

Advancing the Arizona State University Knowledge Enterprise

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Recombinant Antibody Fragments that Selectively Target Oligomeric Tau Aggregates

Alzheimer's disease (AD) is one of the most prevalent and feared neurodegenerative diseases associated with aging, characterized by progressive neuronal loss and cognitive dysfunction. AD affects nearly 5 million Americans, and unfortunately, there is no cure as of yet. Numerous studies have implicated oligomeric amyloid beta (AB) aggregates as toxic species in AD, and increasing evidence also implicates oligomeric forms of tau in the disease pathogenesis of AD and other taupathies. Well characterized reagents that can specifically recognize and distinguish between different aggregated states of tau are critically needed to identify biomarkers of AD and other taupathies and to study toxic mechanisms.

Researchers at Arizona State University in collaboration with researchers at Oligomerix have successfully synthesized recombinant antibodies (nanobodies) for the treatment and early diagnosis of AD and other tauopathies such as Frontotemporal Dementia (FTD) and traumatic brain injury (TBI)-mediated neurodegeneration. These nanobodies specifically target toxic oligomeric tau but do not bind monomeric, fibrillar or non-disease associated form of tau.

These highly specific and selective nanobodies have great utility in diagnosing, treating and imaging tau related neurodegeneration. Moreover, their very specific targeting minimizes unwanted side effects, and may provide a safer long-term therapeutic.

Potential Applications

- Therapeutics to selectively target toxic oligomeric tau aggregates and protect neurons from damage
- Diagnostic tool for early stage AD, FTD, other taupathies or neurodegeneration by detecting oligomeric tau in serum, CSF or other fluid samples
- Labeled imaging agents to detect tau aggregates and neurodegeneration in vivo

Benefits and Advantages

• Specific to only the neurotoxic forms of tau to minimize unwanted side effects

- Targets an early cause of AD, rather than treating symptoms
- Well defined specificities and selectivities for selected tau forms facilitate specific diagnosis of AD and other taupathies
- When used in combination with other protein and morphology specific nanobodies against AB and a-syn, these nanobodies can be used to detect the presence of biomarkers which can readily detect and distinguish many related neurodegenerative diseases including AD, PD, FTD and LBD

For more information about the inventor(s) and their research, please see \underline{Dr} . Sierks' directory webpageDr. Sierks' laboratory webpage