RESEARCH TOPIC MECM_28

Investigating the role of tumor-resident bacteria in dictating organ-specific cancer cell dissemination during metastatic events

Curriculum
MECM Standard

Research Area
Immuno

Laboratory name
Microbiota & mucosal immunology Lab

Research Supervisor
Prof. Maria Rescigno maria.rescigno@hunimed.eu

Abstract
The metastatic process is quite complex and requires cancer cells to leave their primary site, disseminate through the blood, lymphatics, or through direct infiltration of neighboring structure, seed and colonize a secondary site. These metastatic steps are not only driven by genetic and epigenetic modifications within the tumor cell itself but also by its microenvironment, including the microbiota. Emerging evidence highlights a critical role for tumor-resident bacteria—a component of the microbiota—in promoting metastatic dissemination. For example, our laboratory has identified a strain of Escherichia coli capable of inducing pre-metastatic niche formation in the liver [1]. Also, a higher intratumoral microbial load has been shown to enhance the metastatic capacity of tumor cells in nasopharyngeal carcinoma patients [2], while tumor-resident bacteria accelerated cancer metastasis in murine breast cancer models by changing the actin cytoskeleton [3].
Although these interesting observations, many questions remain open: Is the microbial community in the metastatic lesions organ-specific? To which extent metastases and matched primary tumors share the same microbial community? Finally, can the intratumor bacterial signatures be predictive of the distant cancer metastasis?
To address these questions, this project will employ integrated genomic and bioinformatic approaches, leveraging a robust 16S rRNA gene sequencing pipeline developed by our laboratory for high-resolution microbiome profiling. In parallel, culturomic strategies will be used to isolate and characterize bacteria residing within both primary and metastatic tumor sites. Finally, the organ-specific tropism of selected bacterial strains will be evaluated through in vivo preclinical models.
Overall, the results of this study will help to shade light on the microbial community complexity of primary tumors and metastases, with the final goal to propose novel treatments to prevent cancer cell dissemination and, thus, metastatization.

Main technical approaches

During the course of the project, the PhD student will be expected to employ a diverse range of experimental approaches, including culturomics, bacterial culture techniques, flow cytometry as well as in vitro and in vivo studies.

Scientific references

1. Bertocchi, A., et al., Gut vascular barrier impairment leads to intestinal bacteria dissemination and colorectal cancer metastasis to liver, in Cancer Cell. 2021. p. 708—724.e11

2. Qiao, H., et al., Association of Intratumoral Microbiota With Prognosis in Patients With Nasopharyngeal Carcinoma From 2 Hospitals in China. JAMA Oncol, 2022. 8(9): p. 1301–1309

3. Fu, A., et al., Tumor-resident intracellular microbiota promotes metastatic colonization in breast cancer. Cell, 2022. 185(8): p. 1356–1372.e26

Type of contract

PhD scholarship of € 21.000 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984 and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

Borsa di dottorato pari a € 21.000 annui lordi erogata da Humanitas University. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.

Humanitas University – Via Rita Levi Montalcini, 4 – 20072 Pieve Emanuele (MI) Italy
CF 97692990159 – Tel. 02.8224.3777 – info@hunimed.eu – hunimed.eu