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Targeted imaging for personalized medicine: New age for combination cancer treatments

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Introduction: MRI enhancement in the brain may result from primary or recurrent brain tumor, radiation necrosis, metastasis from primary cancer (e.g., lung, breast), stroke, inflammation or infection. Biopsies of the brain are often technically impossible. The purpose was to establish the validity of a polymalic acid (PMLA)-based natural nanobiopolymer, Polycefin™, for the differential tumor-type imaging of metastatic brain tumors.

Methods: Polycefin™ contained covalently attached moieties for tumor-specific targeting (antibodies to EGFR or HER2/*neu*), tumor cell elimination (antisense oligos to EGFR or HER2), transcytosis across blood-brain tumor barrier (anti-transferrin receptor antibody), endosome disruption and drug release into the tumor cell cytoplasm (trileucine), and imaging (MRI tracer Gadolinium, Gd-DOTA). Nude mice had human EGFR+ (MDA-MB-468 breast cancer or A549 lung cancer) and HER2+ (MDA-MB-474 breast cancer) tumor cells stereotactically implanted, each in one brain hemisphere, and nanopolymer injected into the tail vein for imaging. Signals in healthy brain and tumor were quantified over time using 9.4-Tesla small animal MRI system (BioSpec).

Results: After reaching a maximum in the first hour post injection, high signal values prevailed for 3 hours for Gd-DOTA-Polycefin, but declined rapidly for clinical Gd. By differential MRI with anti-HER2 (Trastuzumab) or anti-EFGR (Cetuximab) antibody attached to Polycefin™, it was possible to reliably differentiate HER2+ from EGFR+ metastatic brain tumors by non-invasive imaging.

Conclusions: The Polycefin™ biopolymer appears to be highly suitable for non-invasive differential diagnosis of brain metastases from various tumors based on specific markers. This "virtual biopsy" approach may assist in choosing the right treatment regimen.

Biography

Ljubimova J Y is a Professor and Director of Nanomedicine Research Center at the Department of Neurosurgery at Cedars-Sinai Medical Center. Her major interest is the differential cancer gene expression as a tool for finding novel/early markers of cancer development, and for working out new nanomedicine drugs against these tumor targets for treatment and/or imaging. One of the novel markers, the structural tumor vessel wall protein laminin-411, is currently in a clinical trial as a prognostic and diagnostic marker for human glial tumor progression. These discoveries led to the development of new technologies for drug delivery and engineering of the new class of anti-cancer nanomedicine drugs and imaging agents. Currently her research is supported by three NIH/NCI, private and industry grants. She is the author of over 70 peer review publications, reviews and book chapters as well as an inventor on 12 patents and patent applications.

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