

【Grant-in-Aid for Young Scientists(S)】

Biological Sciences (Medicine, dentistry, and pharmacy II)



Title of Project : Clarification of the metastatic cascade mediated through microRNA in G-I tract carcinomas.

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Research Area : General Surgery, Medicine

Keyword : microRNA pathway, EMT, cancer stem cell, bone marrow, peripheral blood

【Purpose and Background of the Research】

We often have patients with recurrence and metastasis even after the curative operation. This evidence indicated the presence of occult cancer cells that could not be detected by the current technologies for diagnosis. Therefore, the identification of specific marker of recurrence and metastases would be a crew to conquer the intractable cancer cases.

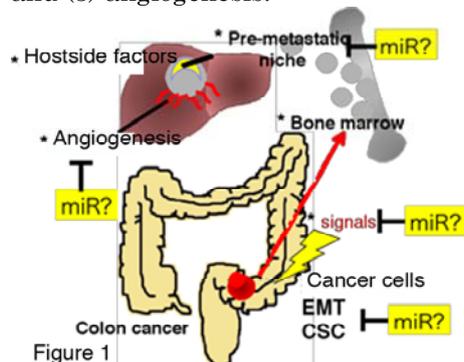
Our previous study¹⁾ proposed us to study recurrence and metastasis comprehensively mediated through not only cancer cells but in host side factors, that formed “the metastatic site society” in GI tract cancer cases.

Recently, as Weinberg et al. in MIT, reported the consecutive role of microRNA (miR) 10b in metastasis in breast cancer cases, miR has been focusing on in the analysis of diverse process of cancer progression. We will identify a bona-fide microRNA-gene pathway regulating metastasis and recurrence in GI tract carcinoma cases.

【Research Methods】

miRs might play an important role in metastasis and recurrence in GI tract cancer cases (gastric cancer and colorectal cancer). In the current study, we are disclosing following three topics (Fig. 1).

1) Identification of miR-gene pathways involving to (1) EMT induction, (2) cell cycle regulation²⁾, and (3) angiogenesis.



2) Clarifying the brand-new miR-gene pathway regulating cancer metastasis.

3) Comprehensive analysis of expression profiles

of cancer cells from primary to the metastatic site via circulating systems will provide the evidence to clarify the metastatic cascade of GI tract cancer cases.

【Expected Research Achievements and Scientific Significance】

Recently, we identified EMT inducible gene, which is recognized as a down-stream molecule in TGF- β in CRC cases. The gene transfected CRC cells can survive under anoikis conditions in peripheral blood and bone marrow. This CRC cells have lost the proliferating ability as well as tumorigenesis even in CD133+ fraction, while have increased ability of tumor invasion. In Figure 2, we validated the loss of intercellular contact by administration of the miR.

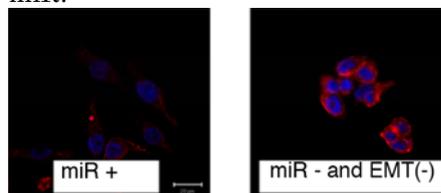


Figure 2

Similar to the above finding, our current study will provide answers to 1), 2) and 3) above. Those findings will conquer cancer metastasis and establish prophylactic strategy against the recurrence after the curative operation.

【Publications Relevant to the Project】

1) Mimori K, et al.: Hematogenous metastasis in gastric cancer requires isolated tumor cells and expression of vascular endothelial growth factor receptor-1. *Clin Cancer Res* 14: 2609-16, 2008

2) Yokobori T, Mimori K.etal.: p53-altered FBXW7 expression determines poor prognosis in gastric cancer cases. *Cancer Res* 2009

【Term of Project】

FY2009-2013

【Budget Allocation】

79,000 Thousand Yen

【Homepage Address and Other Contact Information】

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