creased Expression of AZGP1 Is Associated with Poor Prognosis in Primary Gastric Cancer.//PLoS One. 2013 Jul 23;8(7):e69155.

9. **Iwamoto H, Ojima T, Hayata K, Katsuda M, Miyazawa M, Iida T, Nakamura M, Nakamori M, Iwahashi M, Yamaue H.** Antitumor immune response of dendritic cells (DCs) expressing tumor-associated antigens derived from induced pluripotent stem cells: In comparison to bone marrow-derived DCs.// Int J Cancer. 2013 Jul 3. doi: 10.1002/ijc.28367.
10. **Jin L, Sturgis EM, Zhang Y, Huang Z, Song X, Li C, Wei Q, Li G.** Association of tumor necrosis factor-alpha promoter variants with risk of HPV-associated oral squamous cell carcinoma.//Mol Cancer. 2013 Jul 19;12:80.
11. **Kimple RJ, Smith MA, Blitzer GC, Torres AD, Martin JA, Yang RZ, Peet CR, Lorenz LD, Nickel KP, Klingelhutz AJ, Lambert PF, Harari PM.** Enhanced Radiation Sensitivity in HPV-Positive Head and Neck Cancer.//Cancer Res. 2013 Aug 1;73(15):4791–800.
12. **Laffort C, Le Deist F, Favre M, Caillat-Zucman S, Radford-Weiss I, Debré M, Fraitag S, Blanche S, Cavazzana-Calvo M, de Saint Basile G, de Villartay JP, Giliani S, Orth G, Casanova JL, Bodemer C, Fischer A.** Severe cutaneous papillomavirus disease after haemopoietic stem-cell transplantation in patients with severe combined immune deficiency caused by common gammac cytokine receptor subunit or JAK-3 deficiency.// Lancet. 2004 Jun 19;363(9426):2051–4.
13. **Nizard M, Sandoval F, Badoual C, Pere H, Terme M, Hans S, Benhamouda N, Granier C, Brasnu D, Tartour E.** Immunotherapy of HPV-associated head and neck cancer: Critical parameters.// Oncoimmunology. 2013 Jun 1;2(6):e24534
14. **Rietman EA, Friesen DE, Hahnfeldt P, Gatenby R, Hlatky L, Tuszynski JA.** An integrated multidisciplinary model describing initiation of cancer and the Warburg hypothesis.//Theor Biol Med Model. 2013 Jun 10;10:39.
15. **Susman S, Tomuleasa C, Soritau O, Mihu C, Rus-Ciuca D, Sabourin JC, Bibeau F, Irimie A, Buiga R.** The colorectal cancer stem-like cell hypothesis: a pathologist's point of view.//J BUON. 2012 Apr-Jun;17(2):230–6.

THE EPITHELIUM BARRIER OF THE GASTROINTESTINAL TRACT IN PATHOLOGY

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Introduction. We investigated *H. pylori* infection in children patients with gastrointestinal diseases in Vladivostok, Far Eastern Russia. In this study, we further investigated the role of *Helicobacter pylori* infection in lactase deficiency pathogenesis in children. In the pediatric fields, secondary and transient lactase deficiency was seen during clinical practice of different gastrointestinal diseases. Many previous studies have shown the mucosal conditions of small intestine and duodenum in secondary lactase deficiency; however, local immune responses in gastrointestinal tract have not been examined [1–10]. Especially, conditions of gastric mucosa and epithelium in different pathogenetic variants of lactase deficiency in infants and children under 3 years have not been well studied. In this study, we investigated roles of *H.pylori* infection and immune responses of gastric mucosa and epithelium in, pathogenetic aspects of lactase deficiency in children under 3 years.

Methods. Sixty-three pediatric patients (age: 5 months to 3 years) with different loss of weight in Regional Clinical Center of Maternity, Vladivostok, Russia, were also included during 2008–2011. All patients were diagnosed as lactase deficiency. Morphological changes of gastrointestinal mucosa were examined by endoscopy and dark field microscopy. *H. pylori* in biopsy specimens was detected by immunostaining. CD4-, CD8-, CD 68-, CD163-, or CD204-positive immune cells in the specimens were detected by immunostaining.

