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Regulation of TP63 α /sonic hedgehog axis in n-dimethylnitrosamine-induced liver cancer stem cells

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Nitroso-compounds are critical dietary risk factor of liver cancer. Cancer stem cells (CSCs) play a significant role in the formation and development of cancer. To date, the action of nitroso-compounds on the induction of liver CSCs as well as the underlying mechanisms has not been defined. In the present study, we revealed that chronic N-nitroso dimethylamine (NDMA) exposure induced malignant transformation of human normal liver cells. We further showed that NDMA-induced malignant transformed liver cells exhibited CSCs properties, as evidenced by increased sphere formation capacity in serum-free-medium culture, dramatically elevated expression of liver CSCs markers and increased number of CD133+ cells, along with upregulation of TAp63 α , downregulation of Δ Np63 α , and activation of Sonic Hedgehog pathway. Moreover, we illustrated that suppression of Sonic Hedgehog activity inhibited NDMA-induced liver CSCs properties; over expression of TAp63 α activated Sonic Hedgehog pathway and promoted liver CSCs activity, whereas down expression of TAp63 α inhibited Sonic Hedgehog and suppressed liver CSCs; an opposite action of Δ Np63 α on Sonic Hedgehog pathway and liver CSCs was demonstrated. Taken together, our data suggested for the first time the vital role of TP63 α /Sonic Hedgehog axis in regulating NDMA-induced liver CSCs, and thus could provide new insights into the molecular mechanisms of liver carcinogenesis as well as its target intervention.

Biography

Hongyu Han has completed her PhD from Sun Yat-sen University Cancer Center in 2010. She was a research scientist in University of Pennsylvania and Fox Chase Cancer Center during 2014-2016. Currently, she is a Scientist in the Department of Nutrition in Sun Yat-sen University Cancer Center. Her research interests focus on the effects and mechanisms of dietary factors and cancer development. She has published more than 10 papers in reputed journals.

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