PROJECT 1

Project title
“Role of the atypical chemokine receptor ACKR2 in colon cancer metastasis”

Pre-clinical: Raffaella Bonecchi, raffaella.bonecchi@humanitasresearch.it
Laboratory name: Leukocyte Biology

Abstract
Chemokines are important mediators in cancer-related inflammation. The atypical chemokine receptor 2 (ACKR2) is a scavenger receptor for most inflammatory CC chemokines. ACKR2 acts as a negative regulator in carcinogenesis and inflammation facilitating their resolution. Because of ACKR2 role in regulating the inflammatory trafficking, we decided to deepen its implication in colorectal carcinoma, the third most common cancer worldwide with a tendency to metastasize primarily in liver and lungs.

Previous works shown that ACKR2 deficiency is associated with increased tumor growth and protection against metastasis but its role in the whole metastatic process is not yet understood.

Our aim is testing the hypothesis that ACKR2 negatively affects immune response in metastatic CRC by modulating CCR1-5 chemotaxis of innate immune cells. In order to achieve this purpose, we have set up different murine models of liver and lung CRC metastases.

We are dissecting the phenotype of immune infiltrate into the lesions, characterizing immune cells by multiparametric FACS analysis and RNA sequencing. These preclinical models will be useful to dissect CRC metastatization pathway and to develop novel targets for immunotherapy.

Main technical approaches
- In vivo metastasis models
- Multiparametric FACS analysis

Scientific references
PROJECT 2

Project title
“Role of ACKR2 in trafficking and activation of anti-metastatic innate immunity”

Pre-clinical: Raffaella Bonecchi, raffaella.bonecchi@humanitasresearch.it
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Abstract
The atypical chemokine receptor ACKR2 has been described having a protective role in the carcinogenesis process while it is expression can be detrimental in the activation of innate leukocytes in the context of the metastatization process. The general aim of the project is to identify the role of ACKR2 in mediating the release from the bone marrow and the maturation of innate immune cells endowed with antimetastatic activity. The specific aims are:

to define the mechanisms by which ACKR2 affects differentiation of innate immune cells.
To investigate the role of ACKR2 in the trafficking and polarization of innate tumor-associated leukocytes
To investigate the possible synergism of ACKR2 inhibition with immunotherapy using preclinical models of metastatic melanoma and lung carcinoma.

Main technical approaches
- In vivo metastasis models
- Multiparametric FACS analysis

Scientific references