Highly cytotoxic FGF2-conjugates in targeted therapy for FGFR-expressing cancers

Beneficiary: University of Wrocław

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Partners: Oslo University Hospital
Institute for Cancer Research

Department of Biochemistry
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Akronim: FGF2CON
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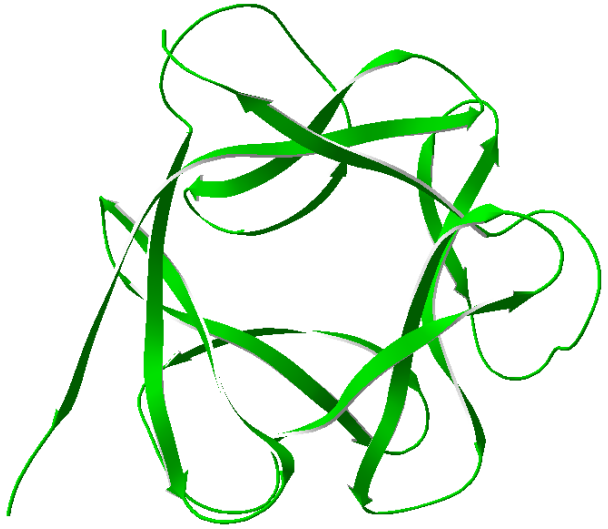
Project objectives



Production and biophysical characterization of FGF2 and FGF2-conjugates suitable for targeted therapy of FGFR-related cancers

Design and production of recombinant FGF2 proteins
Cytotoxic FGF2-conjugates preparation
Biophysical characterization of FGF2-conjugates

Testing and characterization of FGF2 and FGF2-conjugates suitable for targeted therapy of FGFR-related cancers in cellular model – cell line *in vitro study*

Analysis of biological activities of FGF2 constructs
Cytotoxicity studies of FGF2 variants and their conjugates
Examination of the effect of simultaneous use of FGF2-conjugates and specific FGFR tyrosine kinase inhibitors

***In vivo* studies in mouse xenograft models for human cancer and validation of proposed therapy**

Maximum tolerated dose estimation studies of cytotoxic drugs and cytotoxic FGF2-conjugates
Biodistribution and tumor accumulation of fluorescently labeled FGF2
The normal tissue toxicity of FGF2-conjugates
Antitumor activity of FGF2-conjugates alone or in combination with FGFR tyrosine kinase inhibitor

Methods and approach

- Protein production and purification (*E. coli expression system, heparin affinity purification*)
- FGF2-cytotoxic drug conjugation (*monomethyl auristatin E, doxorubicine or epirubicine*)
- Biophysical studies (*MS MALDI TOF or ESI MS/MS, circular dichroism and fluorescence techniques*)
- Protein-protein interaction studies (*SPR- BIAcore3000, fluorescence polarization methods*)
- Receptor binding assay (*competitive binding assay, label-free real time assay)*
- Microscopy (*fluorescence and confocal*)
- Activation of signaling pathway (*Western blotting*)
- Proliferation and cytotoxic studies (*[^{3}H]thymidine incorporation, colorimetric (MTT) or fluorescent (AlamarBlue) assays*)
- *In vivo* studies (*mouse model, biodistribution and tumor accumulation, in vivo fluorescent imaging, subcutaneous xenografts and metastasis model; tumor analysis and histological examination of major organs*)