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iPSZÜRICH

A Lecture Series Focused on Induced Pluripotent Stem Cells

UCL

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KU Leuven, Belgium, and University College London

The 6 infection points of Alzheimer's Disease

For more than three decades, the amyloid cascade hypothesis has framed Alzheimer's disease (AD) as a neuron-centric, linear sequence: amyloid deposition → tau tangles → synaptic loss → dementia. This model provided molecular precision but imposed a deterministic logic that cannot explain resilience, reversibility, or the cellular diversity revealed by modern single-cell and spatial omics. Amyloid-targeting therapies have confirmed that the cascade is biologically real yet mechanistically incomplete: plaques can be cleared, but the disease often persists. We propose that AD is not a linear chain of events but a non-linear systems disorder governed by a limited number of cellular inflection points—qualitative transitions at which adaptive stress responses fail and local homeostasis collapses. Each inflection point represents a reorganization of cellular states across neurons, glia, and vasculature, shifting the brain from compensation to dysfunction. I will present our recent work using spatial transcriptomics and human-mouse xenograft models to chart those inflection points.