ABSTRACT

This bachelor 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 preparation of ^{15}N-labelled DNA-binding domain of FOXO3 protein (FOXO3-DBD) and verification of its native structure using ^{1}H-^{15}N HSQC NMR experiment.

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, although its expression is limited to specific tissues. 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. Some types of tumor cells have developed resistance against chemotherapy by increasing activity of FOXO3 transcription factors. For this reason, it is necessary to look for means to specifically suppress the function of this protein.

This thesis is written in Czech.

Key words

FOXO3, expression, purification, NMR