TUMOR MICROENVIRONMENT UNIT

PROJECT 1

Project title

"Investigation of the immune-associated mechanisms that modulate response to therapy in prostatic cancer"

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Laboratory name: Tumor Microenvironment Unit

Abstract

Effective treatments for advanced prostate cancer (PCa) are still needed and novel therapeutics in this field would have a very high social value. Increasing evidence highlighted the fundamental role of the immune system in the progression of prostatic tumor. Furthermore recent findings suggest that the host immune status determines the tumor responsiveness to standard of care therapies for PCa, such as radiation and androgen deprivation treatments. A large amount of evidence support the concept that combination of standard of care therapies with immunotherapies may result in a strong clinical advantage in cancer. Nevertheless, further investigation is needed to understand the impact of the tumor immune microenvironment in the efficacy of radiotherapy and androgen treatments and to determine the best therapeutic combination. The applicant will profile the immune composition of patients and will investigate immune-mediated mechanisms that modulate response to therapy in prostatic cancer.

Main technical approaches

- Multiparametric Flow Cytometry
- RNA sequencing
- In vitro assays
- Murine models of prostatic cancer

Scientific references

1. Di Mitri, D., et al., Tumour-infiltrating Gr-1+ myeloid cells antagonize senescence in cancer. Nature, 2014. 515(7525): p. 134-7.
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3. Lu, X., et al., Effective combinatorial immunotherapy for castration-resistant prostate cancer. Nature, 2017. 543(7647): p. 728-732.
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PROJECT 2

Project title
"Investigation of the mechanisms that drive the re-education of the innate immune response in in advanced prostate cancer"

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Abstract
Advanced prostatic cancer is the most common cancer in males worldwide and its progression has a strong clinical and social impact. Multiple evidence indicate that the modulation of the functional state of tumor-associated macrophages (TAMs) results in the reduction of tumour progression and recurrence in several cancer types and recent findings suggest that the myeloid compartment may drive progression and therapy resistance in prostate cancer (1-4). The applicant will perform a genetic- and drug- based screening to dissect the mechanisms utilized by the prostatic tumor to re-educate TAMs in its favor (5). In vivo, the applicant will test treatments that re-educate the innate immune response in prostate cancer in order to develop new efficient strategies to treat this incurable disease.

Main technical approaches
- Multiparametric Flow Cytometry
- Crispr-libraries
- Lentivirus handling
- In vitro assays
- Murine models of prostatic cancer

Scientific references
1. Di Mitri, D., et al., Tumour-infiltrating Gr-1+ myeloid cells antagonize senescence in cancer. Nature, 2014. 515(7525): p. 134-7.
2. Solinas, G., et al., Tumor-associated macrophages (TAM) as major players of the cancer-related inflammation. J Leukoc Biol, 2009. 86(5): p. 1065-73.
3. Escamilla, J., et al., CSF1 receptor targeting in prostate cancer reverses macrophage-mediated resistance to androgen blockade therapy. Cancer Res, 2015. 75(6): p. 950-62.
4. Pyonteck, S.M., et al., CSF-1R inhibition alters macrophage polarization and blocks glioma progression. Nat Med, 2013. 19(10): p. 1264-72.
5. Parnas, O., et al., A Genome-wide CRISPR Screen in Primary Immune Cells to Dissect Regulatory Networks. Cell, 2015. 162(3): p. 675-86.