Background: Colorectal cancer, notably colon adenocarcinoma, presents therapeutic challenges, particularly in its advanced stages when metastases have occurred. Despite the revolution in cancer treatment with immunotherapies, such as checkpoint inhibitors, their effectiveness in colorectal cancer has been limited. The heterogeneity of the disease and the complexity of the tumor microenvironment require sophisticated preclinical models to accelerate therapeutic advances. In this context, preclinical xenograft mouse models offer invaluable insights into tumor diseases, allowing the study of molecular characteristics and mechanisms of drug action.

Methods: Capitalizing on the enhanced engraftment capabilities of highly immunodeficient mouse strains, we developed a model for colon adenocarcinoma using a human tumor cell line, SW480. We tested several scenarios: the engraftment of SW480 followed by injection of peripheral blood mononuclear cells (PBMCs), co-engraftment subcutaneously of PBMCs and SW480, and engraftment of SW480 in mice humanized with CD34+ hematopoietic stem cells. Monitoring of tumor growth was conducted three times per week using caliper measurements and biovolume 3D imaging. At the experimental endpoint, we assessed immune infiltration in the tumor microenvironment through flow cytometry.

Results: The SW480 colon adenocarcinoma cell line successfully engrafted in both the CD34+ humanized mice and immunodeficient mice strain. Interestingly, flow cytometry analysis revealed robust immune infiltration in the CD34+ humanized mice bearing the SW480 tumors, mimicking the complex tumor microenvironment of colon adenocarcinoma.

Conclusions: Our findings underscore the utility of the SW480 tumor model in CD34+ humanized mice as a powerful preclinical tool. The successful engraftment and the recapitulation of immune cell infiltration provide a robust platform for testing immunotherapies against colorectal cancer. This model will help us to better understand the intricate tumor-immune interactions and contribute significantly to the development of novel therapeutic strategies to improve patient outcomes.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0455