1. Record Nr. TD18002900

Autore	MASSARA, MATTEO
Titolo	THE NEUTROPHIL ANTI-TUMORAL RESPONSE IN CANCER: ROLE OF ACKR2 AND CHEMOKINE RECEPTORS [Tesi di dottorato]
Editore	Università degli Studi di Milano, 2018-03-16
Lingua di pubblicazione	Inglese
Formato	Tesi di dottorato
Livello bibliografico	Monografia
Note	diritti: info:eu-repo/semantics/openAccess In relazione con info:eu-repo/semantics/altIdentifier/hdl/2434/528533
Sommario	Chemokines are key mediators of inflammation and are involved in both extrinsic and intrinsic pathway of cancer. Their main function is to induce leukocyte migration through the binding of specific seven transmembrane receptors. Beside canonical chemokine receptor a smaller family of atypical chemokine receptors was described. ACKR2 binds with high affinity a broad panel of CC inflammatory chemokines mediating their internalization and intracellular degradation. Due to its chemokine scavenging activity, ACKR2 plays a protective role in chronic inflammation and in the extrinsic pathway of cancer. The objective of my thesis was to investigate the role of ACKR2 in the intrinsic pathway of cancer using the NeuT (HER2) murine model of oncogene-driven breast cancer crossed with ACKR2 KO mice. In this model, we found that ACKR2 plays a dual an opposite role. It slows the primary tumor development while it promotes lung metastasis. We found the same phenotype on metastasis using the orthotopically transplanted 4T1 mammary carcinoma and melanoma B16F10 cell lines were we demonstrated that ACKR2 expression in the hematopoietic compartment acts as a negative regulator of the mobilization of neutrophils with anti-metastatic function. In the last part of my thesis we also investigated the phenotype of circulating and tumor associated neutrophils

	(TANs) in glioma patients, a tumor context characterized by blood neutrophilia and a general immunosuppressive state. We found a higher grade of neutrophilia and an increased rate of immature neutrophils in high grade comparing low grade glioma patients. Finally, we found that the relative abundance of circulating neutrophils on total leukocytes positively correlates with relative abundance of TANs. Collectively taken, these results indicate that neutrophils are a heterogeneous population with both pro and anti-tumoral functions. Targeting of neutrophils in cancer context represent a potential therapeutic approach that limit their pro-tumoral role unleashing the anti-tumoral and anti-metastatic potential.
Localizzazioni e accesso	http://memoria.depositolegale.it/*/http://hdl.handle.net/2434/528533