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Curcumin-Loaded Dual-Targets Nanoparticles with Enhanced Magnetic Resonance Imaging Therapy of Alzheimer's disease in Transgenic Mice

Yuting Ruan* *and* Jun Liu

Sun Yat-Sen University, China

Abstract

Alzheimer's disease (AD) is a common neurodegenerative disease with no curative treatment. Curcumin (cur) has been proved to be effective in treatment of AD. However, the low bioavailability and hydrophobicity of cur which distributed non-targeted after administration and hindered by the blood-brain barrier limit its application. We designed a novel diagnostic and therapeutic nanoparticle, 1,2-dio- leoyl-sn-glycero-3-phosphoethanolamine (DSPE)-n-[poly(ethylene glycol) (PEG)] loaded with cur and super paramagnetic iron oxide (SPION) conjugated with two targets ligands to the surface of the nanoparticles, CRT and QSH, abbreviated as SPIO@DSPE-PEG/Cur-CRT/QSH. CRT specifically targets ligands at the blood-brain barrier (BBB), and QSH has an fine ability to bind with Aβ1-42 which is the culprit of AD pathology. The in vitro parameters of nanoparticle included dynamic light scattering (DLS), transmission electron microscope, saturation of magnetization, flow cytometer analysis. In vivo image of amyloid plaques were detected by MRI scanning, and the spatial learning and memory capability of transgenic APP/PS1 mice were conducted by Morris water maze (MWM). Bielschowsky silver staining, western blotting, immuno staining were among the ex vivo assays to determine the expression of amyloid protein, tau hyper phosphorylation, glial fibrillary acidic protein (GFAP), β-III tubulin (Tuj1). The in vitro assay determined the nanoparticles that possess fine size, zeta potential, r2 relaxivity, increased its cellular uptake. In vivo 7 Tesla MRI images of mice brains which were treated with SPIO@DSPE-PEG/Cur-CRT/QSH showed less amyloid plaques accumulation compared to native cur. The MWM results indicated the SPIO@DSPE-PEG/Cur-CRT/QSH brilliant improved the learning and memory capability of APP/PS1 mice compared with the bald cur. Moreover, SPIO@DSPE-PEG/Cur-CRT/QSH reduce hippocampal tau hyper phosphorylation and β-amyloid deposit, while increase the expression of Tuj1. This nanoparticle would be a potential diagnosis and treatment for AD.

Biography:

Yuting Ruan is a second-year PhD candidate majoring in Neurology at Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University. He mainly focused on the diagnosis and new therapeutic targets for Alzheimer's disease.

Speaker Publications:

1.Shengnuo Fan, Xuan Liu, Wengli Fang,Xiaoyou Chen, Wang Liao, Xiuna Jing, Enxiang Tao, Qiulan Ma, Xingmei Zhang, Rui Guo* & Jun Liu* (2018) "Curcumin loaded PLGA PEG nanoparticles counjugated with B6 peptide for potential use in Alzheimer's Disease". Drug Delivery, 25(1):12.

2. Xiao SH, Zhou DY, Luan P, Gu BB, Feng LB, Fan SN , Liao W, Fang WL, Yang LH, Tao EZ, Guo R*, Liu J*(2016) "Graphene quantum dots conjugated neuroprotective peptide improve learning and memory capability". Biomaterials, 106 : 98~110.

3.Fan SN, Zhang B, Gu BB, Wan Q, Huang XY, Liao W, Liu J*(2015) "PI3K/AKT/mTOR/p70S6K pathway is involved in Aß25-35-induced autophagy". BioMed Research International, 2015: p. 1-9.

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