**K-LG-07** Lower GI Tract

**Biologic Implication of ZKSCAN3 in Terms of Invasiveness for Colorectal Cancers**

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**Background:** We evaluated the role of ZKSCAN3 in invasive signaling pathway with stage 4 colorectal cancer (CRC).

**Methods:** We investigated CRC patients who were curatively resected from 2011 to 2013. A total of 80 patients were included in this study. The expression level of ZKSCAN3 was analyzed by Western blot and RT-PCR.

**Results:** The expression of ZKSCAN3 was significantly higher in the primary tumor compared to the metastatic tissues. The expression of ZKSCAN3 was also positively correlated with the Ki-67 index and negatively correlated with the expression of Mcl-1.

**Conclusions:** ZKSCAN3 plays a crucial role in the invasion of colorectal cancer cells.

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**K-LG-08** Lower GI Tract

**Myeloid Cell Leukemia-1 is Associated with Tumor Progression by Inhibiting Apoptosis and Enhancing Angiogenesis in Colorectal Cancer**

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**Background:** Myeloid cell leukemia-1 (Mcl-1) is a highly expressed anti-apoptotic Bcl-2 protein in cancers. Inhibition of its expression induces apoptosis in cancer cells and enhances sensitivity to cancer treatment.

**Methods:** We investigated the expression of Mcl-1 in 195 patients with colorectal cancer. The expression of Mcl-1 was analyzed by Western blot and RT-PCR.

**Results:** The expression of Mcl-1 was significantly higher in the primary tumor compared to the metastatic tissues. The expression of Mcl-1 was also positively correlated with the Ki-67 index and negatively correlated with the expression of ZKSCAN3.

**Conclusions:** Mcl-1 plays a crucial role in the progression of colorectal cancer.

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**K-LG-09** Lower GI Tract

**Effects of Genetic Variation of Mir-146a on Inflammatory Bowel Disease**

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**Background:** Currently, inflammatory bowel disease (IBD) is considered to be caused by complex interactions of genetic, environmental, and other processes involving immunoregulatory factors. Given the large number of microRNAs (miRNA) annotated in the human genome, 30%-80% of human genes are predicted to be influenced by miRNAs. Among these miRNA, mir-146A acts as a negative feedback regulator to limit TLRF and IRAK/1 mediated signaling and as amplifier to upregulate NO signaling and NO in inflammatory settings. The aim of this study was to investigate the association between miRNA and the chronic inflammation in the Korean population with IBD.

**Methods:** Genotyping of miRNA SNPs rs2910164 (mir146A), rs6505162 (mir423), rs9585189 (mir27A), rs1674913 (mir164A2), and rs3746444 (mir499) was performed in 195 patients with Crohn’s disease (CD), 241 patients with ulcerative colitis (UC), and 149 healthy controls using TaqMan genotyping assays. We checked the mirRNA level and stability using TaqMan real time RT-PCR, FACS analysis, and cell imaging after transfection of miRNA into HT-29 cell, intestinal epithelial cells (IECs), or Jurkat T cell.

**Results:** Among five miRNA, only mir-146A SNP, rs2910164, is significantly correlated patients with UC (P < 0.009 OR: 1.75 (1.14-2.67) in dominant model). mir-146A-B (mir-146A with G allele) displayed increased stability compared with mir-146A-C. mir-146A suppressed the proliferation of HT-29 cell via suppression of EGF signaling, whereas mir-146A increased the proliferation of Jurkat T cell.

**Conclusions:** We have identified the correlation between the variation of mir-146A and UC that established different mechanism between immune cell and IECs. novel molecular regulators identified in the current study would thus serve the possibility of developing better regime to treat IBD pathophysiology.

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**K-LG-10** Lower GI Tract

**The Differential Expressions of Ihom1/2 for Maturation of Tace in Inflammatory Bowel Disease**

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**Background:** TNF-α converting enzyme (TACE) regulates the release of TNF-α and EGFR ligands. Recently, inactive rhomboid protein 2 (Ihom2) was identified as essential for TACE maturation in immune cells. In the aim of this study was to investigate roles of Ihom1/2 for TACE maturation in inflammatory bowel disease (IBD).

**Methods:** Colonic epithelial cells, COLO205, and murine macrophage, RAW264.7, were stimulated with lipopolysaccharide (LPS), and the expressions of Ihom1/2 and TACE were evaluated by RT-PCR and Western blot. For in vivo models, DSS-treated and IL-10 deficient mice were used as acute and chronic colitis, respectively. Colonic biopsy was performed in patients with IBD. The expressions of Ihom1/2 and TACE were determined by RT-PCR and immunohistochemistry in both murine models and IBD patients. Double immunofluorescence staining of Ihom2 and F4/80 was performed in DSS colitis model to define cells expressing Ihom2.

**Results:** In LPS-stimulated COLO205 and RAW264.7, the mRNA and protein expressions of Ihom1/2 and TACE were up-regulated, and the Ihom2 expressions in RAW264.7 were higher than those in COLO205. In acute and chronic murine colitis, the mRNA expressions of Ihom1/2 and TACE were higher than those in controls. For IBD patients, the Ihom1/2 and TACE mRNA expressions increased compared to healthy controls. In both murine colitis and IBD patients, immunohistochemical analysis revealed the increased expression of Ihom2 of inflammatory cells in lamina propria and submucosa. In contrast, the Ihom1 expression was low in inflammatory cells. The double immunofluorescence staining showed that cells highly expressing Ihom2 were macrophages.

**Conclusions:** Ihom2 may play a critical role for TACE maturation and TNF-α secretion in immune cells of colitis, which suggests that Ihom2 could be a novel target for the treatment of IBD.