ABSTRACT

This diploma thesis is part of a project aiming for the development of low molecular compounds which would be capable to inhibit the interaction between human transcription factor FOXO3 and DNA. Main goal of this thesis is the characterization of the interaction between the low molecular inhibitor S9 and the DNA-binding domain of FOXO3 protein (FOXO3-DBD) by using variety of biophysical methods such as NMR, microscale thermophoresis and native electrophoresis.

FOXO transcription factors are important and evolutionary conserved regulatory proteins, which are involved in many crucial cellular processes. The activity of FOXO proteins is regulated by posttranslational modifications, out of which the most important are phosphorylation, acetylation and ubiquitination. Forkhead transcription factors participate in a variety of different cellular functions and are part of several signaling pathways. Its expression might be tissue specific. They contain approximately 100 amino acids long DNA-binding domain composed of several parts. Among its main functions belong the regulation of cell cycle and apoptosis, proliferation and cell differentiation, metabolism control and stress-response regulation. Tumor cells of lymfoblastome have developed resistance against chemotherapy by increasing activity of FOXO3 transcription factors. For this reason, it is necessary to look for specific means of suppression of the function of this protein.

This thesis is written in Czech.

Key words

FOXO3, exprese, purifikace, NMR, MST, EMSA