Conference Proceedings By
United Research Forum, London, UK

ORGANIZED BY
UNITED RESEARCH FORUM
(CONNECT WITH RESEARCH WORLD)

5th International Conference on

Pediatrics and Neonatal Care

July 21-22, 2026 | Vienna, Austria

Adeline Orts-Del Immagine[1], Emma Noël[1], Fabien Guimiot[1,2], Yline Capri[2], Marianne Alison[2], Nicolas de Roux[1,2]

[1]University Paris Cité / NeuroDiderot – INSERM UMR1141, Paris, France
[2]Hospital Robert Debré AP-HP , Paris, France

What Rare Genetic Disorders Reveal About Brain Development and Cell Physiology: Insights from Warburg Micro Syndrome

Warburg Micro syndrome is a rare autosomal recessive neurodevelopmental disorder characterized by severe ocular, neurological, and endocrine abnormalities, most commonly caused by pathogenic variants in RAB3GAP1. RAB3GAP1 encodes the catalytic subunit of the RAB3 GTPase-activating protein, a regulator of Rab-dependent vesicular and membrane trafficking. Although experimental models have suggested a role for RAB3GAP1 in autophagy, how its loss affects Human brain development remains largely unknown.

Here, I present the first detailed neuropathological and molecular analysis of Human Warburg Micro syndrome, based on two related cases: a 23-week gestation fetus and a 3-month-old infant carrying biallelic null RAB3GAP1 variants. Analysis of fetal brain tissue reveals selective vulnerability of the developing cerebral cortex, characterized by thinning of the cortical plate. At the cellular level, loss of RAB3GAP1 expression in the fetal frontal cortex is associated with disruption of neurogenic niches, including depletion of SOX2-positive progenitor cells, disorganization of radial glia, increased apoptotic signaling, and reduced numbers of immature and deep-layer cortical neurons. Notably, while no major cortical malformations are evident at mid-gestation, pronounced cortical abnormalities are present in the postnatal brain, suggesting a progressive neurodevelopmental defect. These developmental alterations are accompanied by marked dysregulation of autophagy markers in the fetal brain, supporting impaired autophagy as a central pathogenic feature of Warburg Micro syndrome. Complementary studies in proband-derived fibroblasts confirm autophagy defects and further underscore the context-dependent impact of RAB3GAP1 dysfunction. Together, these findings establish a direct link between RAB3GAP1 loss, impaired autophagy, and abnormal Human cortical development. However, how defects in autophagy intersect with Rab-dependent intracellular trafficking to drive neurodevelopmental failure remains an open question, which we are now setting out to investigate.

Keywords: Autophagy; Cataract; Corticogenesis; Fetus; Neurodevelopment; RAB3GAP1; Warburg Micro syndrome;

Biography

I am a neurophysiologist with over ten years of experience studying how neural cells integrate volume-transmitted signals conveyed by the cerebrospinal fluid and synaptic inputs during brain development and adulthood, in both physiological and pathological contexts. Since 2022, I have been a Junior Professor at Université Paris Cité in the NeuroDiderot laboratory, where I investigate the mechanisms underlying rare neurodevelopmental disorders in close collaboration with clinicians at Robert Debré Hospital, focusing on how alterations in cell physiology and synaptic homeostasis affect brain development and functions.

https://doi.org/10.51219/URForum.2026.Adeline-Orts-Del-Immagine

ISBN: 978-1-917892-44-5