UNIVERSITY OF ALBERTA
TECHNOLOGY TRANSFER SERVICES

# UNCONJUGATED PLGA NANOPARTICLES IN THE DIAGNOSIS AND TREATMENT OF ALZHEIMER'S DISEASE

ID# 2019046 & 2023012

## HIGHLIGHTS

- Use of native biodegradable nanoparticles in the diagnosis and treatment of Alzheimer's disease (AD).
- Contrary to conventional use of these nanoparticles in delivering drugs to target areas, native PLGA nanoparticles show therapeutic effects in the treatment of AD pathology.

## OPPORTUNITY

Researchers at the University of Alberta found that poly(D,L-lactide-co-glycolide) (PLGA) nanoparticles without conjugation with any drug/agent may be useful in treating Alzheimer's disease (AD). Results obtained so far indicate that these nanoparticles can suppress spontaneous β-amyloid (Aβ) aggregation and trigger disassembly of aggregated Aβ fibers. Additionally, PLGA treatment not only protects mouse cortical cultured neurons against Aβ toxicity but also can mitigate AD-related cognitive deficits/pathology in an established mouse model of AD. Finally, native PLGA nanoparticles were able to attenuate Aβ-induced toxicity in cultured human neurons derived from induced pluripotent stem cells (iPSC) of AD patients, thus highlighting its unique untapped potential in the treatment of AD pathology. In parallel, fluorescent-labelled native PLGA nanoparticles can selectively interact with Aβ plaques in a mouse model of AD, suggesting that these nanoparticles may have utility in diagnostic applications as well. As PLGA nanoparticles are routinely used in drug formulations and have an excellent safety profile, these are promising candidates for drug repurposing.

At present, AD is the leading cause of dementia in the elderly population. Pathological changes that characterize AD indicate that an overproduction or a lack of clearance of Aβ may increase its levels, with the resulting aggregation leading to neuronal loss and development of AD. Currently, there is no solid treatment to prevent/arrest the progression of AD. One of the limiting factors in the treatment of AD is the blood-brain barrier (BBB) which prevents the penetration of the majority of therapeutics into the brain. There is evidence that drug-conjugated PLGA nanoparticles can able to cross BBB. Furthermore, the evidence that labelled PLGA nanoparticles can label neuritic plaques in a mouse model of AD highlights its potential in the diagnosis of AD at an early stage before the onset of symptoms – improvements in molecular diagnostic technologies can lead to better prognosis and treatment strategies for patients. It is well known that Aβ and tau tracers can significantly improve the clinical diagnosis of AD; as such, detecting Aβ deposition at an early stage using labelled PLGA nanoparticles may add in the diagnosis of AD pathology.

## COMPETITIVE ADVANTAGE

- PLGA nanoparticles already approved by FDA are relatively safe and easily delivered to the brain
- May be used as a theranostic for both AD diagnostics and treatment.

## STATUS

- Patents pending; US17/873,751
- Wang, Yanlin, et al. (2020) Significance of cytosolic cathepsin D in Alzheimer's disease pathology: Protective cellular effects of nanoparticles against β-amyloid toxicity. Neuropathol. Appl. Neurobiol. 46: 686-706.
- Anand, Bibin, et al. (2022) "Significance of native PLGA nanoparticles in the treatment of Alzheimer's disease pathology." Bioactive Materials 17: 506-525.
- Wu, Qi, et al. (2022) "Native PLGA nanoparticles regulate APP metabolism and protect neurons against β-amyloid toxicity: Potential significance in Alzheimer's disease pathology." International Journal of Biological Macromolecules, 219: 1180-1196.
- Pallabi, S.P., et al. (2022) "Unconjugated PLGA nanoparticles attenuate temperature-dependent β-amyloid aggregation and protect neurons against toxicity: implications for Alzheimer's disease pathology." Journal of Nanobiotechnology, 20: 67.

- Govindarajan, Karthivashan, and Satyabrata Kar. "Detection of β-amyloid aggregates/plaques in 5xFAD mice by labelled native PLGA nanoparticles: implication in the diagnosis of Alzheimer's disease." Journal of Nanobiotechnology 21.1 (2023): 216.


**INVENTORS**


- Dr. Satyabrata Kar


**MORE INFORMATION**


Quang Tran
Associate Director, Licensing
Technology Transfer Services, University of Alberta
T: 780.492.6254
qmtran@ualberta.ca