



RESEARCH TOPIC MEM12

Role of the microbiota in tumor metastasis formation

Curriculum MEM Standard

Laboratory name

Mucosal immunology and microbiota Unit, Humanitas University

Pre-clinical Supervisor

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Abstract

Metastasis development is facilitated by the formation of a “premetastatic niche” fostered by primary tumor-derived factors 1,2. Colorectal cancer (CRC) patients metastasize primarily to the liver. We recently showed that the premetastatic niche in the liver is induced by bacteria disseminating from primary colorectal tumors³. Intratumoral bacteria disrupt the Gut Vascular Barrier (GVB) an anatomical structure controlling bacterial dissemination along the gut-liver axis 4. Upon GVB impairment bacteria disseminate to the liver, boosted the formation of a pre-metastatic niche and favor the recruitment of metastatic cells. In training and validation cohorts of CRC patients, we found that the increased levels of PV-1, a marker of impaired GVB, is associated with liver bacteria dissemination and metachronous distant metastases.

In this project we want to study the microbiota strain/s responsible for this activity and the molecular players.

Main technical approaches

Microbiology and immunology techniques, in vivo studies

Scientific references

- 1 Costa-Silva, B. et al. Pancreatic cancer exosomes initiate pre-metastatic niche formation in the liver. *Nat. Cell Biol.* 17, 816-826, doi:10.1038/ncb3169 (2015).
- 2 Hiratsuka, S. et al. The S100A8-serum amyloid A3-TLR4 paracrine cascade establishes a pre-metastatic phase. *Nat. Cell Biol.* 10, 1349-1355, doi:10.1038/ncb1794 (2008).
- 3 Bertocchi, A. et al.. Gut Vascular Barrier impairment leads to intestinal bacteria dissemination and colorectal cancer metastasis to liver . *Cancer Cell*, 2021 In press
- 4 Spadoni, I. et al. A gut-vascular barrier controls the systemic dissemination of bacteria. *Science* 350, 830-834, doi:10.1126/science.aad0135 (2015).



Type of contract

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