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Non-Invasive Detection of Biomarkers for Alzhiemer's Disease using Anti-Biofouling Magnetic Nanomaterials

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Alzheimer's Disease (AD) is a neurodegenerative disease with diagnostic and therapeutic challenges. The currently available diagnostic tools are expensive, invasive, and insufficient for early screening. We have constructed a novel, simple and efficient method for the detection of early AD using anti-biofouling magnetic nanomaterials. The anti-biofouling polymer coated Iron Oxide Nanoparticles and their targeting antibody conjugates were prepared as described in the literature. The Fluoresce in Isothiocyanate (FITC) labeled amyloid-beta peptide 1-40 [Aβ(1–40)] and Tetramethylrhodamine-5-(and 6)-isothiocyanate (TRITC) labeled peptide 1-42 [Aβ(1–42)] were dissolved in artificial cerebrospinal fluid (CSF) or Phosphate Buffered Saline (PBS) with Fetal Bovine Serum (FBS) at 50 mg/mL to mimic the human CSF and serum environment respectively. They were then incubated with antibody (Ab)-conjugated IONPs (at final iron concentration of 0.2 mg/mL) or antibody-conjugated Dynabeads for 3 hours before magnetic separation of particles. The separation efficiency (SE) was calculated as the weight ratio of captured peptide to spiked. The protein quantification was verified using micro bicinchoninic acid (BCA) protein assay kit. Furthermore, insulin was purposely added to artificial CSF and PBS with FBS as interference to demonstrate the capture specificity of Ab-conjugated IONPs. The SE of anti-biofouling IONP for Aβ(1–40) in artificial CSF at 0.1, 0.2, 0.5, 1, 2, 5, and 10 microgram/mL were found to be 97, 96.6, 97.7, 92.2, 88.9, 91.4, 89.9% using fluorescence signal and at 98, 95.6, 98.5, 90.2, 93.6, 88.7, and 91.1% with micro BCA protein assay kit. The SE for IONP for Aβ(1–40) in PBS with FBS at the same concentrations were also in the range of 88-95%. When insulin was added to Aβ(1–40) mixture, the separation efficiency of insulin for IONP was only 4.5, 4.7, 6.2, 6.5, 7.7, 9.8, and 12.3% while dynabeads showed no difference in the separation efficiency for both Aβ(1–40) and insulin. Similar results were obtained for Aβ(1–42) and IONP with minimal isolation of insulin in both artificial CSF and PBS with FBS. Dynabeads again showed indiscriminate separation of Aβ(1–42) and insulin.

The antibody conjugated IONP consistently exhibited separation efficiency above 88% for Aβ(1–40), and Aβ(1–42) in both artificial CSF and in PBS containing FBS with good reproducibility. Its ability to selectively detect AD markers were also validated with interference with insulin, demonstrating the IONP's potential application for early AD diagnosis in human serum and CSF.

Biography:

Esther Lim, MD, MBA is currently an associate professor of radiology at PCOM and works in collaboration with Dr. Hui Mao, PhD, Professor of Radiology and Biomedical Engineering and the Director for the Molecular Imaging, Biomarkers, and Probe Development at Emory University. Dr. Yuanchen Li, PhD is a staff scientist at Emory University School of Medicine with expertise in anti-biofouling polymer synthesis for nanomaterial coating and biomarker targeted imaging, drug delivery and therapy.