

3D co-culture platform to study myelination deficits in schizophrenia using hiPSC-derived neurons and oligodendrocyte lineage cells

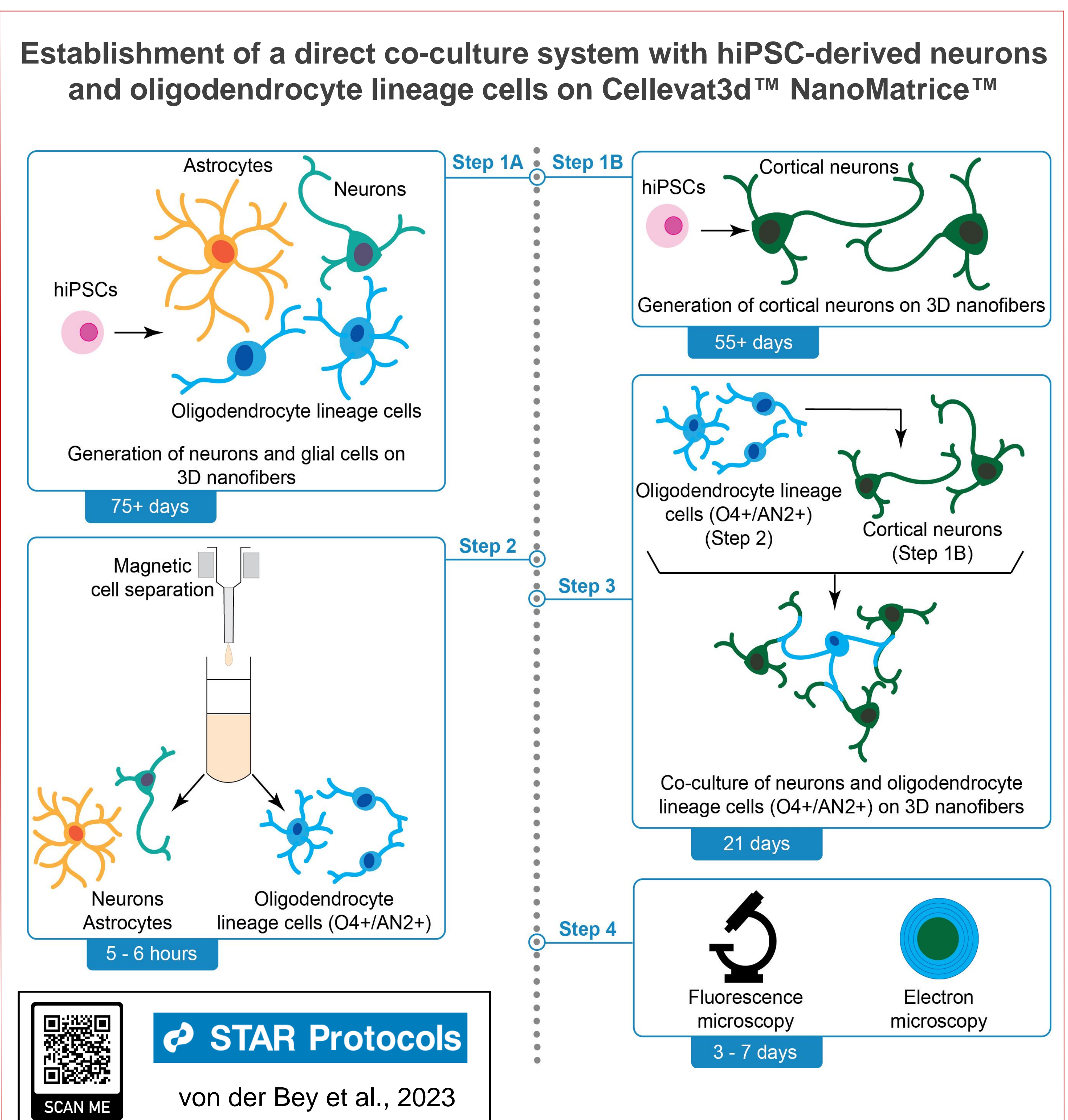
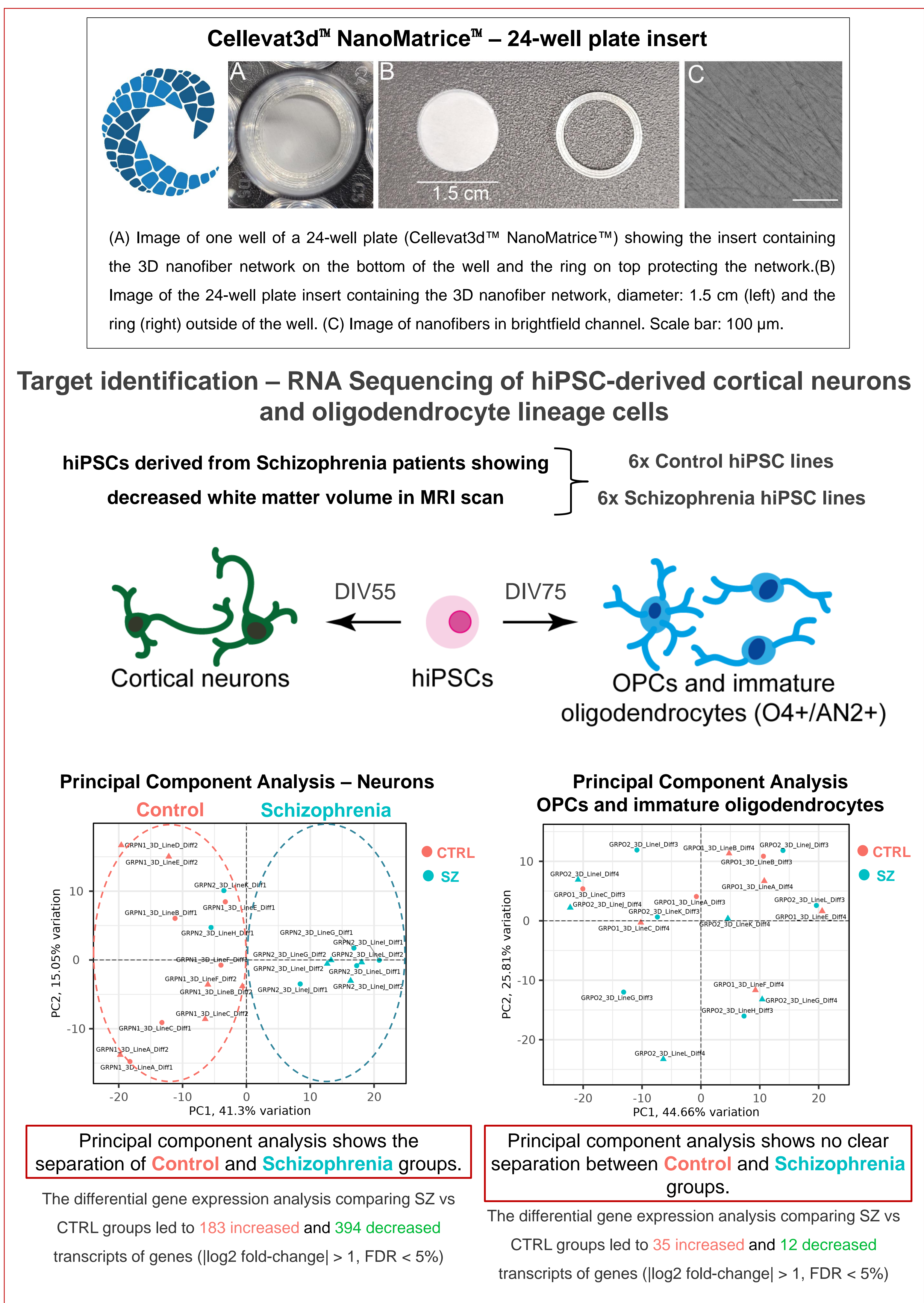
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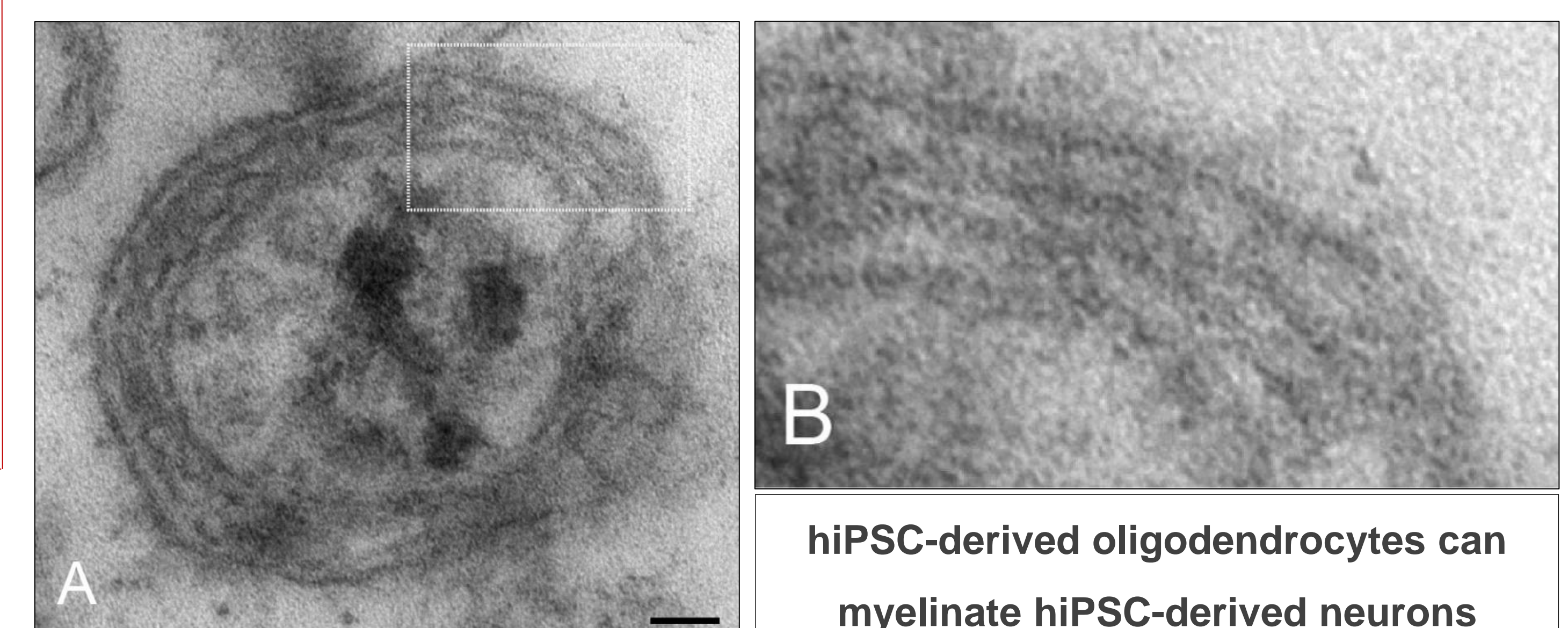
Schizophrenia is a neurodevelopmental disorder that affects about 1% of the population globally. Recent brain imaging studies have shown decreased myelin integrity in white matter tracts of schizophrenia patients. However, the molecular pathways behind the hypomyelination pathology are still unknown.

