Abstrakt v anglickém jazyce

Charles University

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Title of diploma thesis: Radiolabeling of ramucirumab followed with the study of its internalization in vitro.

The process of angiogenesis ensures the formation of the bloodstream at the site of its increased need. Therefore, it is not surprising that angiogenesis is often included in the tumor production process, because it provides the tumor cells nutrition supply and metabolite removal. The targeting of angiogenesis has become a key topic of some scientific research. The process of tumor blood supply formation provides a family of vascular endothelial factors (VEGFs) and their respective receptors, which have become the target of the angiogenesis attenuation in a cancer treatment. One of many therapeutics is the monoclonal antibody ramucirumab targeted against VEGF receptor type 2 (VEGFR-2). Radioactive labeling of ramucirumab with a suitable radionuclide could bring benefits in either radiotherapy or radiodiagnostics.

The aim of this diploma thesis was the indirect radioactive labeling of monoclonal antibody ramucirumab using ^{99m}Tc as radiodiagnostic nuclide via the chelation agent succinimidyl-6-hydrazinonicotinamide (HYNIC) with the subsequent determination of the radiochemical purity of the prepared radiopharmaceutical and particularly its ability to bind VEGFR-2 expressed on human tumor cells followed by the cell internalization. Radiochemical purity was determined using the methods of iTLC and HPLC with the radiometric detection. The cell internalization was tested with the employment of the manual internalization technique and automatic radioimmunoassay with the real-time detection.

The found results showed that the indirect radioactive labeling of monoclonal antibody ramucirumab with the radiodiagnostic nuclide ^{99m}Tc resulted in the radiochemical purity over

99 %. Furthermore, the very good stability of the prepared radioligand was verified for 24 hours. The results of the internalization on two human tumor cell lines confirmed the maintenance of ^{99m}Tc HYNIC-ramucirumab binding to the targeted cellular VEGFR-2.

The found results confirmed the possibility of monoclonal antibody ramucirumab radiolabeling with ^{99m}Tc via the chelating agent HYNIC. The binding ability of the radiolabeled antibody to VEGFR-2 was maintained. Thanks to these findings, the prepared radiopharmaceutical could serve as a promising radiodiagnostic ligand.