COMPARATIVE PROTEOME ANALYSIS OF GROWTH-ARRESTED EBV-POSITIVE LYMPHOMA CELLS

Daniel Tvrdik

Institute of Pathology, General Faculty Hospital,
Studnickova 2, Prague 2, Czech Republic

Introduction and objectives: Transforming growth factor β1 (TGFβ1) induces growth arrest in many cell types, including B lymphocytes. Our experimental DoHH2 cell line model was derived from a patient with malignant non-Hodgkin's lymphoma of follicular origin. Similarly to its effect on normal mouse primary B cells**,** TGFβ1 treatment resulted in significant growth inhibition of the DoHH2 cell line. Interestingly, our model cell line carried EBV genome, which is otherwise associated with marked resistance to TGFβ1-induced growth arrest, both in EBV-positive Burkitt lymphoma cells or EBV-transformed primary B cells. Results: The effect of TGFβ1 on cell cycle progression was studied by flow cytometry. Our result showed that the treatment with TGFβ1 for 48 hours led to a significant increase in the number of DoHH2 cells arrested in G_0/G_1 phase. However, we detected the presence of mRNA transcript of LMP-1 which is a potent inducer of TGFbeta1-resistance and the presence of EBNA-6 mRNA which indicated the fully expressed EBV geonome. In order to determine the plausible mechanism of TGFβ1-induced growth arrest in TGFβ1-sensitive malignant follicular lymphoma cells, we performed two-dimensional gel electrophoresis. We found 102 differences in expressions of proteins after the TGFbeta1 treatment. Conclusions: However, in our study, EBV positive DoHH2 cells retained the sensitivity to TGFβ1 inhibitory action. This implies that EBV-associated resistance to TGFβ1 is not a general phenomenon but that it depends also on B cell type, function and tissue localization.

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Key Words: follicular lymphoma, EBV, TGFbeta1, 2D-gel electrophoresis