

## ALZHEIMER DISEASE

## Localized proteomics distinguishes AD subtypes

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Rapidly progressive Alzheimer disease (rpAD), which is characterized by survival of <3 years after diagnosis, accounts for around 10% of cases of AD. The factors that determine the rate of AD progression are unclear, but a new study indicates that the protein composition of amyloid plaques in different AD subtypes can provide some important clues.

As reported previously, Eleanor Drummond, Thomas Wisniewski and colleagues developed a novel approach to enable proteomic

analysis of amyloid plaques in formalin-fixed, paraffin-embedded (FFPE) tissue. “We found that we could generate comparable proteomic results using FFPE tissue to those reported by other groups who used a similar strategy to analyse frozen tissue,” says Wisniewski. “We were particularly excited by this result, as human FFPE tissue is much more plentiful and easier to work with.”

For the new study, the researchers obtained FFPE brain tissue from 22 patients with rpAD and 22 patients

with typical sporadic AD (sAD). Laser capture microdissection was used to isolate amyloid plaques from these tissue samples, and protein expression in the plaques was measured by means of liquid chromatography–mass spectrometry.

The team identified 141 proteins that were differentially expressed between rpAD and sAD plaques. Plaques from patients with sAD showed elevated levels of astrocytic proteins, whereas rpAD plaques contained an abundance of neuronal proteins. Astrocytes in amyloid plaques are thought to have a neuroprotective role, so absence of these cells might help to explain the accelerated spread of pathology in rpAD.

“The differences in the rpAD plaque proteome provides new direct evidence that amyloid plaques do not all have the same protein composition,” concludes Wisniewski. “Our results suggest that proteomic differences in plaques could provide important insight into the factors that contribute to plaque development and determine the rate of progression of AD.”

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Brain light / Alamy Stock Photo

**ORIGINAL ARTICLE** Drummond, E. et al. Proteomic differences in amyloid plaques in rapidly progressive and sporadic Alzheimer's disease. *Acta Neuropathol.* <http://dx.doi.org/10.1007/s00401-017-1691-0> (2017)

**FURTHER READING** Drummond, E. S. et al. Proteomic analysis of neurons microdissected from formalin-fixed, paraffin-embedded Alzheimer's disease brain tissue. *Sci. Rep.* **5**, 15456 (2015)