THE ROLE OF ENDOCRINE CELLS OF THE COLON IN THE DEVELOPMENT OF METABOLIC DISORDERS

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Annotation: *Endocrine cells of the colon play a key role in regulating metabolism through the production of hormones that affect appetite, glucose and lipid metabolism. Disruption of their morpho-functional organization can lead to the development of obesity, type 2 diabetes mellitus and metabolic syndrome. This article discusses the mechanisms of the influence of intestinal hormones on metabolic processes, as well as the prospects for their use in the treatment of metabolic disorders.*

Keywords: *endocrine cells, colon, intestinal hormones, metabolic syndrome, obesity, diabetes mellitus, GLP-1, PYY, serotonin*

Main text

Endocrine cells of the colon are part of the diffuse neuroendocrine system and participate in the regulation of metabolism by secreting biologically active substances such as glucagon-like peptide-1 (GLP-1), peptide YY (PYY), serotonin and others. These hormones affect the central nervous system, digestive organs and endocrine glands, modulating appetite, insulin secretion and the rate of absorption of nutrients.

Dysfunction of these cells can lead to hormonal imbalance, which contributes to the development of metabolic syndrome. For example, decreased secretion of GLP-1 and PYY leads to increased food intake and insulin resistance , which ultimately contributes to the development of obesity and type 2 diabetes. In addition, disturbances in serotonin production can affect inflammatory processes in the intestine, exacerbating metabolic disorders.

Current research points to the potential of GLP-1 receptor agonists in the treatment of metabolic disorders. Such drugs help reduce body weight, improve glycemic control, and reduce inflammation in the intestines.

Intestinal microbiota (IM) is a set of bacteria that colonize the gastrointestinal tract (GIT). The main representatives of the intestinal microbiota are the types (phyla) Firmicutes , Bacteroidetes , Actinobacteria and Proteobacteria . There is evidence that IM is a "new organ" due to the fact that it directly participates in the functioning of the body. IM is involved in the processes of food digestion, in the metabolism of proteins, fats, carbohydrates and bile acids, has protective properties against pathogenic microorganisms, activating local immunity and stimulating the secretion of mucus by intestinal cells. IM affects peristalsis processes, acts as a trigger for differentiation and cellular apoptosis enterocytes and colonocytes . In addition, CM and its active metabolites take an active part in the synthesis of hormones by enteroendocrine cells (EEC) of the intestine. Disruption of the secretion of these hormones is one of the key links in the pathogenesis of the development of such endocrine diseases as

diabetes mellitus and obesity. Thus, CM is not just an "organ", but an "endocrine organ", the disruption of the composition and functions of which leads to metabolic disorders.

INFLUENCE OF INTESTINAL MICROBIOTA ON INTESTINAL CELLS

One of the main points of application of CM is the intestinal epithelium. Intestinal epithelial cells can be divided into three groups: stem cells, absorptive border enterocytes , and secretory cells. Secretory cells in turn are divided into EECs, goblet cells, and Paneth cells . EECs make up approximately 1% of all intestinal epithelial cells, but at the same time form the largest network of endocrine cells in the human body. EECs are classified depending on the hormone they synthesize: G cells synthesize gastrin , A cells synthesize ghrelin , D cells synthesize somatostatin , I cells synthesize cholecystokinin , enterochromaffin cells synthesize serotonin, K cells synthesize glucose-dependent insulinotropic peptide (GIP), L-cells – glucagon-like peptides 1 and 2 (GLP-1, GLP-2) and peptide YY (peptide tyrosine-tyrosine – PYY).

CM is responsible for adequate functioning of the intestine by activating several mechanisms. On the one hand, CM takes an active part in regulating angiogenesis by influencing the synthesis of active peptides in Paneth cells involved in vascular proliferation processes. This ensures adequate blood supply to the intestine, which allows for the transport of large quantities of hormones, vitamins, nutrients and CM waste products to neighboring intestinal cells, other parts of the gastrointestinal tract and the liver. On the other hand, CM is involved in local (intestinal) and systemic inflammation processes. Thus, CM prevents the development of a cascade of inflammatory reactions by reducing the permeability of the intestinal epithelium, increasing mucus production by goblet cells and regulating the expression of genes responsible for the assembly of tight junctions - proteins that act as adhesion between intestinal epithelial cells. When the composition of CM is disrupted and the number of gram-negative bacteria in the gastrointestinal tract increases, the permeability of the intestinal epithelium increases. This results in gram-negative bacterial lipopolysaccharides entering the intestinal interstitial space and systemic bloodstream, where they bind to Toll - like receptors type 2 (TLR2) on the surface of CD4+ T lymphocytes. This interaction activates gene expression and subsequent synthesis of nuclear factor- κB and activator protein-1, which enhance the synthesis of proinflammatory cytokines – IL-1, IL-6, TNF-α and trigger a cascade of inflammatory reactions.

