

# KAT6B syndrome



**REPORT January, 2026**

**COLLABORATION AGREEMENT BETWEEN UNIVERSIDAD PABLO DE OLAVIDE, SEVILLE, AND THE KAT6 FOUNDATION, FOR THE CONTRIBUTION IN THE DEVELOPMENT OF NEW ALTERNATIVE TREATMENTS OF KAT6B SYNDROME**

## **PREAMBLE**

This report reflects the ongoing collaboration between the KAT6 Foundation and Professor Jose Sanchez-Alcazar's laboratory at the Universidad Pablo de Olavide in Seville, focused on advancing the understanding of cellular dysfunction in KAT6B syndrome and exploring potential agents that may restore more normal cellular functionality.

Through the use of patient-derived cellular models, this work offers early insight into how KAT6B negatively impacts cellular function and how targeted agents may help address these changes. The findings highlight key areas such as reduced gene and protein expression, mitochondrial dysfunction, and potential pharmacological agents that might restore normal function.

While these results are preliminary, they represent an important step toward identifying potential therapeutic strategies; Professor Sanchez-Alcazar's team are continuing studies to explore further agents that may restore cellular functionality in KAT6B. The KAT6 Foundation remains committed to supporting research that moves us closer to improved outcomes for individuals and families affected by KAT6B.

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## **1. Establishment of patient-derived fibroblast cell lines**

Nine fibroblast cell lines derived from KAT6B patients have been successfully established. Cell expansion was performed, and sufficient cryopreserved stocks were generated. Culturing these cell lines proved challenging due to their markedly reduced proliferation rate.

## **2. Initial molecular and functional characterization**

Preliminary analyses performed in three KAT6B fibroblast cell lines revealed:

- Reduced *KAT6B* gene and protein expression
- Decreased expression of KAT6A and BRPF1
- Global reduction in histone acetylation
- Altered mitochondrial bioenergetics
- Reduced Protein levels of PANK2 and ACP
- Increased Reactive Oxygen Species (ROS) accumulation
- Iron accumulation
- Elevated lipid peroxidation

## **3. Pharmacological intervention studies**

Treatment with pantothenate and L-carnitine partially reversed several of the observed pathophysiological alterations in KAT6B fibroblasts, indicating a potential therapeutic effect.

## **4. Future directions**

Following the characterization of the pathophysiological phenotype and the evaluation of responses to pantothenate and L-carnitine, the next steps will include direct cellular reprogramming to induced neurons and RNA sequencing (RNA-seq) analyses, which are planned for the coming months.