

International Conference on Innate Immunity

July 20-21, 2015 Barcelona, Spain

Bacterial stimulated innate immunity against cancer metastasis

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Metastasis is the most lethal feature of cancer. More than 90% of cancer patients die from secondary cancerous growths. Long-term dormancy, drug resistance and multiple growths all contribute to deadly side of metastasis. We have been engineering *Salmonella typhimurium* for cancer therapy and successfully developed a tumor-hypoxia targeting strain YB1, whose growth is strictly regulated by oxygen. Administration of YB1 to tumor-bearing mice partially inhibits the growth of primary tumor, but impressively, largely reduces lung metastasis. To investigate how YB1 treatment affects the process of metastasis, we set up orthotopic and experimental metastasis models on either immunocompetent or immunodeficient mice. The overall process of metastasis includes localized invasion, intravasation, circulation, extravasation and colonization. By implanting mouse breast cancer cells to mice and treating with YB1 at different stages of metastasis, we find that only treatments taken at early stages could reduce lung metastasis. Experimental metastasis model demonstrates further that YB1 treatment interferes with the colonization process of cancer cells to lung, thus reducing metastasis. Direct cytotoxicity of *Salmonella* to cancer cells is excluded as the anti-metastasis mechanism. The proinflammatory cytokine storms induced in tumor and blood circulation by YB1 contribute to the reduction of metastasis. After cytokine storms are induced, intravenously injected 4T1 cells are not able to colonize and form lung metastasis. The same phenomenon can be observed even on immunodeficient NOD SCID mice, indicating that the innate immunity is sufficient to reduce lung metastasis. These results demonstrate the potential of using bacteria as immunotherapy against cancer metastasis.

Biography

Jian dong Huang has completed his PhD at the age of 29 years from University of California, Los Angleles and postdoctoral studies from NCI, NIH. He is the director of Center of Synthetic Biology and Engineering, Shenzhen Institute of Advanced Integration Technology, Shenzhen, China. He has published more than 100 papers in reputed journals and has been serving as Professor at the University of Hong Kong.

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