

Any Relation Between Tumor-Resident Intracellular Microbiota and Metastasis?

Yan Huang¹, Yujiao Liu^{2*}

¹College of nursing and health Science, Wuhan Donghu University, Wuhan 430212, PR China

²State Key Laboratory of Separation Membranes and Membrane Processes, School of Chemistry, Tiangong University, Tianjin 300387, PR China

*Corresponding author: Yujiao Liu, State Key Laboratory of Separation Membranes and Membrane Processes, School of Chemistry, Tiangong University, Tianjin 300387, PR China



ARTICLE INFO

Received:  November 10, 2022

Published:  November 22, 2022

Citation: Yujiao Liu and Yan Huang. Any Relation Between Tumor-Resident Intracellular Microbiota and Metastasis?. Biomed J Sci & Tech Res 47(2)-2022. BJSTR. MS.ID.007469.

ABSTRACT

The recent work of Aikun Fu, et al. published in Cell showed that certain intratumor microbiota promoted cancer metastasis by increasing circulation cancer cells survival rate and reorganizing actin cytoskeleton in response to fluid shear stress. Intracellular microbes are significant for tumor cells metastatic but are not required for primary tumor growth.

Keywords: Intracellular Microbiota; Metastasis; Breast Cancer

Opinion

The most frequently diagnosed cancer among women and the leading cause of cancer death in females is breast cancer [1]. Metastasis and Colonization of tumor cells to the distal organs and tissues is the major cause of breast cancer-related mortality. A clear understanding reveals that both cancer cells synthesized hormones [2,3] and tumor inflammatory microenvironment is crucial for the cancer metastasis? [4]. Tumor inflammatory microenvironment is highly complex and heterogeneous. Any resident in tumor cells could generate the inflammatory reaction and finally induce cancer metastasis. Evidence showed that microbes could modulate cancer susceptibility and tumor progression. And the gut microbiota-immune system interactions contribute a lot on tumor developing and metastasis [5]. Emerging evidence suggests that thousands of intratumor bacteria exist and are active in ~10 cancer types [6]. Due to challenges with the low biomass of intratumor microbiota, knowledge of their functional repertoire and potency remains limited. Until recently, Aikun Fu, et al. found that certain

intracellular bacteria promote tumor metastasis and tumor cells survival by modulating cellular cytoskeleton. To simulate human breast cancer, they built a spontaneous murine breast tumor model mouse mammary tumor virus-polyoma middle tumor-antigen (MMTVPyMT) with significant amounts of intracellular microbiota. Bacteria loaded in normal mouse breast (median 1.73×10^4 / gram) were nearly ten-fold lower than that of breast tumor tissue, determined by optimized qPCR and 16S sequencing.

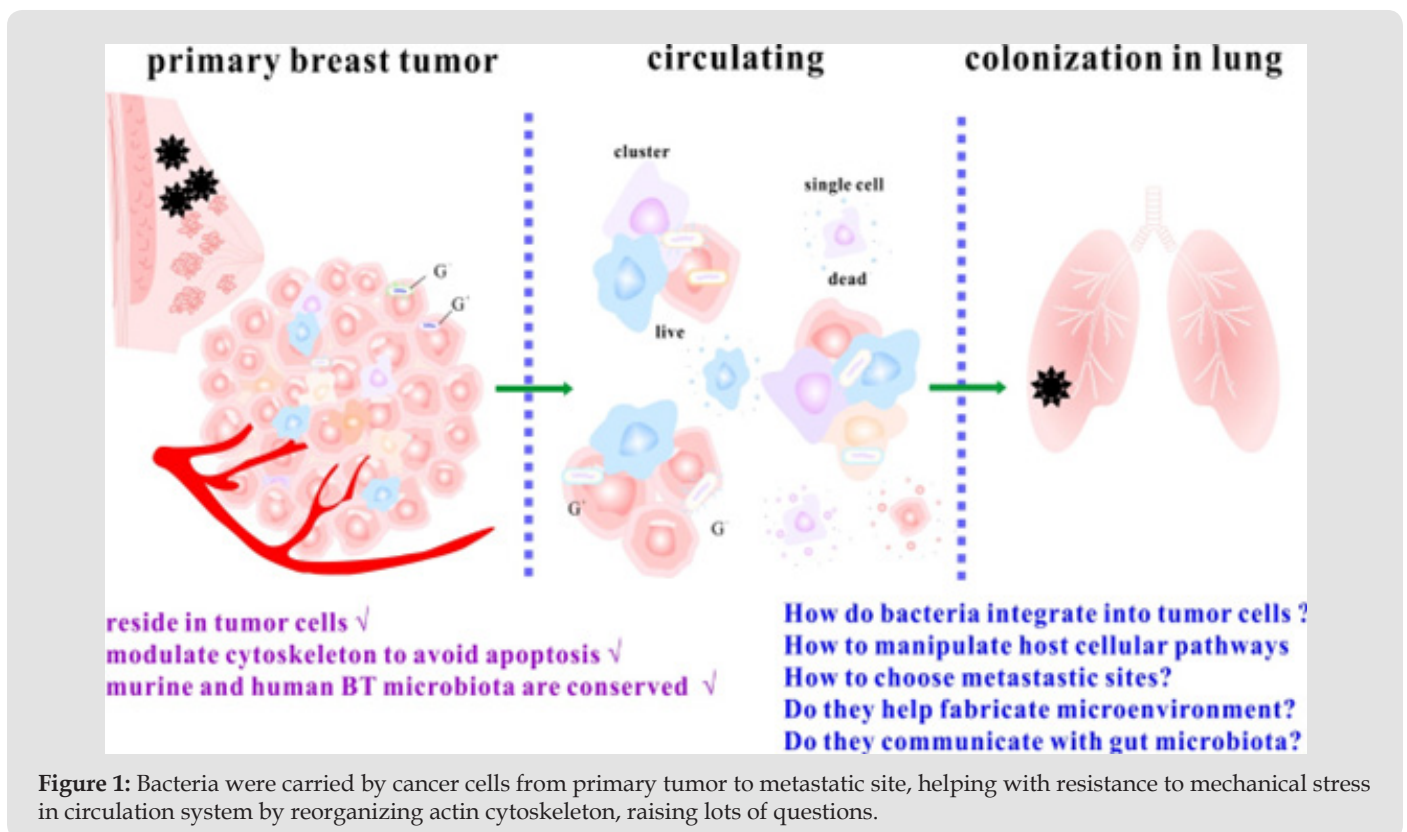
Live bacteria were presented at the perinuclear region of about 3% cells, especially epithelia cells. It was really important evidence for that researchers were not just dealing with contamination and was the initial step for further precision theragnostic [7]. Fu's study showed that tumor microbiota elimination could reduce lung metastasis more than 3-fold under antibiotic treatment, but had no influence on primary tumor weight, suggesting the essential role of intratumor bacteria for metastasis. Primary breast tumor microbiota co-clustered very well with early micro-metastasis

