Abstract

The genetics of Alzheimer’s disease indicate that causal genes induce amyloid plaque formation, while risk genes determine the cellular response to the amyloid plaques. This raises enormous challenges for the modelling of Alzheimer’s disease as it is possible to induce amyloid plaque pathology in mouse brain, but the cellular response mediated by microglia, astroglia, oligodendrocytes and the way this affects neurons are likely very different from the responses in human cells. I will discuss our efforts to model the genetic underpinnings of Alzheimer’s disease using human-mouse xenograft models and demonstrate human specific microglia and neuron responses to amyloid plaques that provide insight in the pathological cascade that leads to the full pathology of the disease.