# Efavirenz use for Niemann-Pick C treatment

**CSIC has developed and brought to preclinical stage a novel non-invasive pharmacological treatment for Niemann Pick disease Type C (NPC) and other lysosomal storage disorders where cholesterol accumulates in the brain.**

**Pharmaceutical and Biopharmaceutical companies are being sought to collaborate through a patent licence agreement.**

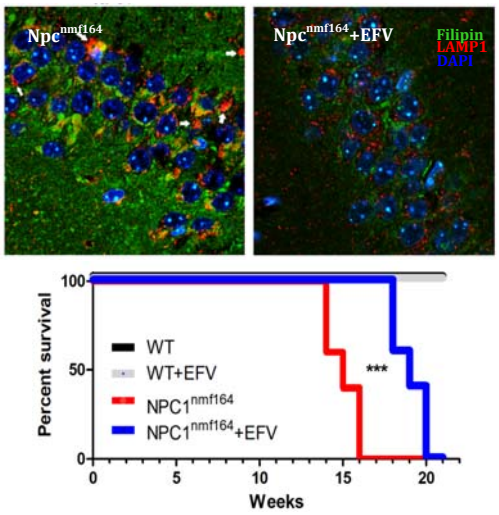
***An offer for Patent Licensing***

## Pharmacological treatment for Niemann-Pick C and other neurological lysosomal storage disorders

NPC is a fatal disease caused by mutations in the cholesterol transport protein Npc1. The accumulation of cholesterol, particularly evident in lysosomes, leads to progressive neurodegeneration and to cognitive and psychiatric alterations in NPC patients. Currently, the only treatment approved for NPC is the iminosugar Miglustat, which prevents accumulation of gangliosides and delays neurological symptoms but does not cure the disease having serious side effects.

We have demonstrated that oral treatment with Efavirenz (EFV), which activates the cholesterol-degrading enzyme CYP46, prevents brain cholesterol accumulation and pathology in a mouse model for NPC ($Npc^{nmf164}$mice).

We propose EFV treatment could be also suitable for many other neurological lysosomal storage disorders where brain cholesterol accumulation is a hallmark.




Cholesterol and lysosome labeling by Filipin (green) and LAMP1 (red) staining, respectively, in the brain of $Npc^{nmf164}$ mice treated or not with EFV. Reduction of cholesterol levels and lysosomal size are evident upon EFV treatment. DAPI (blue) stains cell nuclei. The lower panel shows the 30% increase in life span of $Npc^{nmf164}$ mice treated with EFV

## Main innovations and advantages

- We have shown that Npc1 is not only present in lysosomes but also in synapses where it mediates the cholesterol rearrangement necessary to put in place neurotransmitter receptors.
- Npc1 deficiency leads to cholesterol accumulation in synapses leading to morphological and functional synaptic alterations that result in memory and psychiatric issues.
- In vitro pharmacological activation of the enzyme CYP46 by EFV restores synaptic cholesterol levels and function.
- Oral treatment with EFV prevents brain cholesterol accumulation, memory and psychiatric alterations and extends life span in $Npc^{nmf164}$mice.
- EFV is already used for the chronic treatment of HIV patients at doses much higher than the ones used in our study.

## Patent Status

Priority patent application filed suitable for international extension

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