



## Libro de resúmenes

# I Congreso de Investigadores del PTS

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# I Congreso de Investigadores del PTS

Parque Tecnológico de la Salud

13, 14 y 15 de febrero de 2019

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## PERTURBATION OF SULFIDE METABOLISM UNDER COQ DEFICIENCY IS MAINTAINED AFTER MODIFICATION OF SULFUR AMINOACIDS AVAILABILITY IN THE DIET.

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The Coenzyme Q (CoQ)-junction integrates the oxidation of CoQ in the mitochondrial respiratory chain with the ATP production, the TCA cycle, the  $\uparrow$ oxidation, the shuttling of reduction equivalents from the cytoplasm, the synthesis of pyrimidines, the metabolisms of glycine, arginine and proline and the sulfide oxidation pathway. Recently, we have demonstrated that CoQ deficiency leads to a decrease in the levels of the enzyme Sulfide Quinone Oxidoreductase (SQOR), inducing a disruption in the mitochondrial sulfide oxidation pathway<sup>1</sup>. Because dietary restriction of sulfur aminoacids (SAAR) or supplementation with N-Acetyl-L-cysteine (NAC) can interfere with sulfide metabolism and both strategies have shown therapeutic benefits in a variety of conditions<sup>2,3</sup>, we have tested these two interventions in the Coq9R239X mouse model. Our results show that the severe CoQ deficiency in the kidneys and the brain of Coq9R239X mice persisted under SAAR or after supplementation with NAC. Consequently, the levels of SQOR were significantly reduced in the kidneys and the brain of Coq9R239X mice; and these severe reductions in SQOR levels were maintained under SAAR or after supplementation with NAC.

Curiously, the levels of cystathionine beta synthase (CBS), an enzyme involved in the transsulfuration pathway, were increased in the kidneys and the brain of Coq9R239X mice, compared to Coq9+/+ mice; and SAAR or administration of NAC did not normalize this change. Because sulfide metabolism is related with the glutathione system, we also measured the levels of glutathione and its enzymes. Total GSH levels were reduced in the kidneys of Coq9R239X mice and this change was sustained under SAAR or NAC administration. This result correlates with a reduction in the levels of GPx and GRd in the kidney of Coq9R239X, Coq9R239X + NAC and Coq9R239X + SAAR, compared to Coq9+/+ mice. As a consequence of the lack of effect of SAAR or NAC administration in the sulfide metabolism on Coq9R239X mice, these two interventions were not able to increase the survival in this mouse model. These results demonstrate that the disruption of sulfide and glutathione metabolisms in Coq9R239X mice depends on the levels of CoQ and, therefore, modifications in sulfur aminoacids availability in the diet does not result in therapeutic benefits.