SUMMARY

Background: The apoptosome pathway is interesting as potential therapeutic target because it plays an important role in the cancer chemotherapy- and biological therapy-induced apoptosis as well as in amplifying the death receptor and cytotoxic-granule-induced pathways. The functionality of apoptosome apparatus in non-small cell lung carcinoma (NSCLC) cells and tissues is often impaired due to defects in apoptosome pathway by changes in expression and/or acquired mutations and/or modifications of apoptosome components or its regulators that play a significant role in cancer cell proliferation and treatment unresponsiveness. Therefore, this thesis is aimed at the investigation of the expression status of apoptosome pathway regulators (survivin, HBXIP, XIAP, APIP, and UACA) and of the readiness of apoptosome apparatus activation in non-small cell lung carcinoma cells and tissues.

Methods: Following methods were used in this thesis: isolation and quantification of total RNA, real-time RT-PCR analysis, preparation of cell-free cytosol samples and extracts from cells and tissues, gel-filtration chromatography, Western blot analysis, enzyme analyses and cell culture techniques.

Results and conclusion: Non-small cell lung carcinoma has a higher predisposition to apoptosome-mediated apoptosis than normal lung tissue. The higher propensity of NSCLC tumours to apoptosome-mediated apoptosis is due to several factors. First, the increased expression of activatable apopotosome pathway core protein components, including Apaf-1 and procaspases-9 and -3. Second, the down-regulation of expression of *APIP* and *UACA* genes causing the lack of APIP-mediated apoptosome suppression and UACA-assisted Apaf-1 nuclear entry, which would lead to the failure of DNA damage checkpoint activation in NSCLC cells leading to their genomic instability and contributing to development and progression of NSCLC tumours. However, the functionality of apoptosome is suppressed in some NSCLC cell lines and in a high proportion of NSCLC tumours. There is evidence, that XIAP-mediated inhibition is not the major suppressor mechanism of apoptosome pathway induction in NSCLC tumours. Although overexpressed survivin in NSCLC together with abundant expression of HBXIP could lead to formation of the antiapoptotic survivin•HBXIP complex, which may be preferentially generated in lung tumours to inhibit the apoptosome pathway, in NSCLC cells, failure of the apoptosome-bound procaspase-9 activation may underlie the malfunction of apoptosome pathway.