**Resveratrol induces resilience against age-related neurodegeneration through improvement of proteostasis**

Rubén Corpas1,2, Christian Griñán-Ferré1,3, Mercè Pallàs1,3 and Coral SanfelIU1,2

1 MouseAGE, COST Action BM1402
2 Institut d’Investigacions Biomèdiques de Barcelona (IIBB), CSIC and IDIBAPS, Barcelona, Spain
3 Faculty of Pharmacy, Institut de Neurociències, Universitat de Barcelona and CIBERNED, Barcelona, Spain

AIM: Resveratrol is a natural compound that induces longevity and neuroprotection purportedly by regulating the NAD+ dependent deacetylase SIRT1. We aimed to analyze the effects of resveratrol on the brain status of 3xTg-AD transgenic mice to discern the mechanisms involved in a potential inducement of resilience against age-related neurodegeneration and Alzheimer’s disease.

METHODS: Control NoTg and 3xTg-AD mice were fed a diet supplemented with 100 mg/kg trans-resveratrol during 10 months. The period of 2 to 12 months of age covered a broad period of the AD pathology progression, from the pre-symptomatic to the advanced AD pathology phase. Behavioral tests and immunoblotting of hippocampal tissue were performed.

---

**RESULTS**

1. **Neuroprotection against cognitive loss in 3xTg-AD mice:**

   - **Spatial learning & memory**
     - Morris Water Maze
   - **Acquisition task**
     - NoTg vs 3xTg
   - **Removal test**
     - NoTg vs 3xTg

2. **Protection against amyloid and tau pathology in 3xTg-AD mice**

   - **Aβ levels**
     - APP-CTF
   - **p-Tau levels**
     - NoTg vs 3xTg

3. **Enhancement of the ubiquitin-proteasome system**

   - **Ubiquitin conjugation**
     - Hep70
   - **Ubiquitinated proteins**
     - Tubulin

4. **Activation of SIRT1 pathways**

   - **SIRT1 function**

**CONCLUSIONS**

- Resveratrol induced neuroprotection against memory loss in AD mice and cognitive enhancement in healthy mice.
- Resveratrol protects against amyloid and tau pathologies.
- Resveratrol activates SIRT1 pathways and improves proteostasis in both healthy and AD mice.

This study was supported by SAF2016-77703, MINECO and ERDF.

ruben.corpas@iibb.csic.es