13. Summary

Considering the lack and inconsistency of reports on the clinical value of SATB1 protein in NSCLC and PAC, this dissertation aimed to evaluate the relationship between tissue manifestation of SATB1 and selected clinical, histological, and biological data (TLR2, SMAD3, ezrin, and β-catenin) of the analyzed patient groups. An essential premise of the study was to determine the independent prognostic value of SATB1 expression, taking into account its subcellular localization assessed immunohistochemically in our cohort and publicly available transcriptomic data collected by TCGA project. Considering also that as a global transcription factor, SATB1 is not an isolated 'player' affecting patient prognosis but part of intertwined signaling pathways regulating the dynamic balance of fundamental cellular processes, we decided to assess the biological correlations between SATB1 expression and functionally related proteins: TLR2, SMAD3, ezrin, and β-catenin, as well as their individual and combined effects on patients' overall survival time.

High levels of SATB1 assessed in the nuclear fraction were an independent favorable prognostic factor in patients with NSCLC, while high levels of SATB1 localized to the cytoplasm of the cell proved to be an independent predictor of adverse prognosis. Based on the TCGA dataset, it was shown that *SATB1* mRNA overexpression was significantly associated with more prolonged patient survival. In addition, the stratification of patients with NSCLC based on combinations of SATB1, SMAD3, and TLR2 exposure levels made it possible to distinguish subgroups of patients with the most significant difference in survival time. The opposing prognostic significance of SATB1 depending on the location of staining was also demonstrated in the group of patients with PAC. The presence of an immunohistochemical reaction in the cytoplasmic fraction was an independent adverse prognostic factor in the group of patients with PAC. Analysis related to SATB1 manifestation in the testicular area did not reach statistical significance, but Kaplan-Meier curves separated patients with low expression and unfavorable prognosis from those with high expression and favorable prognosis. High SATB1 mRNA expression proved an independent prognostic indicator for favorable patient survival time. Moreover, the combination of SATB1, SMAD3, Ezrin, and β-catenin expression was associated with patient prognosis independent of conventional risk factors in both our own cohort and the TCGA dataset in the PAC group. In addition, the predicted biological strategy associated with the coexpression of SATB1,

SMAD3, EZR, and CTNNB1 included significant cross-talk with classical tumor-associated regulators.

Regarding clinical utility, this dissertation implies opposite prognostic significance depending on the subcellular distribution of SATB1 in PAC and NSCLC in stage I and II disease. The results presented here indicate the need for individual analysis: of cytoplasmic and nuclear SATB1 to more accurately predict the prognosis of patients with PAC and NSCLC in stage I and II diseases. The analyses carried out in this dissertation make it possible to consider SATB1 and its functionally related proteins as potential therapeutic targets in PAC and stage I and II NSCLC.