Multifactorial diagnostic NIR imaging of CCK2R expressing tumors.

Abstract:
Optical imaging-based diagnostics identify malignancies based on molecular changes instead of morphological criteria in a non-invasive, irradiation free process. The aim of this study was to improve imaging efficiency by the development of a new Cholecystokinin-2-receptor targeted fluorescent peptide that matches the clinical needs regarding biodistribution and pharmacokinetics while displaying superior target specificity. Furthermore we performed multifactorial imaging of Cholecystokinin-2-receptor and tumor metabolism, since simultaneous targeting of various tumor biomarkers could intensely increase tumor identification and characterization. Affinity and specificity of the fluorescent Cholecystokinin-2-receptor targeted minigastrin (dQ-MG-754) were tested in vitro. We conducted in vivo imaging of the dQ-MG-754 probe alone and in a multifactorial approach with a GLUT-1 targeted probe (IR800 2-DG) on subcutaneous xenograft bearing athymic nude mice up to 24 h after intravenous injection (n = 5/group), followed by ex vivo biodistribution analysis and histological examination. We found specific, high affinity binding (Kd = 1.77 nM ± 0.6 nM) of dQ-MG-754 to Cholecystokinin-2-receptor expressing cells and xenografts as well as favorable pharmacokinetics for fluorescence-guided endoscopy. We successfully performed multifactorial imaging for the simultaneous detection...
of the Cholecystokinin-2-receptor and GLUT-1 targeted probe. Prominent differences in uptake patterns of the two contrast agents could be detected. The results were validated by histological examinations. The multifactorial imaging approach presented in this study could facilitate cancer detection in diagnostic imaging and intraoperative and endoscopic applications. Especially the dQ-MG-754 probe bears great potential for translation to clinical endoscopy imaging, because it combines specific high affinity binding with renal elimination and a favorable biodistribution.

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