological fluids) of probiotic strains

(lactobacilli and bifidobacteria) were reported, and their potential application for most effective individualized treatment for gut and distant sites microbiome modulation was preliminary discussed [1].

The objective of our study was to determine in a limited randomized clinical trial the patient- and nosology-specific efficacy of immunobiotics, developed from different original strains of lactobacillus (and their combinations), demonstrating both antimicrobial and immune-modulating functions preliminary examined on animal and cellular models [2].

Patients with infectious-inflammatory diseases of the genitourinary system were recruited from a regional hospital. Eligibility requirements and enrolment procedures were performed in accordance with the EU Regulation No 536/2014. The inclusion criteria for women were age over 18 years, urogenital pathologies of different nosology, and exclusion criteria were detected antibodies to hepatitis B or C; alcohol or drug abuse; HIV infection or antiretroviral therapy; diagnosed diseases of the cervix (dysplasia); menstrual disorders; cancer; pregnancy.

Collected specimens were plated on chromogenic media for detection of cultured urinary tract microbiota representatives and were additionally genetically defined by qRT-PCR (Femoflor®-16, Androflor® REAL-TIME PCR Detection Kit, DNA technologies, Russia). Isolated microorganisms were identified by using the Lachema biochemical tests. Local immune response (IL-10, 17, 1b; TNF-a, SIgA) before and after applied LAB treatment was measured by ELISA. Lactobacilli strains in this study were sequenced and identified as *Lactobacillus casei* (2 strains) and *Lactobacillus acidophilus*.

Individual gender and nosology specific microbiome changes of infectious-inflammatory diseases of the genitourinary system by application of different lactobacilli strains composition

The typical agents (nosologies) of infectious-inflammatory diseases of the genitourinary system were identified. The female bacterial vaginitis was characterized mostly by the predominance of *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* with or without the presence of *Gardnerella, Atopobium, Ureaplasma* or *Mycoplasma.* Different nosologies of the male urogenital tract diseases were characterized mostly by the prevalence of such opportunistic microorganisms as *Streptococcus* and *Staphylococcus* with or without *Ureaplasma*, *Haemophilus*, Enterobacteriaceae, and *Candida.*

Thus, new effective probiotics and their compositions were designed taking into account individual features of the commensal microbiota of the patients and the dominating agents of opportunistic infections of male and female urogenital systems.

It has been proved that the use of the *L. casei* IMV B-7412 probiotic strain was the most effective in mixed infections classified as a significant anaerobic/aerobic microbial ratio of microbiome, a combination of strains *L. casei* IMV-B 7280 / *L. casei* IMV B-7412 enhances the antifungal effect, while the composition of strains *L. casei* IMV B-7280 and *L. acidophilus* IMV B-7279 promotes the restoration of healthy microbiome, providing complete elimination of coliform bacteria and microscopic fungi, and reducing the number of pathogenic staphylococci.

All LAB strains and their compositions were characterized by strain and compositionally specific ability to restore the local and systemic immune response by decreasing the level of IL-17 and SIgA, and increasing the IL-10 level.

Proper combination of LAB strains pragmatically designed is crucial to get prognostic healthy microbiome changes

Efficacy of the application of different pharmabiotics is the subject of great concern since the immunomodulatory properties of its LAB components are mainly strain-dependent and connected to cell walls structure, as was recently demonstrated [3]. There is also an open discussion about oral vs. intraurogenital administration of various LAB based biopreparation. Their efficacy is dependent on the proper combination of LAB strains, correspondingly pragmatically designed content of pharmabiotics is crucial. The combination of commensal strains that are defining the efficacy by producing specific metabolites or preventing adhesion or even physiological competition with strains should also be considered.

Previously, we were able to demonstrate that following the oral administration of synbiotic Bifiten™, the vagina mucosal sites were settled by both commensal and transit microbiota, which in turns led to a reduction of the perinatal complications for the mother and newborn [4]. At the same time, we were able to observe side effects after application of such complex synbiotics to healthy mothers, who did not require any treatment and were initially characterized by a significant number of their own lactobacilli strains.

3PM related conclusion and outlook

Prevention of infection-inflammatory diseases needs to be based on monitoring of individual urogenital system microbiome ratio, since this ratio determines the resistance of the local immune system and initiation of low-grade inflammation.

This approach is in line with proposed 3PM solutions to improve sensitivity and specificity of early stage biomarkers and currently well-discussed [5].

Infants and young people's urogenital health is dependent significantly on women/mothers' health encoding due to early programming self-resistance to potentially pathogenic bacteria, candida, but also viruses, mycoplasma, and chlamydia. This preventive approach is crucial for specific person microbiome-based prophylactics.

Another issue is a specific mixture of etiologic agents causing the infectious-inflammatory urogenital disease—"pathogenic formula", combined with the individual microbiome, connected to specific local immune response, modulation of which is strain-dependent [1, 4]—this issue could be the limitation of recommendation for application of any pharmabiotics strains separately or in combination.

The predictive treatment effect of using any pharmabiotics should be based on the microbiome phenotype of the urogenital system. Then the individual pharmabiotic content selection based on IS models together with ML and databases usage is the way for really prognostic individual efficacy.

3PM requires the understanding of individual differences, thus the "same" nosology needs to be treated differently, based on at least each person's microbial and immune profile.

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Biobanking in 3PM

BRoTHER – a Regional Biobank Network in the Centre of Europe Aimed at Promoting Personalized Medicine Through Digitalization in Biobanking

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Introduction

Biobanking has been a fast-growing field in basic-, clinical- and translational research over the past 30 years. Biobanks collect, store and share biological material alongside associated data and provide a fundamental scientific infrastructure for personalized medicine [1]. Biobanks represent a key resource for predictive diagnostics, research and experimental therapies [2] and follow the whole chain of medical interventions. By placing an emphasis on prevention, prediction and a healthy lifestyle, biobanks have contributed to the current paradigm shift within medicine from "one-size-fits-all" to "individualized medicine" [3, 4]. Biobanking plays a crucial role in the introduction and further optimization of personalized medicine. Samples stored in biobanks provide information about risk factors of diseases. They assist in the discovery of biomarkers that aid in early diagnosis and a personalized treatment choice, as well as biomarkers for the prediction of initial responses to treatment. Biobank samples also serve as unique sources in the search for drugs [5].