＊＊平成 27 年度医学・生命科学セミナー／D1 Medical & Life Science Seminar, 2015＊＊

The role of cellular senescence in vivo: a link between obesity-induced gut microbiota and liver cancer through SASP

Title has been changed.
演題が変更になりました。

- **Lecturer: Prof. Naoko OHTANI[1, 2]**

([1] Department of Applied Biological Science, Faculty of Science and Technology, Tokyo University of Science
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- **Date: October 21st (WED) from 17:30.**
- **Place: Lecture room 2, Medical Education & Library 3 Floor.**

- 講師：大谷　直子　先生
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- 日時：平成 27 年 10 月 21 日（水）17:30
- 場所：医学教育図書棟 3 階　第 2 講義室

Over the past few decades, obesity has become more prevalent in most developed countries, and is increasingly recognized as a risk factor of cancer. Although several events were proposed to be involved in obesity-associated cancer, the exact molecular mechanisms that integrate these events have remained largely unclear. Recently, we found that senescence-associated secretory phenotype (SASP) has crucial roles in promoting obesity-associated hepatocellular carcinoma (HCC) development in mice. 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. The enterohepatic circulation of DCA provokes SASP phenotype in hepatic stellate cells (HSCs), which in turn secretes various inflammatory and tumor-promoting factors in the liver, thus facilitating HCC development in mice after exposure to chemical carcinogen. Notably, blocking DCA production or reducing gut bacteria efficiently prevents HCC development in obese mice. Similar results were also observed in mice lacking an SASP inducer or depleted of senescent HSCs, indicating that the DCA-SASP axis in HSCs has key roles in obesity-associated HCC development. Moreover, signs of SASP were also observed in the HSCs in the area of HCC arising in patients with non-alcoholic steatohepatitis, indicating that a similar pathway may contribute to at least certain aspects of obesity-associated HCC development in humans as well[1)].

[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, Ohtani N.
Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome. **Nature** 499,97-101 (2013)

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