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## Serine protease PRSS8 in gastrointestinal inflammation and tumorigenesis

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PRSS8 is glycosylphosphatidylinositol-anchored serine protease, has physiological and pathophysiological functions and shows important roles in the epidermal barrier function and in the regulation of glucose homeostasis. However, the biological functions of PRSS8 in cancer initiation and progression are unknown. 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 intestinal inflammation and tumors. At the age of 3 months, about 20% of the PRSS8 CKO mice exhibited inflamed rectum and then exerted rectal prolapse. Histopathologic analysis showed that 65% 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, 53 % of the PRSS8 CKO mice developed adenomas, and at the age of 9 months, 75% 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 PRSS8 CKO mouse, assayed by BrdU staining and migration assay. Moreover, PRSS8 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.

### Recent Publications

1. Bao Y, Wang Q, Guo Y, Li, K, Yang Y, Chen Z, Zhang H, Dong H, Shen K, Yang W (2016) PRSS8 methylation and its significance in esophageal squamous cell carcinoma. *Oncotarget* 7(19):28540-55
2. Bao Y, Li K, Guo Y, Wang Q, Li Z, Yang Y, Chen Z, Wang J, Zhao W, Zhang H, Chen J, Dong H, Shen K, Diamond AM and Yang W (2016) Tumor suppressor PRSS8 targets Sphk1/S1P/Stat3/Akt signaling in colorectal cancer. *Oncotarget* 7(18):26780-92
3. Bi X, Shi Q, Zhang H, Bao Y, Hu D, Pohl N, Fang W, Dong H, Xia X, Fan D, and Yang W (2016) c-Jun NH2-terminal kinase 1 interacts with vitamin D receptor and affects vitamin D-mediated inhibition of cancer cell proliferation. *J Steroid Biochem Mol Biol.* 163:164-72.
4. Guo Y, Bao Y, Ma M and Yang W (2017) Identification of Key Candidate Genes and Pathways in Colorectal Cancer by Integrated Bioinformatical Analysis. *Int. J. Mol. Sci.* 18(4):722.
5. Guo Y, Bao Y and Yang W (2017) Regulatory miRNAs in Colorectal Carcinogenesis and Metastasis. *Int. J. Mol. Sci.* doi:10.3390/ijms18040890

### 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. She was promoted to Associate Professor and worked in cancer and cell signal transduction lab since 2012. She was recruited by Jining Medical University as a Professor of Pathology in 2015, and was appointed as Vice Dean of Institute of Precision Medicine. Her study focuses on cancer biology and cell signaling pathways in gastrointestinal carcinogenesis, progression and metastasis. As Principal Investigator, she was funded by the National Natural Science Foundation of China. She has published 22 papers and was awarded three patents.

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