Abstract

Ubiquitination complex CRL4 (Cullin Ring Ligase) attracts a lot of attention due to its involvement in physiological and pathological processes, especially in the development of cancer. Cullin4 a/b proteins are reported to serve as oncoproteins in various malignancies. Due to their role in the regulation of cancer drugs targeting CRL4 have been identified, including thalidomide and its derivatives inhibiting one of the substrate receptors of the complex, the Cereblon protein. The adapter protein within the CRL4 complex - DDB1, which is involved i.a. in DNA repair, also has a role in cancer. However, the mechanism of this function has not yet been fully elucidated.

The subject of this master thesis was to study the effects of elimination and suppression of CRL4 complex functions in the prostate cancer cell line LNCaP. Significantly variable changes in cell proliferation and migration have been observed if the complex functions were affected by thalidomide. The creation of the LNCaP cell line with conditionally suppressed DDB1 function was used to study tumor dynamics in a mouse model. Results show that suppression of DDB1 function has an inhibitory effect on tumor cell proliferation but increases their ability to invade adjacent tissues. Complete deletion of the *DDB1* gene in the LNCaP cell line resulted in cell lethality. The variable and context-dependent properties of the *DDB1* gene encourage further studies.

Key words

cancer, metastasis, CRL4, prostate, ubikvitinace, knock-out, knock-down, LNCaP