Mutations in the \(BRI2\) gene cause rare neurodegenerative diseases referred to as familial British dementia (FBD) and familial Danish dementia (FDD). These disorders are both associated with neurodegeneration and extensive amyloid deposition in the CNS. FBD and FDD are distinguished from Alzheimer's disease (AD) and other dementing disorders by plaque deposition in the cerebellum and an accompanying cerebellar ataxia. In both lesions, 34-amino acid long peptides are generated (\(ABri/ADan\)), which share homology in their first 22 amino acids although they completely differ at their C-termini. Both peptides start with a glutamate at position 1, however, it has been demonstrated using mass-spectrometry that the majority of these peptides are N-terminally modified starting with a pyroglutamate (pGlu) residue at position 1. So far nothing is known about the immunohistochemical profile of pGlu-modified \(ABri/ADan\) peptides in brain tissue. This type of post-translational modification is also known in AD where a large proportion of A\(\beta\) peptides are N-terminally truncated carrying the pGlu-modification at position 3 (A\(\beta3pGlu\)). In AD, this modification leads to a higher aggregation propensity, disturbed proteolytical degradation and increased toxicity of A\(\beta\) peptides. We have generated antibodies detecting the pGlu-modification at the N-terminus and characterized their specificity using western- and dot-blot analyses. Immunohistochemical stainings of human brain samples of FBD and FDD patients revealed the presence of pGlu-modified peptides in parenchymal and vascular deposits. In addition, an age-dependent increase in pGlu-modified ADan deposits was detected in the parenchyma and vessel walls of transgenic mice overexpressing the Danish mutant form of Bri2.