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Novel cytotoxic conjugates of peptibodies targeting Fibroblast Growth Factor Receptors (FGFR)

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Fibroblast growth factor receptors, involved in progression and development of certain types of cancer, are currently being targeted by multitude of different anticancer therapies. The goal of our project is to develop cytotoxic conjugates, in a format of peptibody conjugated with monomethylauristatin E (MMAE), that would target FGFR-expressing cancer cells. The natural ligands of FGF receptors – FGFs – are screened in this project to isolate binding regions interacting with receptor and minimize these regions down to linear peptides, which will be then reformatted into Fc-fusions, ie. peptibodies. Peptibodies showing FGFR-dependent internalization will be conjugated with the cytotoxic drug and tested for the FGFR-specific cytotoxic effect on cells. We have already shown that two of the FGF2 sequence-derived peptibodies are internalized into FGFR-expressing cells and, after conjugation with the cytotoxic drug, decrease their viability down to 20%. The peptibody conjugated with a drug functions as a selective drug-delivery system that shows a potential to reach its target without harming the neighboring cells. The results we show indicate that this format can work as a basis for targeted therapies aiming at cancer cell with the overexpression or malfunctioning of the FGFRs.

Biography

Natalia Skinder is a Master student completing her project in the Department of Protein Engineering at the University of Wroclaw. The research she is involved in currently is focusing on development of anticancer targeted therapies using cytotoxic conjugates as basis for the treatment. Karolina Jendryczko is a PhD student in Department of Protein Engineering in University of Wroclaw. Her research interests are focus on the novel cancer therapy based on peptide-Fc fusions. Prior to her PhD, she was associated with the Foundation of Cardiac Surgery Development in which sheworked on a biological scaffold enriched with mesenchymal stromal cells.

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