During its vital activity, the CM is able to metabolize indigestible carbohydrates to short-chain fatty acids (SCFA), the main ones of which are butyrate, acetate, propionate and succinate . In the cells of the intestinal epithelium, succinate , butyrate and propionate participate in intestinal gluconeogenesis . Intestinal gluconeogenesis is the process of glucose synthesis by intestinal epithelial cells. Glucose formed in the epithelial cells enters the portal vein. The endings of the periportal nerve plexuses located in the wall of the portal vein perceive an increased concentration of glucose and send an impulse to the brain to activate the saturation center. Also, information about the concentration of glucose in the portal vein reaches the liver and peripheral tissues through the fibers of the nerve plexuses. This leads to a decrease in the formation of glucose by the liver and increases the glucose tolerance of peripheral tissues.

Thus, CM is directly involved in maintaining the vital activity of intestinal epithelial cells, affecting angiogenesis , mucus production, cellular permeability, inflammation and energy supply. In addition, CM, through SCFA, affects glucose homeostasis in the body and is involved in the processes of central appetite regulation. However, these are not the only points of application of CM. Currently, the effect of CM on the processes of activation of the synthesis of hormones of the gastrointestinal tract, pancreas (PG), and adipose tissue is being actively studied.

INFLUENCE OF INTESTINAL MICROBIOTA ON THE SYNTHESIS OF GASTROINTESTINAL HORMONES

CM and its active metabolites affect the synthesis of most gastrointestinal hormones, namely, GLP-1, GLP-2, GIP, PYY, ghrelin , cholecystokinin , serotonin. In addition, there is evidence that CM is involved in the synthesis of hormones such as leptin and insulin. The receptor and enzymatic pathways by which CM affects hormone synthesis are shown in Fig. 1.

