

Study of changes in the intestinal microbiota of rats caused by implantation of a biopolymer construct based on poly-3-hydroxybutyrate and alginate

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Biopolymer constructions are widely used in tissue engineering, in particular, for regeneration of bone, muscle, epithelial and other tissues. Studies in the field of colon regeneration were considered to be of interest, since several severe diseases such as Crohn's disease, colitis, and colon cancer demand for new methods of treatment. The main feature of the intestine is a close symbiotic relationship with a complex bacterial community, so any factor or effect on the gastrointestinal tract significantly could change the composition of the microbiota. Thus, the composition of the microbiota can play the role of a marker for indirect assessment of animal status after intestinal implantation. The aim of the work was to assess changes in the intestinal microbiota after implantation of a 3-dimensional biopolymer construct into the large intestine of Wistar rats.

Poly-3-hydroxybutyrate (PHB) and alginate were obtained by bacterial synthesis of culturing the bacterial strain *Azotobacter agile* 12. Bacteria were grown in liquid Burke medium with a minimum level of aeration for the synthesis of PHB, and with a maximum level of aeration for the synthesis of alginate. The isolation of biopolymers from biomass was carried out after 48 hours of cultivation. The implantable composite structure consisted of a porous PHB-based substrate in the form of a tube 2 cm long and 0.5 cm in diameter coated with alginate hydrogel. The construct was implanted into Wistar rats in the large intestine. One week later, rats were dissected and biomaterial was selected for metagenomic analysis.

Metagenomic analysis was performed on the hypervariable region of V4 of the 16S rRNA gene. DNA was amplified with primers F515 (GTGBCAGCMGCCGCGGTAA) and R806 (GGACTACHVGGGTWTCTAAT). Sequencing was performed on an Illumina MiSeq™ System. Sequencing reads processing and data analysis were carried out in the QIIME program.

Data analysis showed that bacteria from Firmicutes phylum dominates in preoperative and postoperative samples. Significant quantitative differences were found at the genus level - outbreaks of 3 bacterial genera appear in the experimental samples: *Ileibacterium sp.*, *Lachnoclostridium sp.*, *Faecalibaculum sp.* and an OTU from *Christensenellaceae* family. A sharp decrease of *Erysipelatoclostridium sp.* abundance was found.

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