Abstract

Non-Hodgkin lymphomas (NHL) represent the most common hematologic malignancies. Patient-derived xenografts (PDX) are used for various aspects of translational research including preclinical in vivo validation of experimental treatment approaches. While it was repeatedly demonstrated that PDX keep majority of somatic mutations with the primary lymphoma samples, from which they were derived, the composition of PDX tumor microenvironment (TME) has not been extensively studied. We derived 15 PDX models from patients with various subtypes of aggressive lymphomas. We implemented complex genetic and immunohistochemical analysis of the established PDX models head-to-head with the patient´s primary lymphoma cells, from which the PDXs were derived. We clearly confirmed that the established PDX cells shared majority of somatic mutations with the patient´s primary cells, from which they were derived. Thus, from the genetic perspective the PDX models represent relevant tools for the study of lymphoma biology. Immunohistochemistry analysis of selected antigens revealed some differences between the PDXs and patients´ primary cells. Importantly, the analysis demonstrated complete loss of non-malignant cellular components of the tumor microenvironment frequently observed in lymphoma infiltrated lymph nodes, including T-cells, macrophages or NK cells. In addition, the PDX tumors had significantly lower extent of microvessel density and microvessel area composed exclusively of vessels of murine origin. Although PDX models represent relevant tools for translational study of malignant lymphomas, the differences described in our study must be taken into account during experiments that address the tumor microenvironment, e.g. experimental anti-angiogenic treatment approaches, various forms of immunotherapy, or nanotherapeutics that rely on enhanced permeability and retention (EPR) effect.