Tumor-associated HEVs: specialized blood vessels for lymphocyte entry into tumors

JEAN-PHILIPPE GIRARD

Institut de Pharmacologie et de Biologie Structurale, CNRS-Université de Toulouse

Keywords: blood vessel / endothelial cell / lymphocyte / anti-tumor immunity / cancer immune-therapy

Results: Blood vessels and tumor angiogenesis are generally associated with tumor growth and poor clinical outcome of cancer patients. However, we discovered that some blood vessels present within the tumor microenvironment can be associated with favorable prognosis by contributing to tumor suppression rather than tumor growth (Martinet, … and Girard, Cancer Res 2011). These specialized blood vessels, designated high endothelial venules (HEVs), are normally found in lymph nodes where they mediate lymphocyte entry from the blood (Girard et al., Nat Rev Immunol 2012). A high density of tumor-associated HEVs in human breast carcinomas and melanomas was associated with high levels of cytotoxic lymphocyte infiltration, indicating that HEVs may participate in the eradication of tumors by facilitating access of ‘killer’ lymphocytes into tumor tissues. Therefore, the type of blood vessels found in the tumor microenvironment is critical for clinical outcome, and increasing the density of the ‘good’ HEV blood vessels within solid tumors represents a promising novel strategy for cancer therapy. It is thus important to better characterize HEV blood vessels at the molecular level and to define the mechanisms involved in their regulation. These mechanisms are still poorly understood, despite our results indicating a critical role for dendritic cells in the process (Mousson and Girard, Nature 2011).

The role of HEV blood vessels in cancer will be presented in this seminar. Our recent data on the characterization of HEV blood vessels by single cell RNA-Seq, intravital microscopy and multiphoton in vivo imaging, and the influence of tumor-associated HEVs on the response to cancer therapeutics (including cancer immunotherapy) will be discussed.

References: