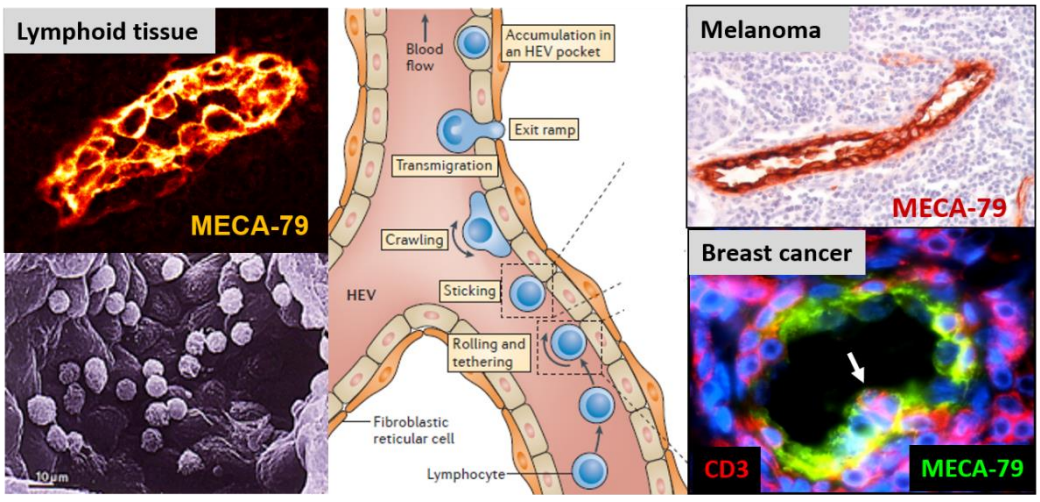
Post-doctoral position at the interface Cancer / Immunology / Vascular Biology (M/F)

A post-doctoral position (30 months) at the interface between Cancerology, Immunology and Vascular Biology is available in the team of Dr Jean-Philippe GIRARD ('Equipe Labellisée LIGUE 2023', Laboratory of Excellence 'Toulouse Cancer' (LABEX TOUCAN), IPBS-CNRS, University of Toulouse, France; https://www.ipbs.fr/endothelial-cells-in-immunity-inflammation-and-cancer/).

Project title: HEV blood vessels and lymphocyte infiltration in tumors during anti-tumor immunity and cancer immunotherapy

Key-words : cancerology, immunology, blood vessel, lymphocyte trafficking, cancer immunotherapy

Abstract : Cancer immunotherapy with immune checkpoint blocking antibodies (ICB, anti-PD-1 and/or anti-CTLA-4 antibodies) has revolutionized cancer treatment. Unfortunately it does not work for all patients, nor for all cancers. To make the treatment effective in a larger number of patients, we need to better understand how it works. Immunotherapy is based on activating the patient's own T cells, especially CD8+ cytotoxic T cells ('killer cells'). However, almost nothing is known about such fundamental aspects as the mechanisms controlling the access of lymphocytes to tumors. How can activated lymphocytes eliminate cancer cells if they do not enter into tumor and never encounter tumor cells?



The originality of our team is to focus on the mechanisms regulating the entry of lymphocytes into tumors, a step that is absolutely essential but very little studied until now. **We have recently discovered that specialized blood vessels expressing the MECA-79 marker and related to the HEV ('high endothelial venule') blood vessels of lymphoid organs (Moussion and Girard, Nature 2011), constitute the major gateways for lymphocytes to enter tumors (Asrir*,... and Girard, Cancer Cell 2022** ; 65 citations in the Web of Science, 'highly cited paper'; article selected in 'Best of Cancer Cell 2022'). By combining different approaches (scRNA-seq, intravital microscopy,...), we have shown that tumor-associated HEVs (TA-HEVs) have a unique bi-functional phenotype, and are the near-exclusive gateways for lymphocytes in different preclinical models of tumors treated with anti-PD-1/anti-CTLA-4 cancer immunotherapy.

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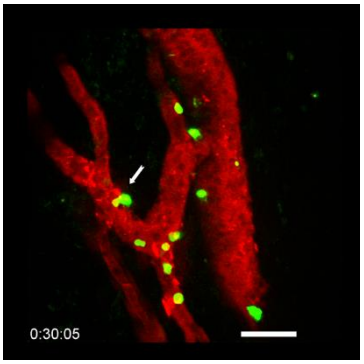
In humans, a high TA-HEV score in metastatic melanoma lesions is associated with a better response to treatment and a longer survival of patients treated with anti-PD-1 plus anti-CTLA-4 immunotherapy. Finally, we performed a proof of concept in a preclinical model that revealed that increasing the number of TA-HEVs and their functionality, improves the efficacy of immunotherapy. These latest results suggest that modulation of HEVs in tumors may increase lymphocyte infiltration and thus make immunotherapy effective in a larger number of patients.



For a more detailed description of our discovery published in Cancer Cell 2022 - see our Lecture at the Collège de France on May 20, 2022:

https://www.college-de-france.fr/site/hugues-de-the/symposium-2022-05-20-16h45.htm

The two main objectives of the Post-doctoral project are to better define the function and regulation of HEV blood vessels during anti-tumor immunity and anti-cancer immunotherapy:

1) Role of TA-HEVs in lymphocyte infiltration in tumors;

2) Methods to increase the number of TA-HEVs in tumors.

Multidisciplinary approaches will be used (flow cytometry, intravital microscopy and in vivo multiphoton imaging, homing assays, single cell sequencing scRNA-seq, multiplex IHC immunohistochemistry, in situ hybridization 'RNA scope',...) and both preclinical murine tumor models and human clinical samples (collaboration with clinicians from different cancer centers).

Based on our preliminary results, we are convinced that the project will lead to several major advances.

Context: Post-doctoral work carried out at the IPBS-Toulouse, a large Research Center of the CNRS and the University of Toulouse (www.ipbs.fr), in the multidisciplinary team of JP Girard which gathers 14 people (CNRS, Inserm and University researchers, CNRS engineers, PhD students and post-docs). The host team has a unique expertise on HEV blood vessels which is recognized at the highest international level (Girard and Springer, Immunity 1995; Moussion and Girard, Nature 2011; Girard et al Nature Rev Immunol 2012; Asrir* et al. Cancer Cell 2022). All necessary resources (biological and financial resources, state-of-the-art technological facilities) will be available.

Supervisor: Jean-Philippe GIRARD, Director of Research of Exceptional Class at Inserm, CNRS Silver Medal, 'Highly Cited Researcher' in the Web of Science (HCR index 2019, 2020, 2022 and 2023), one of the two world leaders on HEVs (30 years of expertise).

Profile: PhD in Immunology or Cancerology. We are looking for a creative and highly motivated post-doctoral researcher. Experience in preclinical murine tumor models and flow cytometry and/or in vivo microscopy and/or multiplex IHC and/or RNA scope and/or scRNA-seq would be a plus.

Funding : CNRS researcher fixed-term contract (30 months) funded by the National Cancer Institute (INCA). The salary will be in accordance with the CNRS salary scale. Social security and health benefits will be included.

How to apply: Please send your application file including cover letter, CV and list of publications to jean-philippe.girard@ipbs.fr (The position will remain open until it is filled; only the selected candidate will be contacted).

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