SELECTED OPPORTUNITIES IN RARE DISEASE – SENSORY ORGANS

Modulator of WIP1 levels to treat Wolfram syndrome (BIO15148)

MODULATOR OF WIP1 LEVELS TO TREAT WOLFRAM SYNDROME (BIO15148)

Product factsheet

POC in vitro and in vivo

- **Product: WIP1 gene therapy / inhibitor of WIP1 degradation**
- **Potential applications:** Wolfram syndrome (WS) is an autosomal recessive neurodegenerative disorder characterized by diabetes insipidus/mellitus, optic atrophy and deafness.
- Loss of function of WFS1 is responsible for WS
- Gene therapy aiming at WFS1 normal expression is impossible due to the size of the WFS1 gene
- **Mechanism:** unexpected key role of WFS1 and WIP1 in ER-mitochondria crosstalk which reconciles the ER expression of WFS1 with the mitochondrial phenotype
  - WFS1 forms a complex with WIP1 (official name undisclosed), to promote ER-mitochondrial Ca2+ transfer in response to stimuli that generate inositol-1,4,5- triphosphate.
  - WFS1 associates with WIP1 to prevent its degradation by the proteasome.
  - WIP1 regulates VDAC expression and mitochondrial respiratory chain.
- **Phase of development: POC in vitro and in vivo**
  - WS patients fibroblasts show diminution of WIP1 protein expression
  - WS patients fibroblasts treatment with proteasome restores levels of WIP1 to a level comparable to normal patients
  - Expression of WIP1 in WS patients fibroblasts can overcome WFS1 deficiency and restore mitochondrial respiration
- **Patents: PCT/EP2017/056940, TARGETING THE NEURONAL CALCIUM SENSOR 1 FOR TREATING WOLFRAM SYNDROME**

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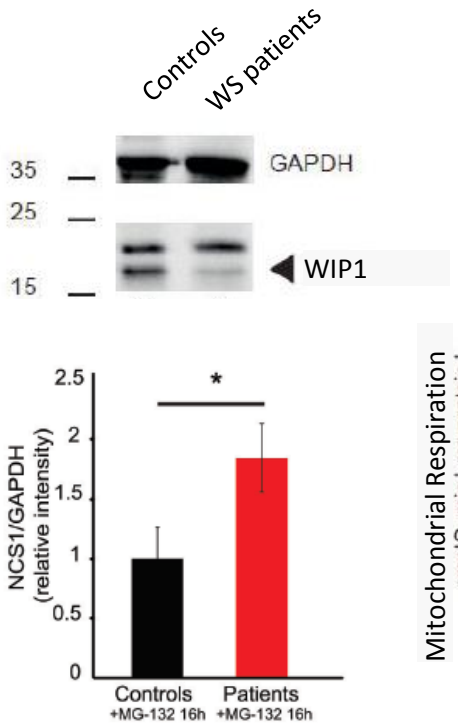
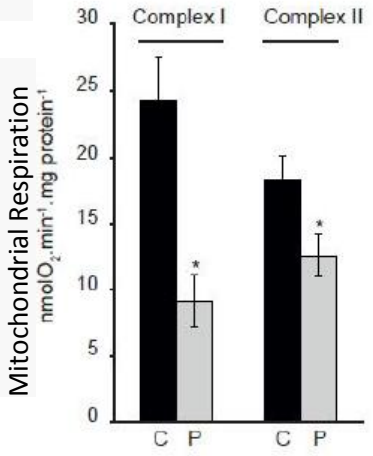
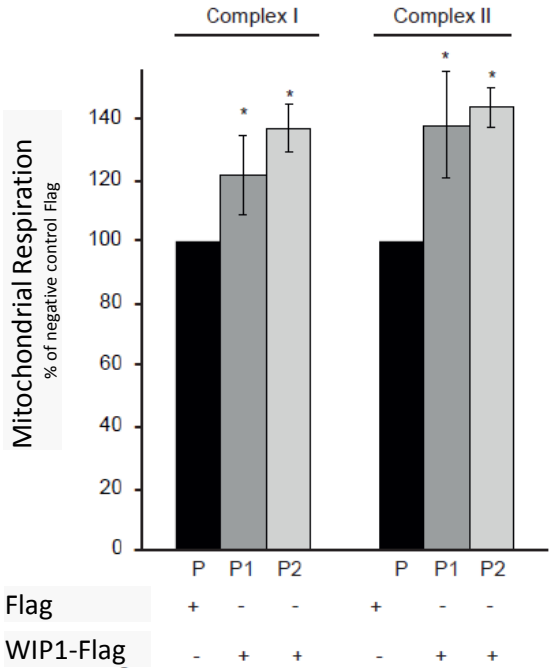
Proof of concept

Restoration of WIP1 expression in cells of WS patients can overcome WFS1 deficiency and mitochondrial respiratory defects







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