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Development of a quick, robust and chemically-defined differentiation protocol from human induced pluripotent stem cells towards cortical neurons to phenotype Alzheimer's Disease

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In an aging world, neurodegenerative diseases, such as Alzheimer's Diseases start to appear more and more in society. Unfortunately, only drugs ameliorating the symptoms, but no preventive or curative medications are available. One underlying reason is that only animal models exist that do not fully reflect the human pathophysiology, leading to the difficulty of translating findings into humans. Therefore, it is of great importance to access an authentic in vitro cell culture system to study disease. Such a cell culture system would also have the potential to be used in later stages of drug discovery and drug development.
Here, a quick, robust and chemically-defined xeno-free differentiation protocol was developed to obtain a human induced pluripotent stem cell (hiPSC)-derived cortical neuron cell culture system. Several factors influencing variability of differentiation were addressed and identified, leading to faster generation of cells, greater robustness and wide applicability among different hiPSC lines. Further, it was shown that the derived culture system is suitable for disease modeling in Alzheimer's Disease as the Aβ-pathology could be recapitulated in the cells, already at a very early time point of differentiation. The established differentiation protocol is a promising tool in disease modeling of Alzheimer's Disease and other tauopathies, without the need of animal-derived cell culture supplements and reagents.