Leukemia Inhibitory Factor-loaded Nanoparticles with Enhanced Stability and Anti-Inflammatory Activity for Ischemic Stroke Treatment

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Purpose:
To prolong the stability and both neuroprotective and anti-inflammatory activities of leukemia inhibitory factor (LIF), an anti-inflammatory cytokine that has shown promise as a therapeutic agent for permanent ischemic stroke.

Methods:
LIF was packaged in nanoparticles made of poly(ethylene glycol)-poly(lactic acid) (PEG-PLA) polymer to form LIF-loaded nanoparticles (NanoLIF). The surface of NanoLIF was also modified with the CD11b antibody (CD11b-NanoLIF) targeting activated peripheral macrophages to increase cytokine delivery to inflammatory macrophages. ELISA was used to quantify bioactive cytokine inside and releasing from NanoLIF. NanoLIF biological activity was measured using the M1 murine leukemia cell proliferation assay.

Results:
NanoLIF and CD11b-NanoLIF had diameters of approximately 30 nm, neutral surface charge, and physicochemical stability retaining biological activity of the cytokine during incubation at 25°C for 12 h. NanoLIF particles released LIF relatively fast from 0-6 h after incubation at 37°C followed by slow release from 24-72 h according to a two-phase exponential decay model. NanoLIF and CD11b-NanoLIF significantly decreased M1 cell proliferation over 72 h compared to free LIF.

Conclusions:
NanoLIF and CD11b-NanoLIF preserved the metabolic stability and biological activity of LIF in vitro. These results are promising to improve the therapeutic potential of LIF in treating neurodegenerative and inflammatory diseases.