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MicroRNAs play important roles in the formation of lung adenocarcinoma in conditional knockout mice

Zhen-Guo Zhao, Jun-Yu Jin, Jian-Guo Sun & Zheng-tang Chen
Third Military Medical University, China

Abstract:

To obtain key microRNAs (miRNAs) and identify their biological functions during the formation of pulmonary adenocarcinoma in conditional knockout mice.

Methods:
After intranasal infection with Ad-Cre adenovirus, lung adenocarcinoma formed in LSL-Kras G12D mice within 30 days. Sca-1+CD34+ cells were sorted by flow cytometry and tested for the ability to undergo self-renewal and differentiation. MiRNA profile was obtained from the microarray. The targets of miRNAs were predicted and verified by dual-luciferase reporter vectors, qRT-PCR and western blot.

Results:
Lung adenocarcinoma was induced in LSL-Kras G12D mice. Isolated by flow cytometry, Sca-1+CD34+ cells were cultured as non-adherent and multicellular spheres in serum-free medium. In vivo, the tumor formation ability of Sca-1+CD34+ cells was 25 times stronger than control cells. In Sca-1+CD34+ cells, 145 miRNAs increased and 72 miRNAs decreased from 0 day to 30 days after virus inhalation. Four successively up-regulated miRNAs (miR-15a*, miR-203, miR-294, and miR-295*) and three successively down-regulated miRNAs (miR-19b, miR-483, and miR-615-5p) were validated by qRT-PCR. Among them, miR-294 could significantly decrease the protein level of MMP3 and inhibit the migration and invasion of Lewis lung cancer cells. Conclusion MiRNAs, characteristically expressed in tumor-initiating Sca-1+CD34+ cells, play important roles in the formation of lung adenocarcinoma.

Biography:

Jian-Guo Sun received his PhD in oncology in 2004 from Third Military Medical University, China. He is an associate professor and vice director of Cancer Institute of Xin-Qiao Hospital. He is a member of West China Radiotherapy Association, a winner of West China Talent Project, and a visiting scholar in the Department of Radiation Oncology, Stanford University. Over the past 17 years, he has been a physician and an oncology researcher, who has published about 20 articles in international journals. His current research focuses on the influence of circulating cells on revascularization and regrowth of lung cancer cells after radiation.