binding to proteins and regulating cellular metabolism. The aim of this study was to identify a certain lncRNA promoting the progress of advanced colorectal cancer (CRC) with a therapeutic perspective.

Methods We screened out highly expressed lncRNAs using samples from patients with stage IV CRC compared with matched adjacent normal tissues. The proteins interacted with linc00920 was confirmed with RNA pull-down and mRNA immunoprecipitation (RIP) assay. The proliferation and metabolic alteration of CRC under linc00920 inhibition were tested in vitro and in vivo.

Results Linc00920 was upregulated in CRC with poor overall survival and inhibition of linc00920 resulted in impaired growth of CRC cell lines. Moreover, knocking down of linc00920 was consistent with a lower level of insulin-like growth factor 2 mRNA-binding protein 2 (IGF2BP2), which is known as a m^6A ‘reader’ and mRNA stabilizer. Linc00920 bound to the ubiquitination sites of IGF2BP2 and prevented its autophagic degradation, maintaining the MYC-mediated glycolysis in CRC. Moreover, inhibition of linc00920 suppressed the proliferation of tumors from patient-derived xenograft (PDX) models.

Conclusions Linc00920-IGF2BP2-MYC axis promotes the progress of CRC as a promising therapeutic target.

IDDF2019-ABS-0269 OVEREXPRESSION OF PDEF SUPPRESSES CELL AGGRESSIVENESS IN COLORECTAL CANCER
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Background Prostate-derived Ets factor (PDEF) belongs to the Ets family of transcription factors. It plays an important role in tumorigenesis and progression of many tumors such as prostate cancer, breast cancer, and gastric cancer. However, its biological function in colorectal cancer (CRC) is still unclear.

Methods A lentivirus vector overexpressing PDEF was constructed and transfected into SW620 cells with lipofectamine. In order to knock down the expression of PDEF, PDEF-custom si-RNA was transfected into SW620 cells. The expression level of PDEF was detected by western blot and real-time-polymerase chain reaction. The proliferation, invasion, migration and cell cycle of SW620 cells were investigated after transfection. Meanwhile, transfected SW620 cells were subcutaneously injected into nude mouse, and the specimens were harvested from the injection site for histological analysis after six-weeks injection.

Results Cell proliferation was significantly inhibited when PDEF was overexpressed. Transwell tests showed that PDEF overexpression could suppress the migration and invasion of SW620 cells. In contrast, the ability of proliferation, migration and invasion became stronger when PDEF was knocked down. Further flow cytometry showed that overexpression of PDEF could reduce the ratio of cells at the G2/M phase. In addition, subcutaneous transplanted tumors overexpressing PDEF in the xenograft model were significantly smaller than the control group.

Conclusions Overexpression of PDEF could inhibit the proliferation and invasion of CRC cell in vitro and in vivo. Our study suggested that PDEF could serve as a potential tumor biomarker and drug target in CRC.

IDDF2019-ABS-0270 ECT2 INCREASES EGFR EXPRESSION AND TUMORIGENICITY BY PROMOTING CDC42 ACTIVITY IN PANCREATIC CANCER
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Background The poor prognosis of patients with pancreatic ductal adenocarcinoma (PDAC) is partially attributed to the invasive and metastatic behavior of this disease. Epithelial cell transforming 2 (ECT2) is a guanine nucleotide exchange factor (GEF) of the Rho family of GTPases. It has also been reported that upregulation of ECT2 in pancreatic cancer, but the role and mechanism of ECT2 have not been previously determined.

Methods Expression of ECT2 in PDAC and PDAC cell lines was characterized using immunohistochemistry and Western blotting. ECT2 was overexpressed via retroviral transduction and knocked down in PDAC cells using shRNA. Cell proliferation was determined using a colorimetric cell viability assay, and cell migration and invasion using transwells. Expression of markers of epithelial-mesenchyme transition (EMT) was assayed by Western blotting. ECT2 and cell division cycle 42 (Cdc42) were interrogated by immunoprecipitation and Western blot. The functional role of Cdc42 was determined using siRNA.

Results We found ECT2 was significantly upregulated in PDAC tissues and cells, correlated with more advanced clinicopathological features. ECT2 regulated invasion and migration of PDAC cells in vitro and in vivo. ECT2 silencing downregulated EGFR expression via accelerating EGFR degradation in pancreatic cancer cells. Immunoprecipitation assay further confirmed that ECT2 interacted with Cdc42. More importantly, ECT2 silence markedly decreases Cdc42 activity. The promoting effect of ECT2 on migration can be decreased by the siRNA against Cdc42.

Conclusions Overall, this study shows that ECT2 increases EGFR and promotes tumorigenicity of pancreatic cancer cells by enhancing Cdc42 activity.

IDDF2019-ABS-0275 DECREASED EXPRESSION OF TLE1 PROMOTES CELL APOPTOSIS AND INDUCES ABERRANT AUTOPHAGY IN CROHN’S DISEASE
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Background Transducin-like enhancer of split 1 (TLE1) has been reported as co-repressor of multiple transcriptional factors. The association between TLE1 and the pathogenesis of
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.

IDDF2019-ABS-0277

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.