UNIVERSITY OF WARSAW | CeNT CENTRE OF NEW TECHNOLOGIES

invites to a seminar by

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Neurodevelopmental origins of schizophrenia - new lessons from induced Pluripotent Stem Cells

7th of June 2018 at 12 p.m.

Venue: Centre of New Technologies, Banacha 2C,
Lecture Hall 0142 (Ground floor)

Host: Marta B. Wiśniewska

Studies of induced pluripotent stem cells (iPSCs) from schizophrenia patients and control individuals revealed that the disorder is programmed at the preneuronal stage, involves a common dysregulated mRNA transcriptome, and identified Integrative Nuclear FGFR1 Signaling a common dysregulated mechanism. We use human embryonic stem cell (hESC) and iPSC-derived cerebral organoids from controls and schizophrenia patients to model the first trimester of in utero brain development. The schizophrenia organoids reveal an abnormal scattering of proliferating Ki67+ neural progenitor cells (NPCs) from the ventricular zone (VZ), throughout the intermediate (IZ) and cortical (CZ) zones. TBR1 pioneer neurons and reelin, which guides cortico-petal migration, are restricted from the schizophrenia cortex. The maturing neurons are abundantly developed in the subcortical regions, but are depleted from the schizophrenia cortex. The decreased intracortical connectivity is denoted by changes in the orientation and morphology of calretinin interneurons. In schizophrenia organoids, nuclear (n)FGFR1 is abundantly expressed by developing subcortical cells, but is depleted from the neuronal committed cells (NCCs) of the CZ. Blocking FGFR1 activity reproduces both the loss of nFGFR1 and cortical neuronal maturation in hESC cerebral organoids. We report for the first time, progression of the cortical malformation in schizophrenia and link it to altered FGFR1 signaling. Targeting INFS may offer a preventive treatment of schizophrenia.