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Title: Cetuximab administered through pulmonary route in a mice model of lung tumor

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Body: Introduction: Emerging evidences indicate that monoclonal antibodies delivered through pulmonary route may be a promising treatment for lung diseases. We assessed the efficacy and tumor distribution of cetuximab, an anti-EGFR antibody, delivered through the pulmonary route in a murine model of lung tumor. Methods: A549-luc cells were orotracheally inoculated into lungs of Balb/C nude females to develop an orthotopic murine model of NSCLC sensitive to cetuximab. Nine days after inoculation, tumor were treated with cetuximab intraperitoneally (n=15), aerosol cetuximab (n=17) at a dose of 10 mg/kg or NaCl aerosol (n=16), once a week for three weeks. Bioluminescence imaging was used to homogenise group before treatment and to follow up tumor growth. For intratumoral biodistribution study, cetuximab was conjugated to a fluorophore and delivered in the orthotopic mouse model of NSCLC either through ip, iv or the pulmonary route. Three dimensional near-infrared fluorescence imaging (NIRF) was used to determine tumor uptake of cetuximab. Results: As shown by bioluminescence imaging, the growth of A549-luc tumors was statistically decreased by 40% in mice treated with aerosolized cetuximab and 24% in the group treated with ip cetuximab comparatively to the control group ($p<0,05$). The molecular mechanisms underlying the therapeutic efficacy are currently under evaluation. 3D NIRF revealed that tumor uptake of cetuximab was different depending on the route of administration. Conclusion: The pulmonary delivery of mAb, such as cetuximab, may be relevant for treating respiratory diseases, but further investigations are required to understand the molecular mechanisms associated with the therapeutic response.