ABSTRACT

Hypoxia, or lack of oxygen, is a major factor in the tumour microenvironment that might contribute to suppression of immune system. Hypoxia is known to alter epigenetic regulation, and this might be the key to hypoxia's mechanism of immune suppression. We aim to investigate the effect of hypoxia toward CD8+ T cell, how hypoxia would impact the interaction between CD8+ T cell and triple-negative breast cancer (TNBC) cell line, and how the use of epigenetic drugs might help to reverse hypoxia-induced immune suppression. CD8+ T cells were cultured under normoxia and hypoxia, and the expression of their effectors were analysed by RT-qPCR and flow cytometry. CD8+ T cells were also co-cultured with BT549 and MD231-LM2 (LM2) TNBC cell line to analyse the expression of proteins on the TNBC cells that respond to immune activity. Several epigenetic drugs were administered to CD8+ T cells under hypoxia, and the expression of their effectors were analysed by RT-qPCR and flow cytometry. Expression of CD8+ T cells effector, namely perforin, granzyme B, TNFα, and IFNγ was reduced under hypoxia, and TNBC cells' expression of IRF1 and PD-L1 was decreased, confirming the decreased activity from the CD8+ T cells. EZH2- and class I HDACs-targetting drugs were shown to upregulate the previously suppressed CD8+ T cell effectors. We found that hypoxia suppresses CD8+ T cell activity, and the use of drugs that target histone regulators resulted in reversal this suppression.