CO-ORGANIZED EVENT

13th International Conference on Clinical Gastroenterology & Hepatology
&
2nd International Conference on Digestive Diseases

December 07-08, 2017 Madrid, Spain

Characterization of novel mouse model of gastrointestinal cancer

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Colorectal cancer (CRC) is one of the most common cancers and a leading cause of cancer-related death in worldwide. Several decades effort have revealed that the development and progression of colorectal cancer is linked to the oncogenic signaling activation, particularly, the activation of Wnt/β-catenin or chronic colitis-associated inflammatory signaling, etc. We have found that PRSS8 was significantly reduced in esophageal and colorectal cancers and acted as a tumor suppressor in colitis-associated colorectal cancer through targeting Sphk1/Stat3/Akt signaling pathway. To determine the roles of PRSS8 in colorectal cancer in vivo, we developed a conditional knockout mouse model - Intestine-specific deletion of Prss8 in mice (Prss8 fl/fl-Cre+, Prss8 CKO), and found that PRSS8 deletion caused spontaneous formation of colitis and intestinal tumors. At the age of about 3 months, about 20% of the Prss8 CKO mice exhibited inflamed rectum and then exerted rectal prolapse. Histopathologic analysis showed that 60% Prss8 CKO mice had developed chronic inflammation in large intestine at 3 months. Interestingly, 45% Prss8 CKO mice had developed hyperplasia in small intestine at 3 months. At the age of 6 months, 80% of the Prss8 CKO mice developed adenomas, and at the age of nine months, 100% of the Prss8 CKO mice developed adenomas. Further studies showed that gastrointestinal tumorigenesis was linked to the Disruption of intestinal epithelial cell maturation: more proliferative cells and moved faster in the Prss 8 CKO mouse, assayed by BrdU staining and migration assay. Moreover, Prss 8 CKO mouse intestine exhibited less mature mucin drops and goblet cells at the crypts of small and large intestine in comparison with the WT mice. Gene profile using mouse intestinal epithelial cells and gene set enrichment analysis showed that the tumorigenesis was associated with oncogenic signaling pathways, including Wnt/beta-catenin and inflammatory signaling. The underlying mechanisms are under further investigation.

Biography

Yonghua Bao has completed her graduation from Jiamusi Medical University, China with a Clinical Medicine background, PhD in Biochemistry and Molecular Biology from Jilin University and Post-doctoral training in Biochemistry and Molecular Biology at the State Key Laboratory of China Agricultural University.

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