IDDF2018-ABS-0230 TRANSGLUTAMINASE 2 MODULATES INFLAMMATION-ASSOCIATED ANGIOGENESIS VIA VEGFR2 PATHWAY IN CROHN'S DISEASE

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Background Angiogenesis is a vital component of the pathogenesis of inflammatory bowel disease (IBD). Vascular endothelial growth factor A (VEGF-A) and its receptors VEGFR2 are the pivotal component of angiogenesis in IBD. Recent studies suggest that transglutaminase 2 regulates angiogenesis in cancer and physiological conditions through VEGFR2 pathway. However, whether transglutaminase 2 are involved in this process of IBD remains elusive.

Methods We use real-time PCR and Western blotting to validate the expression of TGM2 in CD patients' biopsy samples and TNBS-induced murine colitis. Furthermore, we use immunohistochemistry and immunofluorescence of surgical specimen and TNBS/DSS-induced murine colitis section to investigate the location of TGM2 in CD. To investigate the role of TGM2 in CD, human intestinal microvascular endothelial cells (HIMEC) and mouse intestinal microvascular endothelial cells (MIMEC) was treated with inflammatory cytokines. Finally, TNBS murine colitis model was treated with IL-9 neutralising antibody and weight loss, intestine length, as well as microvessel density, was evaluated after treatment.

Results We found that the TGM2 was up-regulated in colonic mucosa of CD patients and TNBS-induced colitis. In addition, TGM2 expression mainly locates in microvessel. (figure 1) Furthermore, after treating with IL-9, TGM2 and VEGFR2 were significantly upregulated in HIMEC and MIMEC. In contrary, weight loss, intestine length, as well as microvessel density in TNBS murine colitis model, was significantly improved after treating with IL-9 neutralising antibody.

Conclusions Our findings provide new evidence that TGM2 plays an important role in angiogenesis in CD, thus TGM2 may represent a novel therapeutic target for IBD.

IDDF2018-ABS-0231 ACIDOSIS PROMOTES THE STEMNESS OF CANCER STEM CELLS THROUGH VITAMIN D-VITAMIN D RECEPTOR SIGNALLING PATHWAY IN COLORECTAL CANCER

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Background The tumour recurrence, metastasis and treatment resistance of colorectal carcinoma (CRC) are closely related to acidic tumour microenvironment and colorectal cancer stem cells (colorectal CSCs). Here we identified the regulatory effects of the acidic tumour microenvironment on vitamin D receptor (VDR) and the regulation of the signal axis on the self-renewal of colorectal stem cells.

Methods Using western blotting and relative quantitative PCR to detect VDR expression in 43 pairs of normal and CRC samples and acidic condition. Self-renewal ability of colorectal CSCs was detected by sphere formation assay, limited dilution assay and flow cytometry. Chromatin immunoprecipitation, *gain of function* and *loss of function* assay was used to screen the target genes of VDR and their effects on colorectal CSCs.

Results Firstly we found VDR mRNA decreased under acidic condition. And the expression of VDR in CRC tissue compared to adjacent normal tissue was decreased significantly. In addition, the VDR protein expression was the lowest in colorectal CSCs compared to normal, and CRC cells, VDR expression in colorectal cancer cells with strong metastatic ability was also reduced. Over-expressing VDR in CRC sample cell line resulted in decreased cell migration and invasion ability. The proportion of PROM1 (prominin 1) positive cells decreased when over-

Abstract IDDF2018-ABS-0230 Figure 1