The role of glial cells in amyloid-beta clearance: pathophysiological studies

Accumulation of amyloid-beta (Aß) in the brain is thought to be the driving force in Alzheimer's disease (AD) pathogenesis. Aß can rapidly aggregate into several aggregation forms such as oligomers and fibrils. Oligomers are the most toxic species in the human brain, whereas the fibrils will eventually deposit in amyloid plaques. This Aß accumulation and deposition can be caused by a disbalance between Aß production and Aß clearance in the brain. In patients with sporadic AD (about 90% of all AD patients) there is no (genetic) evidence for an increase in amyloid-beta production and it has been hypothesized that Aß clearance is hampered.

One important route via which Aß can be cleared from the brain is via cellular uptake and proteolytic degradation by glial cells. These cells consists mainly of astrocytes and microglia and they are closely associated with Aß plaques. It remains however unclear what causes the failure in Aß clearance by astrocytes and microglia. In order to investigate this we work in close collaboration with the Netherlands brain bank and we can obtain human brain tissue to isolate and culture primary human astrocytes and microglia. The use of primary human cells enables us to investigate the role of these cells in amyloid-beta clearance and try to unravel why glial cells seem to fail in correct Aß clearance.

Depending on the project several technique can be used:

- Isolation of primary human astrocytes and microglia
- Cell culture work
- Aß aggregation experiments
- Flow cytometry
- Electrophoresis and Westernblot analysis
- ELISA
- Immunohistochemical staining of cells and/or human brain tissue

Because the exact research projects can change over time, a more specific description can be given upon request or in an interview.