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Engineered minibody mediated targeting of head and neck cancer

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Cetuximab, a chimeric monoclonal antibody developed for targeting the epidermal growth factor receptor (EGFR), has been intensively used to treat cancer patients with metastatic colorectal cancer and head and neck cancer. Intact immunoglobulin G (IgG) antibody like cetuximab, however, has some limitations such as high production cost and low penetration rate from vasculature into solid tumor mass due to its large size. In attempt to overcome these limitations, we engineered cetuximab to create single chain variable fragments (scFv-CH3; Minibody) that were expressed in bacterial system. Among three engineered minibodies, we found that MI061 minibody, which is composed of the variable heavy (VH) and light (VL) region joined by an 18-residue peptide linker, displays higher solubility and better extraction properties from bacterial lysate. In addition, we validated that purified MI061 significantly interferes ligand binding to EGFR and blocks EGFR's phosphorylation. By using a protein microarray composed of 16,368 unique human proteins covering around 2,400 plasma membrane associated proteins such as receptors and channels, we also demonstrated that MI061 only recognizes the EGFR but not other proteins as compared with cetuximab. These results indicated that engineered MI061 retains both binding specificity and affinity of cetuximab for EGFR. Although it had relatively short half-life in serum, it was shown to be highly significant anti-tumor effect by inhibiting ERK pathway in A431 xenograft model. Taken together, our present study provides compelling evidence that engineered minibody is more effective and promising agent for in vivo targeting of solid tumors.

Biography

Jee Min Chung has completed her B.S at the age of 22 years from Wonkwang University and a master's and doctorate integrated course studies from Ajou University School of Medicine.

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