sample and circulating tumor cell clusters, indicating bacteria transferring from the primary tumor to metastatic sites in clusters, and indirectly supporting emerging evidence that circulating tumor cell clusters derived from primary tumor greatly contribute to the metastatic [8]. Bacteria with strong invasion efficiency significantly increased the number of colonized metastatic tumor foci. The cancer cell invasion of various bacteria enhances stem cell activity by turning on many immunity-related signals and triggers the fluid shear stress pathway through RhoA signaling, indicating that the intrinsic signaling modulation was sufficient to drive metastatic colonization and providing therapeutic targets.

The similar microbial community profile and dynamics of murine and human breast tumor supports the hypothesis that microbiota in human breast tumor is essential in the human cancer pathogenesis and progression. Aikun Fu, et al. emphasized that diverse microbiota residence in tumor cells and certain intracellular bacteria promote lung metastasis, raising numerous questions that require further study. Bacteria with strong invasion efficiency significantly increased the number of colonized metastatic tumor foci, while weakly invasive bacteria had limited effect. But those bacteria both reside in tumor cells, how do they invade tumor cells and distinguish normal cells? Bacteria of metastatic sites come from primary tumor; bacteria intravenous injection can't load them into metastatic sites, and bacteria reside in macrophages,

implying that they may be transported to tumor by something, may be through the migration of immune cells. Disrupted physical barriers and suppressed immunity may cause leakage in tumor microenvironment and enable bacteria invasion. The intracellular bacteria have no influence on the tumor cell heterogeneity or primary tumor weight but can modulating cytoskeleton and viability of circulating tumor cell clusters. The low biomass may be responsible for this difference. And then, how does the intratumor microbiota manipulate host cellular pathways, encoding some effectors or interacting with metabolism? How they communicate with immune cells in circulation system? Gut bacteria modulate immune-response even at distant sites.

The clusters may carry some signal on the cell surface from primary tumor microenvironment to avoid immune clearance. How do clusters choose metastatic sites? Breast tumor metastasizes to lymph nodes, lung, bone and brain in general through lymphatic fluid and blood (Figure 1). Is there any possibility to prevent the colonization in these organs? After colonization in metastatic sites, do the intratumor bacteria help with tumor environment fabrication and how? Is there any possibility that gut microbiota cooperates with intratumor microbiota to interfere tumor environment? These open questions may unlock the next wave of precision cancer diagnostics and therapeutics.



Acknowledgment

This study was financially supported by Hubei Province education department scientific research item (B2018291).

Declaration of Interests

The authors declare no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, et al. (2021) Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians* 71(3): 209-249.
2. Obradović MMS, Hamelin B, Manevski N, Couto JP, Sethi A, et al. (2019) Glucocorticoids promote breast cancer metastasis. *Nature* 567(7749): 540-544.
3. Wellenstein MD, Coffelt SB, Danique EM, Duits DEM, Miltenburg MH, et al. (2019) Loss of p53 triggers WNT-dependent systemic inflammation to drive breast cancer metastasis. *Nature* 572(7770): 538-542.
4. Risom, T, Glass DR, Averbukh I, Liu CC, Alex Baranski A, et al. (2022) Transition to invasive breast cancer is associated with progressive changes in the structure and composition of tumor stroma. *Cell* 185(2): 299-310.
5. Sepich Poore Gregory D, Zitvogel L, Straussman R, Hasty J, Wargo JA, et al. (2021) The microbiome and human cancer. *Science* 371(6536): 4552-4564.
6. Nejman D, Livyatan I, Fuks G, Gavert N, Zwang Y, et al. (2020) The human tumor microbiome is composed of tumor type-specific intracellular bacteria. *Science* 368(6494): 973-980.
7. Dolgin E (2020) Tumors Appear Rife with Bacterial Lodgers. *Cancer discovery* 10(8): 1085-1086.
8. Aceto N, Bardia A, Miyamoto DT, Donaldson MC, Wittner BS, et al. (2014) Circulating Tumor Cell Clusters Are Oligoclonal Precursors of Breast Cancer Metastasis. *Cell* 158(5): 1110-1122.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2022.47.007469

Yujiao Liu. Biomed J Sci & Tech Res



This work is licensed under Creative Commons Attribution 4.0 License

Submission Link: <https://biomedres.us/submit-manuscript.php>



Assets of Publishing with us

- Global archiving of articles
- Immediate, unrestricted online access
- Rigorous Peer Review Process
- Authors Retain Copyrights
- Unique DOI for all articles

<https://biomedres.us/>