To unravel the mechanisms of hypomyelination in schizophrenia, we focus on neurons and oligodendrocyte lineage cells. Therefore, we differentiated human induced pluripotent stem cells (hiPSCs) derived from six healthy controls and six schizophrenia patients into neurons and oligodendrocyte lineage cells on a 3D nanofiber network and performed differential gene expression analysis.

To further study the interaction of neurons and oligodendrocytes, in particular the process of myelination, we established a controlled direct co-culture system of hiPSC-derived neurons and oligodendrocyte lineage cells in a 3D micro-environment. This co-culture system provides an *in vitro* assay to study myelination biology in health and disease on a microscopic and ultrastructural level.



Transmission Electron Microscopy (TEM) – 21 days of co-culture:



Transmission electron microscopy of hiPSC-derived neurons (DIV108) and oligodendrocytes (DIV96) co-cultured for 21 days on 3D nanofibers: (A) Representative image of a cross section of a myelinated axon. (B) Zoom in of the white dashed rectangle showing four myelin sheath wraps. Image acquisition with JEOL JEM-1400 electron microscope. Scalebar: 100 nm.

Our 3D co-culture system provides an *in vitro* assay to study myelination biology in health and disease.

Outlook: Using 3D culture system of hiPSC-derived neurons and oligodendrocyte lineage cells for the validation of candidate targets

References: von der Bey et al., 2023

