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New class of nanomedicines to image and treat primary and metastatic tumors

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Abstract

Nanopolymers are highly promising vehicles for multi-targeting and can provide molecular combination therapy and thus, personalized therapy based on specific marker expression profiles. In our work, a natural nanobiopolymer, polymalic acid (PMLA), was used as a nanoplatform for the family of Polycefin^{TM} drugs to treat primary and metastatic tumors.

Treatment efficacy was examined in treatment of primary brain and breast and metastatic tumors with polymer-attached antisense oligonucleotides (AON) to four molecular markers: α and β laminin, EGFR, HER2 and tumor-specific corresponding monoclonal antibodies (mAb) to either EGFR (Cetuximab)or HER2 (Herceptin), and transferrin receptor (TfR) for delivery through mouse endothelial system including brain blood and tumor barriers (BBB/BTB).

In brain tumors treated with Polycefin nanobiopolymer bearing AON against chains of tumor vascular protein, laminin-411, the vascular area was significantly decreased and tumor size was reduced 10-fold. For HER2-positive primary breast cancer, more than 90% growth inhibition was achieved *in vivo* in a mouse model using Polycefin-attached HER2 AON. Treatment of primary TNBC by another Polycefin version, where PMLA had anti-TfR mAb for transcytosis, nucleosome-related antigen binding 2C5 mAb for tumor cell targeting, and anti-EGFR AON to block tumor cell growth, also led to a significant reduction of tumor size. Polymer-treated tumors exhibited significant cell apoptosis identified by the cleaved PARP method.

Polycefin drugs were also used to treat brain metastases. Animal survival after Polycefin treatment of lung metastasis, HER2-positive breast cancer and TNBC was significantly: 65% for lung cancer, 47% for HER2-positive breast cancer, and 81% for TNBC.

Overall, these nanoconjugates showed significant anti-tumor activity to teat primary cancers and metastases to the brain.

Biography

Ljubimova is a Professor and Director of Nanomedicine Research Center at the Department of Neurosurgery at Cedars-Sinai Medical Center. She works in clinical and basic cancer research in her entire career. The 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. Currently her research is supported by three NIH/NCI, private and industry grants. She is the author of over 70 publications, reviews and book chapters as well as an inventor on nine patents and patent applications.