ABSTRACT

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Title od diploma thesis: The effect of trabectedin on the cells derivated from colorectal carcinoma

Trabectedin is alkaloid, which occurs naturally in sea tunicate *Ecteinascidia turbinata.* Its mechanism of action consist of creation complexes with DNA, transcription factors and nuclears proteins. This cause blocade of transcription and defect of repair mechanism of DNA in cell. We can use it in therapy of some types of cancer, in this particular work we was researching influence on colorectal carcinoma. We tested this substance on two cancerous cell lines SW 480 – derivated from primary deposit of adenokarcinoma and SW 620 – metastatic line from lymph nodes from same patient. Prime cell cultures marked as 36B and 39B were secured from patients in University Hospital in Hradec Králové and their following cultivation. Both samples 36B and 39B were derived from the primary colon tumor deposit. On all cell lines was performed cytotoxicity assay and then was individualy calculated IC_{50}. These values were used in migration assay for cells 36B and 39B. After treatment with trabectedin both samples showed a decrease in migration capacity. With RT-PCR and immunobloting we discovered significant decrease in expresion of observed adhesive and invasive molecules (EpCAM, ICAM-1, E-cadherin, N-cadherin, FAK, p-FAK) on line 36B at a trabectedin concentration of 5 μg/ml. By our measurement was this line most sensitive to selected levels of trabectedin. Achieved result on other lines were not clear. Some observed molecules have here decreased levels, some have not shown significant changes and some have increased levels. Trabectedin has been shown to be promising for FAK and phospho-FAK proteins whose levels have decreased in most cell lines and primary cultures.