Abstract

Adhesion signalling plays a key role in biological processes, including the formation of immunological synapses that are important for efficient interaction between effector and target cells of the immune system. Disturbances in adhesion mechanisms can lead to cancer progression in the development of leukemia and in treatment resistance and relapsing disease. The aim of this thesis is to study the effects of blinatumomab and tyrosine kinase inhibitors (TKIs) on adhesion signalling in B-lymphoblastic acute leukemia (B-ALL) cells. The effect of blinatumomab, a bispecific antibody targeting CD3 and CD19, and TKIs (including dasatinib and ponatinib) on the proliferation, viability, and expression of adhesion molecules on the surface of B-ALL cells are described in detail. Thesis includes experimental evaluation of the effect of these drugs on key potentially oncogenic signalling pathways, particularly Src family kinases, and changes in phosphorylation of key proteins such as Erk and Akt kinases that provide regulation of cell proliferation and viability. The findings of this work suggest that the combination of blinatumomab and TKIs may have a significant impact on the adhesion properties of leukemia cells, which could help explain the increased incidence of relapse in extramedullary tissues in patients treated with blinatumomab.