Crohn's disease (CD) is obscure. The aim of the study is to identify the expression and function of TLE1 in CD.

Methods TLE1 expression was detected in peripheral blood mononuclear cells (PBMC) and intestinal biopsies (diseased/non-diseased mucosae) in 43 patients with active ulcerative colitis (UC), 40 patients with active CD and 37 healthy controls (HC) by real-time polymerase chain reaction or immunohistochemistry. We transfected TLE1-siRNA into HEK293, SW480 and LoVo cells to inhibit TLE1 expression and then to detect cell apoptosis by FITC Annexin V/PI and Hoechst staining. Apoptosis-related and autophagy-related proteins were tested by Western blot, and co-immunoprecipitation (Co-IP) was conducted to study the interaction of TLE1 and autophagy-related proteins.

Results TLE1 mRNA expression significantly decreased in both PBMC ($p=0.030$) and intestinal tissues (diseased mucosae: $p=0.028$; non-diseased mucosae: $p=0.031$) in active CD compared to HC. Protein expression of TLE1 in active CD's intestinal biopsies, especially in diseased tissues, was also lower than it in active UC and HC (figure 1). Cell experiments showed that Cleaved caspase-3 and Cleaved caspase-9 was markedly upregulated and cell apoptosis was highly activated after TLE1 silencing. In addition, the decrease of LC3-II/I value and the increase of ATG16L1 degradation were observed, indicating the inhibition of autophagy formation. Co-IP in HEK293 cells revealed the possible direct interaction of TLE1 and ATG16L1/ATG7 proteins.

Conclusions There is a significant and specific decrease of TLE1 in active CD. Its low expression promotes cell apoptosis by upregulating Cleaved caspase-3 and Cleaved caspase-9 as well as induces aberrant autophagy by activating ATG16L1 degradation. TLE1 may directly interact with ATG16L1 or ATG7. TLE1 could be promisingly introduced as a new study target in CD pathogenesis and a potential biomarker for CD diagnosis.

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KLF13 REGULATES CRC DEVELOPMENT VIA CHOLESTEROL BIOSYNTHESIS

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Background Colorectal cancer (CRC) is one of the most common malignancies worldwide. The Kruppel-like factors (KLFs) are a set of zinc finger DNA-binding proteins that regulate gene expression. It has been reported that KLFs play important roles in cancer development. However, the role of KLF13 in CRC remains unclear. In this study, we investigated the involvement of KLF13 in CRC development.

Methods Lentivirus-mediated knockdown was used to silence KLF13 in CRC cells. Protein alterations were detected with Western blotting. Gene expression of tissues was detected by qPCR. Growth-inhibitory effects on CRC cells were evaluated in vitro with cell number estimation and colony formation assay.

Results We found that KLF13 was down-regulated in CRC tissues comparing with the normal tissues based on the TCGA database and our qPCR results. We used lentivirus-mediated knockdown to silence KLF13 in CRC cells. KLF13 down-regulation promoted the proliferation and colony growth of both HCT-116 and HT-29 cells. Cholesterol content in CRC cells was increased after KLF13 knockdown. At the molecular level, KLF13 negatively regulated the expression of 7-Dehydrocholesterol reductase (DHCR7), which is critical for the sterol biosynthesis that converts 7-dehydrocholesterol (7-DHC) to cholesterol. We also found that cholesterol biosynthesis inhibitors reduced the colony growth of HCT-116 and HT-29 cells.

Conclusions Our study highlights the important role of KLF13 in regulating cholesterol biosynthesis and CRC development.

Abstract IDDF2019-ABS-0275 Figure 1 Staining images and immunohistochemical scores of TLE1 in diseased and non-diseased intestinal mucosae of active Crohn's disease and ulcerative colitis patients compared to healthy controls