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Chronic colitis and colitis-associated colorectal carcinogenesis

The activation of Wnt/beta-catenin signaling pathway and chronic colitis malignant transformation are the two major causes to colorectal cancer. The former is well studies, but the mechanisms of colitis develop and how 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 validated and were found significantly down-regulated or up-regulated 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 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 and activation of oncogenic signaling in colorectal epithelial cells, leading 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 has obtained his MD degree and was trained as a Pathologist from China and received his Postdoctoral training on Cancer Biology from Rockefeller University and Albert Einstein Cancer Center and then worked as an Assistant Professor. In 2006, he moved to the Department of Pathology, University of Illinois at Chicago. His research focuses on the determination of mechanisms of gastrointestinal carcinogenesis, identification of biomarkers for cancer detection and patient selection for chemotherapy and implication of precision medicine in cancers. He has published about 90 articles and has brought important impact in clinical significance.

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