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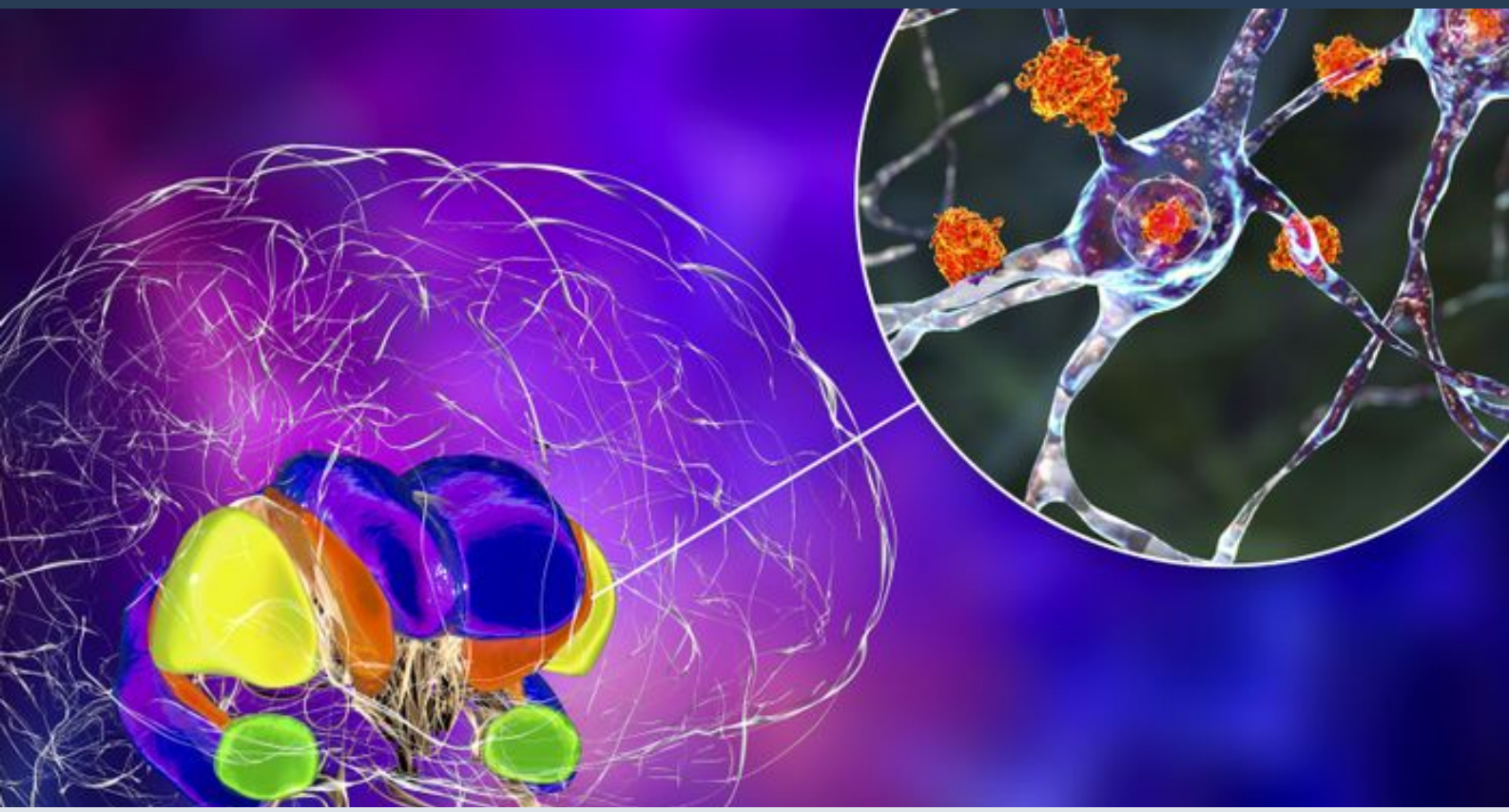
Sphingo- and Phospholipids as Biomarkers in Neuroacanthocytosis

Unravelling a new lipid-neuro network and the role of sphingo- and phospholipids as disease biomarkers in Neuroacanthocytosis

Reference: NA Biomarkers



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Seeking

Development partner

About **LMU Munich**

Ludwig-Maximilians-Universität München is the University in the heart of Munich. LMU is recognized as one of Europe's premier academic and research institutions. The LMU Munich community is engaged in generating new knowledge for the benefit of society at large.

Background

Emerging data show sphingo- and phospholipids as key factors in neurologic conditions, such as Parkinson´s, Huntington´s and Alzheimer´s disease.

VPS13A disease (Chorea Acanthocytosis, ChAc; chorein protein; *VPS13A* gene) and McLeod Syndrome (MLS; XK protein; _XK_ gene) are core neuroacanthocytosis (NA) syndromes, a group of rare progressive disorders with the main clinical characteristics of neurological abnormalities (movement disorders, e.g. chorea) and malformed, spiky red blood cells (acanthocytes).

Little is known about the pathophysiology of these diseases. LMU Munich related European Multidisciplinary Initiative on Neuroacanthocytosis consortium detected recently ground-breaking information regarding VPS13 mechanisms: (i) Vps13 proteins act as interorganelle contact sites in lipid transfer; (ii) VPS13A and XK colocalize in human cells, (iii) XK re-localizes VPS13A from lipid droplets on the endoplasmic reticulum and (iv) XK mutations disrupt VPS13A localization. The simultaneous neurologic and erythrocyte symptoms strengthen the hypothesis of the role of sphingo- and phospholipids in disease development.

However, biomarker candidates for these fatal movement disorders are lacking and most of the research in this field has been inconclusive. Diagnosis, disease activity measurement and prognosis are still essentially based on clinical evaluation, thus diagnostic delay is extended. The identification of biomarkers for early diagnosis and prognosis is therefore a relevant unmet medical need.

This project aims to unravel the presumed, yet never explored role of sphingo- and phospholipids in disease manifestation and as diagnostic biomarkers in human patients. Furthermore, the project opens the door for experiments on therapeutic interventions in these genetic diseases.

Tech Overview

During the last decades, the LMU Munich group has collected the worldwide largest international NA patient cohort, with >700 blood samples, detailed clinical information and informed consent.

In the project, the researchers will carry out (a) genetics, (b) lipidomics, (c) Western blot analyses in human samples, compare mutation effects on the VPS13-XK link in (d) yeast and in (e) zebrafish.

This will be the first bed-to-bench study, to reveal a completely novel intracellular network in NA, and the role of lipid metabolism. The team will analyse the organelles altered by lipid traffic disruption. Know-how and human samples grant an internationally unique and incomparably strong team.

Special innovations: whole-genome sequencing, lipidomics, neuropathology markers that have never been used in NA research.

Further Details

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Benefits

- Unravel pathology-causing lipids and candidate biomarkers for diagnosis and prognosis
- Describe a novel pathomechanism in a group of genetic movement disorders
- Point out associations between proteins and diseases, such as ChAc and MLS
- Develop a whole organism *in vivo* screening tool in the zebrafish model for therapeutic drug target

Applications

- Biomarkers for early diagnosis in Neuroacanthocytosis
- Biomarkers for disease prognosis in Neuroacanthocytosis

Opportunity

Development partner: NA diseases are rare and currently not curable. The search for a development partner is therefore challenging and at the same time an essential need.

For further information, please contact us.

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