

PhD student position

Engineered antibodies as theranostics for cancer imaging and therapy

Summary: Monoclonal antibodies (mAbs) often need to be engineered to circumvent their inherent limitations. We have recently developed and patented the 5D3 mAb that specifically recognizes prostate-specific membrane antigen (PSMA), an established cancer marker. The project is aimed at the protein engineering efforts to prepare different types of 5D3 derivatives that will be incorporated into several experimental platforms targeting PSMA-positive tumors *in vitro* and *in vivo*.

Project: Parent 5D3 will be engineered into several types of derivatives including single chain variable fragments Fab fragments and diabodies. They will be heterologously overexpressed and purified and their biophysical, biological and structural characteristics evaluated. The best performing derivatives will be then incorporated into three distinct platforms to assess their potential for cancer management: (i) chelator fusions loaded with imaging and therapeutically relevant metals; (ii) cytotoxic fusions; and (iii) BiTE (bispecific T-cell engagers) fusions that elicit cytotoxic effects by retargeting immune cells to PSMA-positive tumors. The fusion platforms will be evaluated in a series of *in vitro* assays and the efficacy of the most promising candidates assessed *in vivo* using the mouse xenograft model of prostate cancer.

Methodology: Used methodology includes cloning, mutagenesis, heterologous protein expression in various systems (*E.coli*, insect and mammalian cells), and protein purification. Biophysical/structural characterization includes microscale thermophoresis, ELISA, SPR, nanoDSF, and X-ray crystallography. Immunofluorescence microscopy, FACS, cytotoxic assays, ROS production monitoring will be used for cell-based (immunological) assays. The project is supported by the grant from the Czech Science Foundation and will be carried out in collaboration with M. Pomper lab, Johns Hopkins Medical Institutions, Baltimore, USA.ue.

Qualifications: Applicants should have a solid background in molecular biology and biochemistry or cell biology. We expect good communication skills, analytical thinking and the ability for teamwork. The successful candidate will participate in a PhD program at Charles University in Prague. The starting date is summer/fall 2018.

How to Apply: For more information please contact Cyril Bařinka (cyril.barinka@ibt.cas.cz) directly.

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