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Genetic and epigenetic alterations in chronic colitis malignant transformationWancai Yang^{1,2} and Yonghua Bao¹¹University of Illinois at Chicago, USA²Jining Medical University, China

Chronic colitis malignant transformation is one of major causes to colorectal cancer, but the mechanisms of colitis develops and how the chronic colitis progress to malignance is largely unknown. Using a unique mouse model, we have demonstrated that the mice with targeted disruption of the intestinal mucin gene *Muc2* spontaneously develop chronic inflammation at colon and rectum at early age, whose histopathology was similar to ulcerative colitis in human. In the aged mice, *Muc2*^{-/-} mice develop colonic and rectal adenocarcinoma accompanying severe inflammation. To determine the mechanisms of the malignant transformation, we conducted miRNA array on the colonic epithelial cells from *Muc2*^{-/-} and *+/+* mice. MicroRNA profiling showed differential expression of miRNAs (i.e. lower or higher expression enrichments) in *Muc2*^{-/-} mice. Based on relevance to cytokines and cancer, the miRNAs were validate and were found significantly downregulated or upregulated in human colitis and colorectal cancer tissues, respectively. The targets of the miRNAs were further characterized and their functions were investigated. More studies from the *Muc2*^{-/-} mice showed disorder of gut microbiota. Moreover, a novel tumor suppressor PRSS8 also plays a critical role in colorectal carcinogenesis and progression, for instance, tissue-specific deletion of the PRSS8 gene resulted in intestinal inflammation and tumor formation in mice. Gene set enrichment analysis showed that the colitis and tumorigenesis were linked to the activation of Wnt/beta-catenin, PI3K/AKT and EMT (epithelial-mesenchymal transition) signaling pathways. Taken above, the disorder of gut microbiota could result in genetic mutations, epigenetic alterations, leading to the activation of oncogenic signaling, in colorectal epithelial cells, and finally, to colitis development, promoting malignant transformation and mediating colorectal cancer metastasis.

Biography

Wancai Yang is the Dean of the Institute of Precision Medicine and School of Basic Medical Sciences, Jining Medical University, China, and a Professor of Pathology, University of Illinois at Chicago, USA. He is also an Adjunct Professor of Biological Sciences, University of Texas, El Paso, USA. He obtained his MD degree and was trained as a Pathologist from China and received Post-doctoral training on Cancer Biology from Rockefeller University and Albert Einstein Cancer Center, US, and was promoted as Assistant Professor. In 2006, he moved to the Department of Pathology, UIC and serving as a Grant Reviewer for the National Institutes of Health (USA) and the National Nature Science Foundation of China. His research focuses on: (1) the determination of mechanisms of gastrointestinal carcinogenesis, (2) identification of biomarkers for cancer detection and patient selection for chemotherapy, (3) implication of precision medicine in cancers. He has published more than 80 peer-reviewed articles and has brought important impact in clinical significance.

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