IMMUNOPHARMACOLOGY

PROJECT 1

Project title

"Characteriztion of the biochemical and biological properties of a novel molecule associated to M2 polarization of macrophages"

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Laboratory name: Immunopharmacology

Abstract

Migration Stimulating Factor (MSF) is a protein expressed by tumour cells and by cells present in the tumour microenvironment (1-3). We recently found that MSF is expressed by M2 macrophages and tumor-associated macrophages (TAM) (3-5). A deep knowledge of MSF biology is still lacking, thus this project has the aim to elucidate the main biochemical and biological properties of MSF. MSF folding, structural characteristics, glycosylation patterns and the migratory responses induced by the protein on leukocytes subpopulations and on cancer cells will be investigated. Based on a first set of data, efforts will be devoted to the identification of the receptor for MSF on monocytes and of the signaling pathways involved. The project will be carried out in collaboration with the Biomedicine Research Institute (IRB) in Bellinzona (Switzerland).

Main technical approaches

Biochemical techniques for protein purification; Chemotaxis assay; CRISP-Cas9 gene targeting strategy using commercial libraries for receptor identification; molecular modelling.

Scientific references

1. Schor et al. 2003. Migration-stimulating factor: a genetically truncated onco-fetal fibronectin isoform expressed by carcinoma and tumor-associated stromal cells. Cancer Res. 63:8827-8836.
2. Schor & Schor 2010. Angiogenesis and tumour progression: migration-stimulating factor as a novel target for clinical intervention. Eye (Lond) 24:450-458.
3. Solinas et al. 2010. Tumor-conditioned macrophages secrete migration-stimulating factor: a new marker for M2-polarization, influencing tumor cell motility. J. Immunol. 185:642-652.
4. Mantovani et al. 2008. Cancer-related inflammation. Nature. 454:436-44.
5. Mantovani et al. 2017. Tumour-associated macrophages as treatment targets in oncology. Nat. Rev. Clin. Oncol. 14:399-416.

PROJECT 2

Project title
"Role of molecules associated to M2 polarization of macrophages in cancer progression"

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Abstract
Tumor-associated macrophages (TAMs) are prototypic inflammatory cells infiltrating tumors characterized by an M2-like phenotype. TAM are key orchestrators of the tumor microenvironment directly affecting neoplastic cell growth, neoangiogenesis, and extracellular matrix remodeling (1,2). We recently identified the expression profile of M2 and M2-like polarized macrophages (3,4). Aim of this project is to characterize one of the molecules differentially expressed by M2 macrophages. In particular we will investigate the capacity of this molecule to stimulate cancer cell invasion using in vitro assays and in vivo approaches. Proof of concept of therapeutic targeting in models of metastatic dissemination of cancer cells will be pursued in mice. The use of imaging techniques, both in vitro and in vivo, will be the core of this project.

Main technical approaches
In vitro invasion assays and silencing of signaling pathways; RT-PCR, SDS-PAGE and western blot will be used for EMt analysis; in vivo analysis of tumor growth and metastatic dissemination in orthotopic models; use of confocal microscopy, 2-photon and in vivo imaging techniques.

Scientific references
1. Mantovani et al. 2008. Cancer-related inflammation. Nature. 454:436-44.
2. Mantovani et al. 2017. Tumour-associated macrophages as treatment targets in oncology. Nat. Rev. Clin. Oncol. 14:399-416.
3. Solinas et al. 2010. Tumor-conditioned macrophages secrete migration-stimulating factor: a new marker for M2-polarization, influencing tumor cell motility. J. Immunol. 185:642-652.
4. Schor et al. 2003. Migration-stimulating factor: a genetically truncated onco-fetal fibronectin isoform expressed by carcinoma and tumor-associated stromal cells. Cancer Res. 63:8827-8836.