

## Summary

### **Study of metastatic processes and response to chemotherapy in primary cultures obtained from colorectal carcinoma and lymph node metastases**

Colorectal carcinoma is one of the most common malignant diseases in the Czech Republic. Despite an implementation of primary population screening to detect premalignant lesions, the incidence and the mortality of the disease do not appear to decrease significantly. A significant percentage of patients still manifest with late (metastatic) stage of the disease.

Isolation of primary cell cultures of colorectal carcinoma is a method in which a large number of tumour cells is obtained relatively rapidly under „in vitro“ conditions. With a low number of passages the cells can retain most of the characteristics of the original cells "in vivo". Therefore, cell cultures are an ideal model for studying the efficacy of chemotherapeutics and chemoresistance, as well as markers involved in carcinogenesis and metastasis of colorectal carcinoma.

Overall, samples from 60 patients with colon adenocarcinoma were obtained. Our intention was to take one sample from the primary tumour and another sample from the lymph node from each patient. From the primary tumours we successfully obtained 26 primocultures with a success rate of 45 % (26/58); from the collected lymph nodes we obtained 17 primocultures with a success rate of 47 % (17/36). However, in almost half of the collected lymph nodes, no metastasis was detected histologically. The real success of cell culture isolation from metastatic affected lymph nodes was higher; 74 % (14/19). In ten cases the isolation of cell cultures from the primary tumour and also from the lymph node metastasis was successful.

In all of our tested samples, the results showed significant variability in the sensitivity to the chemotherapeutic agents used and in the expression of EMT markers before the application of chemotherapeutics and after their use. This variability is probably the result of different staging, grading and interindividual heterogeneity of the samples, but it may also reflect the difference in EMT process dynamics.

By comparing the effect of irinotecan and oxaliplatin on biological behaviour and expression of EMT markers in paired colorectal carcinoma cell lines we found out that both chemotherapeutics reduced metastatic cell motility and migration activity; irinotecan being more efficient.

Obtained results broaden the basic knowledge of the properties and behaviour of colorectal carcinoma cell lines and describe the mechanisms by which the tumour cells may overcome cell death.