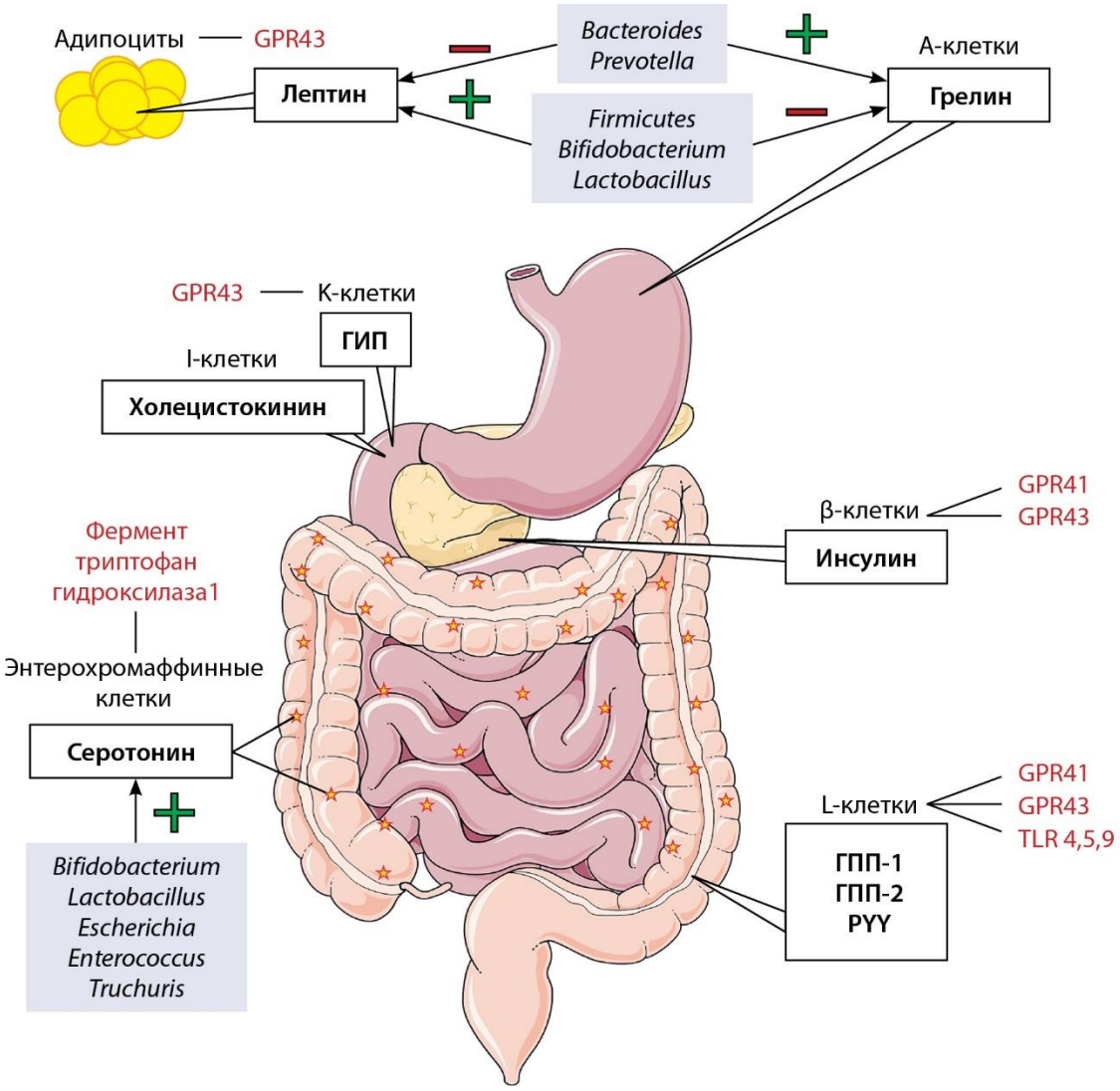

Figure 1. Receptor and enzymatic pathways through which gut microbiota influence hormone synthesis.

Note. The intestinal microbiota , via its active metabolites, binds to the receptors GPR41; GPR43; TLR 4,5,9. This leads to the activation of intracellular processes leading to the synthesis of hormones. Also, short-chain fatty acids affect the synthesis of serotonin by

reducing the activity of the enzyme tryptophan hydrolase 1. In addition, there is evidence of a direct effect of intestinal bacteria on the synthesis of hormones.

GIP - glucose dependent insulinotropic peptide, GLP-1, GLP-2 – glucagon-like peptides 1 and 2; PYY – peptide YY.

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Glucagon-like peptide 1

GLP-1 is a hormone produced by L-cells in the distal ileum and in small quantities in the colon. GLP-1 is secreted in response to an oral glucose load. This hormone stimulates insulin secretion by beta cells and reduces glucagon synthesis by alpha cells of the pancreas. In addition to its insulinotropic effect, GLP-1 has a protective effect on beta cells of the pancreas, heart and kidneys, helps slow intestinal peristalsis, relax the muscular apparatus of the proximal stomach, reduces appetite, and has an anti-inflammatory effect [15].

There are a number of studies proving the effect of CM on the secretion of GLP-1 through the production of active metabolites: SCFA, hydrogen sulfide (H2S), indole. There is also data on the effect of some types of bacteria on the secretion of GLP-1.

SCFAs are synthesized by bacteria mainly from indigestible carbohydrates, i.e. carbohydrates that are not broken down by gastrointestinal enzymes (cellulose, pectin, etc.). SCFAs activate two types of receptors: GPR41 and GPR43, which are also called free fatty acid receptors (FFAR3 and FFAR2). These receptors are present in the gastrointestinal tract, liver, white adipose tissue, muscles, beta cells and alpha cells of the pancreas. It has now been established that activation of GPR41 receptors by butyrate and propionate in the gastrointestinal tract does not affect GLP-1 secretion, since mice lacking GPR41 do not have impaired glucose homeostasis and GLP- 1 secretion. Unlike GPR41, activation of the SCFA GPR43 leads to a cascade of intracellular reactions aimed at increasing calcium ions in L-cells and initiating the synthesis of GLP-1 by these cells. Due to the fact that the GPR41 and GPR43 receptors are more than 75% identical in amino acid sequence, activation of these receptors can lead to cross-effects. In other words, it is highly likely that the GPR41 receptor is involved in the secretion of GLP-1, which requires further evidence.

Conclusion

Endocrine cells of the colon play an important role in maintaining metabolic homeostasis. Their dysfunction contributes to the development of diseases such as obesity and type 2 diabetes. Studying the mechanisms of their work and developing targeted therapeutic approaches may become an effective way to prevent and treat metabolic disorders.

REFERENCES:

1. Hugon P Dufour JC, Colson P et al. A comprehensive repertoire of prokaryotic species identified in human beings. Lancet Infect Dis. 2015 Oct ;15 (10):1211-1219. https://doi.org/10.1016/S1473- 3099(15)00293-5. Epub 2015 Aug 23.

2. Jazani N, Savoj J, Lustgarten M, Lau W, Vaziri N. Impact of Gut Dysbiosis on Neurohormonal Pathways in Chronic Kidney Disease. Diseases. 2019. https://doi.org/10.3390/diseases7010021

3. Qin J, Li R, et al. A human gut microbial gene catalog established by metagenomic sequencing. Nature. 2010 Mar 4 ;464 (7285):59-65. https://doi.org/10.1038/nature08821

4. Qurbanova , L. M., & Toshboyeva , S. K. (2021). KIMYOVIY TAJRIBALAR-O'QUVCHILARNING KIMYODAN TAYYORGARLIK DARAJASINI OSHIRISHDA MUHIM OMIL. *Journal of Natural Sciences* , *1* (3).

