

Abstract

Testicular germ cell tumors (TGCT) are rare in general but they are also the most commonly occurring malignant tumors in adolescent and young males. Predispositions for the incidence of TGCT include genetic factors – a number of discovered DNA risk loci, epigenetic changes in DNA, alterations of various signaling pathways and also external environmental risk factors. These tumors usually respond to cisplatin therapy very well, nevertheless some patients develop a resistance to this cytostatic medicament. There is still relatively small amount of research dedicated to the cause of cisplatin resistance, as well as to bio-molecular characteristics of TGCT and their role in the pathogenesis. As a result, there is only a little development in TGCT therapy to this day and thus there is no targeted therapy available, which would be highly effective for treating patients with developed cisplatin resistance and/or poor prognosis of their disease. As a result of the fact that TGCT incidence is increasing in the recent decades, it can be considered an actual problem requiring urgent addressing in order to improve the survival rate and quality of life of patients with advanced TGCT.

Theoretical part of this thesis deals with the main currently known molecular characteristics of TGCT as well as cisplatin resistance, mechanisms of their origin, and lastly the influence of external risk factors and interpopulation variability of TGCT incidence. The aim of the practical part is to identify and interpret molecular aberrations in TGCT samples of patients resistant to cisplatin from Department of Oncology of 1st Faculty of Medicine and Thomayer University Hospital. These patients are included in an ongoing research study and the gathered material consists of primary tumor samples, metastasis and cell free DNA (cfDNA) samples which were analyzed by whole-exome sequencing. The main goal of this thesis is to find those molecular aberrations that could be associated with development of the disease and with cisplatin resistance and therefore could be used as a basis for new therapy methods and targeted biological therapy.