

## **Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome**

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Obesity is associated with an increased risk of several types of cancer, but the mechanisms connecting obesity and tumorigenesis remain poorly understood. Here, we show that dietary or genetic obesity induces alterations of gut microbiota, thereby increasing the levels of deoxycholic acid (DCA), a gut bacterial metabolite known to cause DNA damage in mice. The enterohepatic circulation of DCA provokes DNA damage and consequent cellular senescence in hepatic stellate cells (HSCs), which in turn, secretes various inflammatory and tumour promoting factors in the liver, thus facilitating hepatocellular carcinoma (HCC) development in mice after exposure to chemical carcinogen. Interestingly, signs of senescence-associated secretome were also observed in the HSCs in the area of HCC arising in patients with non-alcoholic steatohepatitis (NASH), implying that a similar pathway may contribute to at least certain aspects of obesity-associated HCC development in humans as well.

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### EDUCATIONS/TRAINING

1987	Tokyo University of Science, Japan, BSc.
1989	Tokyo University of Science Graduate School, Japan, MSc.
1993	Tokyo University of Science Graduate School, Japan, Ph.D.

### POSITIONS AND HONORS

1993-1994	Postdoctoral Fellow, University of California, Berkeley, USA
1995-1997	Postdoctoral Fellow, Imperial Cancer Research Fund Laboratories, UK
1998-2003	Group Leader, Paterson Institute for Cancer Research, UK
2003-2008	Professor, Institute for Genome Res., University of Tokushima, Japan
2008 - Present	Chief, Cancer Institute, Japanese Foundation for Cancer Research, Japan
2005	Inoue Foundation for Science, Inoue Fellow
2012	Japanese Foundation for Cancer Research, Academic Award

### RECENT PUBLICATIONS

1. Yoshimoto S, Loo TM, Atarashi K, Kanda H, Sato S, Oyadomari S, Iwakura Y, Oshima K, Morita H, Hattori M, Honda K, Ishikawa Y, Hara E and Ohtani N. Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome. *Nature* 499: 97-101, 2013.
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