

PI	<i>Garlanda Cecilia</i> <i>Jaillon Sebastien</i>
PROJECT TITLE	Cellular and molecular dynamics of innate immunity in cancer
ABSTRACT	<p>Exploration of the tumor immune contexture is crucial for the development of new therapeutic approaches.</p> <p>We revealed the role of neutrophils in resistance to primary sarcomagenesis by driving type 1 polarisation of a subset of unconventional T cells (UTCs) (Ponzetta A et al, 2019. Cell).</p> <p>UTCs display an innate-like signature and express IL-1R8, an IL-1 receptor family member with negative regulatory functions. IL-1R8 acts as a checkpoint in NK cells (Molgora M et al, 2017. Nature). IL-1R8 is also expressed by other effector cells, including CD8+ and subsets of UTCs.</p> <p>By combining state-of-the-art technologies, genetically engineered mice, primary carcinogenesis models and human samples, we aim to dissect:</p> <ul style="list-style-type: none"> - the heterogeneity of neutrophils in cancer - the cellular and molecular mechanisms involved in the neutrophil-UTC antitumor axis, and its potential activity in cancer immunoediting and immunotherapy. - the role of IL-1R8 in lymphocyte functional activity and as therapeutic target in cancer.
FUNDING REFERENCE (AMOUNT, STARTING DATE AND DURATION)	<p>- AIRC to SJ: Amount: 825 000 € Starting date: 02/01/2020 Duration: 5 years</p> <p>- AIRC to CG: Amount: 746 000€ Starting date: 02/01/2019 Duration: 5 years</p>
MAIN TECHNICAL APPROACHES TO CARRY OUT THE PRESENT PROJECT	<ul style="list-style-type: none"> -Flow cytometry -Animal handling (Murine models of carcinogenesis) -Cellular Biology (purification and culture of cells from blood and tissues, proliferation, cytotoxicity, cross-talk between different cell types) -Molecular Biology (single cell RNA sequencing) -Bioinformatics analysis -Imaging
SCIENTIFIC REFERENCES RELATED TO THE PRESENT PROJECT (max 5)	<p>1. Complement activation promoted by the lectin pathway mediates C3aR-dependent sarcoma progression and immunosuppression. Magrini E, Di Marco S, Mapelli S, Perucchini C, Pasqualini F, Donato A, De la Luz Guevara Lopez M, Carriero R, Ponzetta A, Colombo P, Cananzi F, Supino D, Reis E.S, Peano C, Inforzato A, Jaillon S, Doni A, Lambris</p>

J.D, Mantovani A, **Garlanda C**. **Nature Cancer**. 2021. 2, 218–232

2. Neutrophil diversity and plasticity in tumour progression and therapy.
Jaillon S, Ponzetta A, Di Mitri D, Santoni A, Bonecchi R, Mantovani A*. **Nature Reviews Cancer**. 2020. Sept; 20(9):485-503.

3. Neutrophils driving unconventional T cells mediate resistance against murine sarcomas and selected human tumors.
Ponzetta A, Carriero R, Carnevale S, Barbagallo M, Molgora M, Perucchini C, Magrini E, Gianni F, Kunderfranco P, Polentarutti N, Pasqualini F, Di Marco S, Supino D, Peano C, Cananzi F, Colombo P, Pilotti S, Alomar SY, Bonavita E, Galdiero MR, **Garlanda C**, Mantovani A, **Jaillon S**. **Cell**. 2019. Jul 11;178(2):346-360.

4. IL-1R8 is a checkpoint in NK cells regulating anti-tumor and anti-viral activity.
Molgora M, Bonavita E, Ponzetta A, Riva F, Barbagallo M, **Jaillon S**, Popović B, Bernardini G, Magrini E, Gianni F, Zelenay S, Jonjić S, Santoni S, **Garlanda C**, Mantovani A. **Nature**. 2017. Nov 2;551(7678):110-114

5. PTX3 is an extrinsic oncosuppressor regulating complement-dependent inflammation in cancer.
Bonavita E, Gentile S, Rubino M, Maina V, Papait R, Kunderfranco P, Greco C, Feruglio F, Molgora M, Laface I, Tartari S, Doni A, Pasqualini F, Barbati E, Basso G, Galdiero M.R, Nebuloni M, Roncalli M, Colombo, P., Laghi, L., Lambris J.D, **Jaillon S**, **Garlanda C**, Mantovani A. **Cell**. 2015. Feb; 160(4):700-14.