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Angiogenin promotes colorectal cancer metastasis via tiRNA production

Muxiong Chen, Siqi Li, Xiaoliang Shi, Ningqin Xu, Desen Sun, Rongpan Bai, Haiyan Chen, Kefeng Ding, Jinghao Sheng and Zhengping Xu
Zhejiang University, College of Xinjiang Medical University, China

Colorectal cancer (CRC) is one of the most common malignancies worldwide, as well as a major cause of cancer-related deaths. Despite considerable improvement in the therapeutic modalities, over 50% of CRC patients eventually developed recurrent disease and metastasis leading to death within 5 years of diagnosis. To date, the mechanisms that cause CRC metastasis are not fully understood. Angiogenin (ANG), a member of the ribonuclease A superfamily, not only activates endothelial cells to induce tumor angiogenesis, but also targets tumor cells to promote cell survival, proliferation, and/or migration. However, its clinical significance and underlying mechanism in CRC metastasis are still largely unknown. Here, we found that both RNA and protein levels of ANG were upregulated in CRC tissues. Statistical analysis indicated that higher ANG expression was strongly associated

with metastasis in CRC patients. We then revealed that ANG enhanced CRC growth and metastasis both in in vitro and in vivo systems. Intriguingly, the ANG rescue assay suggested that its ribonucleolytic activity was crucial in promoting CRC metastasis. Indeed, a bunch of tRNA-derived stress-induced small RNAs (tiRNAs), produced through ANG cleavage, was enriched in both CRC tumor tissues and highly metastatic cells. Further studies confirmed that these tiRNAs promoted CRC cell migration and invasion and functioned in ANG-promoted CRC metastasis. Moreover, higher serum 5'-tiRNA-Val level was observed in CRC patients and was correlated with the serum ANG level. Taken together, we propose that a novel ANG-tiRNAs-cell migration and invasion regulatory axis promotes CRC metastasis, which might be of potential for developing new measures for CRC diagnosis, prognosis, and treatment.

Biography

Muxiong Chen, Ph.D student, biochemistry and molecular biology, Zhejiang University School of Medicine. Muxiong focuses on the new functions and mechanisms of angiogenin, a tumorigenesis and angiogenesis factor. He is now interested in the roles of angiogenin in the colorectal cancer metastasis.

mxchen92@163.com

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