5. Kurbanova, L. M., Khidirov , Z. E., & Abduraimov , Z. A. (2021). CLINICAL AND EPIDEMIOLOGICAL FEATURES OF THE COURSE OF BRUCELLOSIS IN THE AGE ASPECT IN THE SAMARKAND REGION. *Achievements of Science and Education* , (1 (73)), 61-68.

6. Uktamovich, K. E., Oblakulovich , KS, Murodullaevna , K. L., Hidirovna , L. Z., & Aslamovna , K. G. (2021). Effects of cellular cord blood on skin pathology in laboratory animals. *Central Asian Journal of Medical and Natural Science* , *2* (1), 116-122.

7. Narzullaevna, KS, Esirgapovich , KA, Xalimovich , JM, Murodillaevna , BRSKL, Solijonovna , UO, & Naimovich , BB (2021). What is Ecology ?. *Annals of the Romanian Society for Cell Biology* , *25* (5), 3341-3345.

8. Erkinovich , XZ, Murodullavena , KL, Mamadievich , RZ, Mamirkulovich , MZ, Xidirovna , LZ, & Oblakulovich , KS (2021). Improving the Surgical Treatment of Patients with a Biliary Disease Complicated by Mirizzy Syndrome. *Annals of the Romanian Society for Cell Biology* , *25* (6).

9. Oripov, F. S., Kurbanova , L. M., & Kurbanov , X. R. (2022). Epithelial barrier of the colon in normal and ulcerative colitis. *Open Access Repository* , *8* (7), 9-16.

10. Tastanova, G. Y., Kurbanova , L. M., & Olimjonova , D. U. (2025). MORPHOLOGICAL STATE OF THE STRUCTURE OF THE LARGE INTESTINAL TISSUE AFTER EXPERIMENTAL MINIGASTROSHUNT OPERATION. *SHOKH LIBRARY* .

11. Oripov, F. S., Kurbanova , L. M., & Kurbanov , X. R. (2022). Epithelial barrier of the colon in normal and ulcerative colitis. *Open Access Repository* , *8* (7), 9-16.

12. Sh, B. R., Ch , X. N., & Kiyamov , I. E. (2022). Environmentally Friendly Product is a Pledge of Our Health. *Texas Journal of Multidisciplinary Studies* , *9* , 48-50.

13. Murodullayevna, Q. L. (2022). ICHAK YALLIG'LANISH KASALLIGIDA MORFOLOGIK O'ZGARISHLAR. *Journal of new century innovations* , *15* (3), 236-240.

14. Murodilloevna, K. L., Sur'atovich , O. F., & Deev , R. V. (2024). SPECTRUM OF DISEASES CAUSED BY MORPHO-FUNCTIONAL DISORDERS ORGANIZATION OF ENDOCRINE CELLS IN THE COLON.

15. Chhajer , M., & Kurbonova , L. M. (2024). MODERN THYROID GLAND DISEASES CLINICAL LABORATORY DIAGNOSTIC METHODS. *TADQIQOTLAR. UZ* , *38* (7), 128-130.

16. Sadinovich, U.S., Chhajer , M., & Murodilloyevna , K. L. (2024). COMPARISON OF MORPHOLOGY AND MORPHOMETRIC INDICATORS OF

LIVER TISSUE IN WHITE NONBRED RATS UNDER THE INFLUENCE OF 3 DIFFERENT DRUGS OF ANTI-INFLAMMATORY DRUGS IN NORMAL AND POLYPHARMACY. *TADQIQOTLAR. UZ* , *38* (7), 140-147.

17. Muradkosimov , S., Ermanov , R., Turakulov , J., & Kurbanova , L. (2021). Epidemiological situations of infectious diseases among migrants of the Samarkand region. *Journal of Biomedicine and Practice* , *1* (3/2), 207-211.

18. Kurbanova, L. M., & Kholyarova , G. R. (2024). In both normal and ulcerative colonitis , the epithelium is the colon's barrier.

19. Kurbanova , L. M., Kholyarova , G. R., & Kamalova , M. I. (2023). ISSUES OF DIFFERENTIAL DIAGNOSIS OF INFLAMMATORY AND FUNCTIONAL INTESTINAL DISEASES (LITERATURE REVIEW). *World Bulletin of Public Health* , *21* , 171-174.

20. Kurbanova, L. M., Chhajer , M., & Kholyarova , G. R. (2024). A REVIEW OF THE LITERATURE RELATING TO THE DIFFERENTIAL DIAGNOSIS OF FUNCTIONAL AND INFLAMMATORY INTESTINAL DISEASES.