with 2 weeks in High WNT media and 1 week in differentiation media based on established protocol. Colonoids are present in the model throughout the 3 week culture time. 2 sets of macrophages are added with the first set added after the first week of culture and the second set replacing the first set after the second week.

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GREEN TEA POLYPHENOL EPIGALLOcatechIN-3-GALLATE DIFFERENTIALLY MODULATES ENDOPLASMIC RETICULUM STRESS-MEDIATED WOUND HEALING PROCESS IN SUBEPITHELIAL MYOFIBROBLASTS

Chao Li, John Kuemmerle

Epigallocatechin-3-gallate (EGCG) has multifaceted roles in the preclinical treatment of diseases including liver and lung fibrosis. EGCG has also been tested with fewer reported side effects than therapeutic drugs. Previously we showed that increase in endoplasmic reticulum (ER) stress response in subepithelial myofibroblasts (SEMF) contributes to activation of TGF-β1 and resultant intestinal fibrosis in patients with fibrotic Crohn's disease. Moreover, different migratory potential of myofibroblasts isolated from inflamed, fibrotic, or fistulized Crohn's disease mucosa could be an explanation for impaired or excess wound healing and subsequently for fistula or fibrosis in patients with Crohn's disease. To investigate the effect of EGCG on ER stress-mediated wound healing process, SEMF were isolated from normal ileum and affected ileum in the same patient with Crohn's disease. Cells were cultured and treated with EGCG (10 μg/ml), AG1024 (a tyrosine kinase inhibitor, 6 μM), U1026 (an ERK inhibitor, 6 μM), LY294002 (a PI3K inhibitor, 10 μM), SB202190 (a p38 inhibitor, 50 nM), 4-PBA (a chemical chaperone, 10 μg/ml), and MG132 (a NF-KB inhibitor, 3 μM) for 2 hours in serum free medium. Cell lysates were obtained for Western blot analysis. An ER stress agonist tunicamycin (5 μg/ml) was incubated with SEMF for different time points. Wound healing assay was used in a cell monolayer, capturing the images at the beginning and at regular intervals during cell migration to close the wound, and comparing the images to quantify the migratory potential of the cells. In vivo effect of EGCG was tested in a murine TNBS colitis model and observed by Storz Coloview standard operating procedures. Here we showed that EGCG further decreased endogenous GRP78 protein expression by 18-29±1.5% in SEMF compared to that treated with different inhibitors targeting other non-ER stress signals. EGCG prevented tunicamycin-induced migratory potential of SEMF isolated from normal ileum by 40±2.5%, 65±3.3% after 48 and 72 hours, as well as cell proliferation by 85±3.3%, 120±6.1% after 48 and 72 hours, respectively. Moreover, EGCG also further decreased cell migratory potential of SEMF isolated from affected ileum by 15±2.1% and 50±1.8% compared to the control group after 48 and 72 hours, respectively. Coloview showed that EGCG decreased inflammatory activity in the mice colon compared to TNBS colitis group after 8-week treatment. Ongoing study includes methylene blue staining of the colonic mucosa during endoscopy, endoscopic scoring of inflammation activity, and trichrome staining of collagen production in a colonic biopsy. Taken together, EGCG alleviates ER Stress response, leads to greater inhibition of migratory potential of SEMF, and decreases TGF-β1 and collagen productions, which is the major molecular feature of fibrosis.

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TARGETED COLON DELIVERY OF NIPEP-IM-0127 PEPTIDE FOR INFAMMATORY BOWEL DISEASE (IBD) TREATMENT

Deogil Kim, Dong Woo Lee, Beom Soo Jeon, Young Seong Park, Dong Hyeon Pyung Chung

Under inflammatory bowel disease (IBD), autoantibody-type VII collagen complex can induce autoimmune reaction and continue with the inflammation. Here, we introduced synthetic 19 amino acid sequenced peptide termed as NIPEP-IM-0127 that inhibits autoantibody-type VII collagen complex formation. The NIPEP-IM-0127 was further formulated for oral administration. Primary function of NIPEP-IM-0127 selectively localizes to wound gut barrier and masks exposed type VII collagen, which is the starting of autoimmune reaction. Disrupted type VII collagen by the disease was bound to the applied peptide, which interfere autoimmune complex formation by competitive binding inhibition between antibody and peptide. NIPEP-IM-0127 thus recovered inflammatory cytokine level by the inhibition of immune complex creation. The orally applied NIPEP-IM-0127 peptide was primarily detected at the surface of colon tissue after 9 hours of administration, while no distributions were shown in other organs. Most importantly, significant mucosal regeneration and healing has been achieved by NIPEP-IM-0127. The following GLP toxicity studies, including safety pharmacology, genotoxicity, single and repeated dose toxicity, demonstrated that NIPEP-IM-0127 showed no significant toxic effect in in mouse and monkey. Taken together, the NIPEP-IM-0127 is suggested to be a novel therapeutic candidate for IBD treatment by the dual effects combining immune modulation and intestine barrier healing.

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A NEW TREATMENT APPROACH FOR INFLAMMATORY BOWEL DISEASE: INTRACOLONIC BIFIDOBACTERIUM AND XYLOGLUCAN APPLICATION

Huseyin Bozkurt

Background: Inflammatory bowel disease (IBD) pathogenesis includes the altered gut microbiota, environmental factors, human immune responses and genetic. Reduced bifidobacteria level is associated with IBD. Xyloglucan is a plant based prebiotic oligosaccharide. Bifidobacteria level is increased in the presence of xyloglucan.

In this article we aim to share the results of our cases; Ulcerative colitis (UC) patients treated by intracolonic single administration of *Bifidobacterium animalis* subsp. *lactis* and Xyloglucan combination with colonoscopic laboratory and clinical examination.

Results: Age, sex, diagnosis, disease location, previous medications are summarized in Table 1. All the patients had active ulcerative colitis disease before the administration. The Mayo Score was used to assess the severity of UC. 2 cases had extensive colitis and 8 patients had left-sided colitis. After 6 weeks of the administration mucosal healing and resolution of colonic symptoms were seen. These results are summarized in Table 2. Of the 10 cases, 7 were undertaken 5-ASA +Azathiopurine and three were undertook vedolizumab treatment. Intracolonic single *Bifidobacterium animalis* subsp. *lactis* and xyloglucan administration was found effective in the mucosal healing and resolution of colonic symptoms in ulcerative colitis patients. Conclusions: Herein we reported the importance of Bifidobacterium and xylooligosaccharide combination in IBD. Colonoscopic single *Bifidobacterium animalis* subsp. *lactis* and xyloglucan administration is a new method that has no side effect and easy to apply for treatment of IBD. This application might provide enhancement of non-stimulatory status and higher biodiversity in colonic mucosa so mucosal healing may be improved rapidly. However, it would be necessary to develop diagnostic strategies in order to discriminate which patients would benefit from this strategy.