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## Internalization of antibody fragments directed against FGFR1

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Fibroblast growth factors (FGFs) and their plasma membrane-localized receptors (FGFRs) regulate signaling pathways that govern developmental processes and metabolism. Numerous tumors are characterized by the overproduction of FGFR and this is considered a bad prognostic factor for patient survival. Antibody drug conjugates (ADCs) targeting cancer cells with the elevated level of FGFR represent one of the most attractive therapeutic strategies. ADCs are composed of the antibodies raised against tumor-specific biomarkers linked to the highly cytotoxic drugs. After selective binding to the cancer cells ADCs are internalized and delivered to the lysosomes by intracellular vesicular transport system. The lysosomal proteolysis of ADCs results in the release of the cytotoxic drugs, leading to the cell death. A prerequisite for an ADC approach is efficient internalization of the antibody-target complex. Although the biology of FGFRs and their ligands has been broadly studied, the requirements for the effective internalization of antibodies that target FGFR remain elusive. We analyzed the internalization of antibody fragments in various formats that target FGFR1. The antibody fragments in the monovalent scFv format bind to FGFR1, but are not internalized into the model cells that overproduce FGFR1. In contrast, the same scFv proteins in the bivalent scFv-Fc format are efficiently internalized via FGFR1-mediated clathrin and dynamin dependent endocytosis. Interestingly, the receptor kinase function of FGFR1 is dispensable for endocytosis of scFv-Fc-FGFR1 complexes. Binding of the bivalent scFv-Fc induces FGFR1 dimerization without simultaneous receptor activation, suggesting that oligomerization of FGFR1 triggers receptor endocytosis.

### Biography

Lukasz Opalinski has completed his MS in Biotechnology from the University of Wroclaw, Poland. In 2012, he obtained his PhD from the University of Groningen, Netherlands. His PhD work was focused on peroxisome proliferation and involvement of peroxisomes in antibiotics production by filamentous fungi. In 2012, he obtained EMBO Long Term Fellowship to study molecular mechanisms of mitochondria biogenesis at the University of Freiburg, Germany. Since 2015, he is working as a Faculty of Biotechnology in the University of Wroclaw, Poland, where he is working on the endocytosis of antibody fragments generated against FGFR1.

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