Understanding the Effect of Aspartate β-Hydroxylase Inhibition On T Cell-Mediated Immunity Using Single-Cell RNA Sequencing

S. Johari [1], K. Krausová [1], B. Číhařová [1], I. Poláková [1], M. Olsen [2,3],M. Šmahel [1]

[1] Department of Genetics and Microbiology, Faculty of Science, Charles University, BIOCEV, Vestec, Czech Republic
[2] Department of Pharmaceutical Sciences, College of Pharmacy – Glendale, Midwestern University, Glendale, AZ, USA
[3] Crenae Therapeutics, Phoenix, AZ, USA

Abstract:
Overexpression of aspartate β-hydroxylase (ASPH) was found in 70-90% of solid tumors but is negligible in normal tissues. Increased ASPH contributes to tumor cell proliferation, migration, and invasion but can also affect immune cells. In this study, we showed that ASPH inhibition with the small molecule inhibitor MO-I-1151 enhanced the anti-tumor effect stimulated by DNA immunization and activated an adaptive immunity mediated by $CD4^+$ and $CD8^+$ T cells. To reveal the mechanisms involved, we performed single-cell RNA sequencing with $CD45^+$ tumor-infiltrating cells. Seurat and QIAGEN Ingenuity Pathway Analysis showed that inhibition of ASPH induced differences in infiltration with immune cells and cytokine/chemokine profiles of T cells in tumors of immunized mice. These results suggest a suppressive effect of ASPH on anti-tumor adaptive immunity that could be eliminated by ASPH inhibition.