Results. In our previous study, 89.9% of patients (age, 15 to 80 years) were *H. pylori*-positive, regarding the virulence genotype of *H.pylori*, 79.4% were cagA-positive. As for EPIYA motif of cagA, ABC type was the most prevalent and accounted for 73.2%; ABCC type for 14.6%; AB or ABCCC type for 4.9%, and novel AAABC type for 2.4%. No ABD type was detected.

In this study, 95% of children under 3 years with secondary lactase deficiency were *H. pylori*-positive. We have established changes of immune cell; numbers and condition in cellular and humoral immunity according to clinical manifestations of this disease. Increase of proliferative activity of immune cells in epithelial layers and the cells without contact to epithelial wall in mucosa were found. Immunostaining showed the increase of immune cells positive for CD4, CDS, CD 68, CD163, and CD204 in gastrointestinal epithelium in *H. pylori*-positive lactase deficiency patients.

Discussion. In our previous study, *cagA*-positive *H. pylori* mainly belonged to Western type (EPYIA-ABC type) although Vladivostok is geographically located in East Asia.

Present study is the first investigation of lactase deficiency with H. pylori infection in children under 3 years in Vladivostok, Russia. Our data suggest mechanisms of pathogenicity of lactase deficiency under *H. pylori* infection. Our data are also useful for development of immune response algorithm during medication of those patients and for monitoring of morphological condition of gastrointestinal mucosa in children during various pathologic processes associated with malabsorption and lactase deficiency. Further investigation is required to reveal the exact mechanisms of lactase deficiency under *H. pylori* infection.

References

1. **Ahmad R, Raina D, Trivedi V, Ren J, Rajabi H, Kharbanda S, Kufe D.** MUC1 oncoprotein activates the IkappaB kinase beta complex and constitutive NF-kappaB signalling. Nat Cell Biol 9: 1419–1427, 2007. doi:10.1038/ncb1661.
2. **Al-Sadi R, Ye D, Dokladny K, Ma TY.** Mechanism of IL-1beta-induced increase in intestinal epithelial tight junction permeability. J Immunol 180: 5653–5661, 2008. doi:10.4049/jimmunol.180.8.5653.
3. **Canny G, Levy O, Furuta GT, Narravula-Alipati S, Sisson RB, Serhan CN, Colgan SP.** Lipid mediator-induced expression of bactericidal/permeability-increasing protein (BPI) in human mucosal epithelia. Proc Natl Acad Sci USA 99: 3902–3907, 2002. doi:10.1073/pnas.052533799.
4. **Chibishev A, Simonovska N, Shikole A.** Post-corrosive injuries of upper gastrointestinal tract.//Prilozi. 2010;31(1):297–316.
5. **Dann SM, Eckmann L.** Innate immune defenses in the intestinal tract. Curr Opin Gastroenterol 23: 115–120, 2007. doi:10.1097/MOG.0b013e32803cadf4.
6. **Frank DN, St Amand AL, Feldman RA, Boedeker EC, Harpaz N, Pace NR.** Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proc Natl Acad Sci USA 104: 13780–13785, 2007. doi:10.1073/pnas.0706625104.
7. **Kamada N, Núñez G.** Regulation of the immune system by the resident intestinal bacteria. Gastroenterology 146: 1477–1488, 2014. doi:10.1053/j.gastro.2014.01.060.
8. **Lopetuso LR1, Scaldaferri F, Bruno G, Petito V, Franceschi F, Gasbarrini A.** The therapeutic management of gut barrier leaking: the emerging role for mucosal barrier protectors.// Eur Rev Med Pharmacol Sci. 2015;19(6):1068–76.
9. **Viggiano D, Ianiro G, Vanella G, Bibbò S, Bruno G, Simeone G, Mele G.** Gut barrier in health and disease: focus on childhood.//Eur Rev Med Pharmacol Sci. 2015;19(6):1077–85.
10. **Wells JM, Brummer RJ, Derrien M, MacDonald TT, Troost F, Cani PD, Theodorou V, Dekker J, Méheust A, de Vos WM, Mercenier A, Nauta A, Garcia-Rodenas CL .** Homeostasis of the gut barrier and potential biomarkers.// Am J Physiol Gastrointest Liver Physiol. 2017 Mar 1;312(3):G171–G193. doi: 10.1152/ajpgi.00048.2015.