CELL METABOLIC PHENOTYPE AND IMMUNE ESCAPE IN ACUTE MYELOID LEUKEMIA

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Importance of the immune system for cancer cell elimination during tumor development and therapy is increasingly recognized for virtually all tumor types including acute myeloid leukemia (AML). Tumor cells employ a variety of mechanisms to escape recognition by cytotoxic immune cells or inhibit immune cell activation. In AML, certain recurrent genetic aberrations modify in parallel cell metabolic preferences and immune escape. In addition, cell extrinsic factors may activate selected immune escape mechanisms. One of the most prominent inhibitory mechanisms involves interaction between the PD-1 receptor on cytotoxic lymphocytes and its ligand PD-L1 on cancer cells. Blocking antibodies against PD-1/PD-L1 are being tested in many clinical trials, in various tumor types.

We have shown previously that high PD-L1 expression levels at diagnosis are associated with worse prognosis in AML (Brodská et al. 2019). Our subsequent experiments showed that overnight culture of AML blasts from the peripheral blood often results in a large increase in PD-L1 surface levels. The effect strongly correlated with cell glycolytic activity measured as the extracellular lactate production (ECAR) using the Seahorse platform (Spearman r = 0.7, p less than 0.0001). In contrast, no significant correlation was observed between PD-L1 levels and the cell respiration rate. Furthermore, primary cells with high glycolytic rates also induced PD-L1 expression on co-cultured AML cell line.

Our results suggest that glycolytic AML cells are able to promote immune escape, probably through lactate production. This effect could be specifically important in the hypoxic bone marrow environment, which may favor the metabolic switch from oxidative phosphorylation to glycolysis. The work was supported by the Ministry of Health, Czech Republic (research organization No 00023736).