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Gene therapy for colorectal cancer using adenovirus-mediated full-length antibody cetuximab

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Cetuximab is a mouse-human chimeric monoclonal antibody, approved for marketing to treat patients with advanced colorectal cancer and head and neck squamous cell carcinoma in several countries around the world. It works by blocking the epidermal growth factor receptor (EGFR) from receiving signals or interacting with other proteins to promote its normal function. The demand of cetuximab is increasing in clinic to treat patients with certain cancers due to its specificity and sufficient effect, however, the complicated technologies and high cost limit its wide applications. Here, we generated an adenovirus-mediated cetuximab for cancer gene therapy, results in rapid, high-level antibody expression after one single intramuscular injection while at a low cost. The full-length gene cetuximab was cloned into two serotypes of adenoviral vector, respectively, termed AdC68-CTB and Hu5-CTB. Indirect fluorescence assay and binding ELISA were performed to verify binding specificity and affinity, data suggested that cetuximab expressed by both recombinant adenoviruses carries the same bioactive as commercial Erbitux. After infected with AdC68-CTB or Hu5-CTB, the viability of colorectal cancer cells NCI-H508 and DiFi were inhibited and the cells displayed the phosphorylation status of EGFR and its downstream effectors mitogen-activated protein kinase kinase (MEK) and extracellular signal-regulated kinase (ERK) down-regulated. Our results further showed that a single administration of AdC68-CTB or Hu5-CTB induced sustained expression of cetuximab at a high serum level and tumor volume were dramatically reduced in NCI-H508 or DiFi-inoculated nude mice. In conclusion, adenovirus expressing full-length cetuximab could be a novel alternative method to effectively treat colorectal cancer.

Biography

Man Xing has completed her Bachelor's degree from Jilin University in 2013. She is currently pursuing her Master's degree in Institut Pasteur of Shanghai, Chinese Academy of Sciences. She has published a paper in *Emerging Microbes and Infections* in 2014 and applied for a patent in 2015.

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