Study of mitochondrial function in experimental models for SOD1-linked familial ALS by genetic manipulation of the p66Shc-dependent molecular pathway

Call for projects 2009
Grant: 100 000 €
Project Duration: 2 years

Investigator: Maria Teresa Carri, University “Tor Vergata”, Rome, Italy

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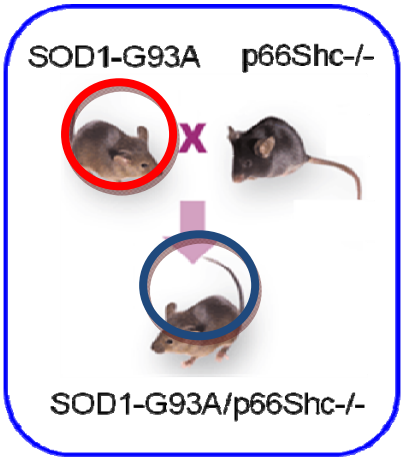
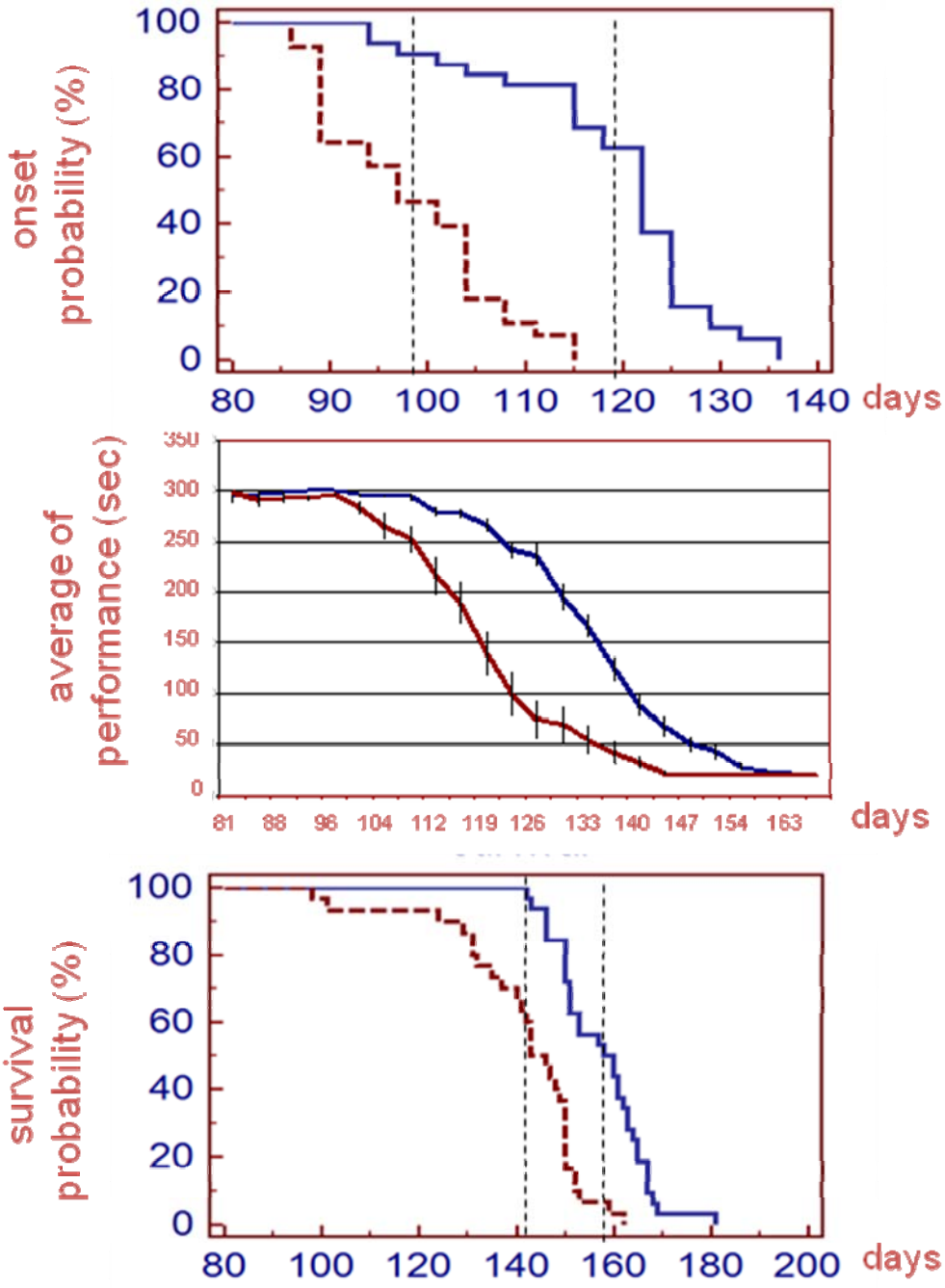
A wealth of evidence indicates that intracellular organelles called *mitochondria* are one of the primary locations of damage in Amyotrophic Lateral Sclerosis. These organelles are most important in the life of motor neurons because they possess the ability to convert nutrients into energy, and they also play an essential role in calcium metabolism and in oxidative stress and therefore in the control of cell survival. Dysfunction of mitochondria is observed early in patients (and in experimental models for ALS) and causes the death of neurons, which underlies onset of paralysis and death of patients.

In this project, we have attempted rescue of correct mitochondrial function in mice models for familial ALS by genetic removal of a protein called p66Shc that controls oxidative stress and mitochondrial damage in cells.

We have been able to demonstrate that deletion of this protein robustly ameliorates mitochondrial function, delays onset, improves motor performance and prolongs survival in transgenic mice modelling ALS. We have also been able to understand why this protein is important in ALS and at least part of the molecular pathway(s) underlying mitochondrial damage in this disease.

Thus, our results provide the proof of principle for a new strategy for therapeutic intervention in ALS. We plan to further pursue this line of research with a pre-clinical study on the pharmacological interception of the p66Shc pathway in mice.





Red: ALS mice (expressing ALS-G93ASOD1)
Blue : same mice as above, but lacking p66Shc

STUDY OF MITOCHONDRIAL FUNCTION IN EXPERIMENTAL MODELS FOR SOD1-LINKED FAMILIAL ALS BY GENETIC MANIPULATION OF THE P66SHC-DEPENDENT MOLECULAR PATHWAY

MT. Carri , Italy
Grant: € 100 000

Recent evidence indicates that intracellular organelles called mitochondria are one of the primary location of damage in Amyotrophic Lateral Sclerosis.

Mitochondria are “the powerhouse of the cell” because of their ability to convert nutrients into energy. They also play an essential role in calcium metabolism, in oxidative stress and in the control of cell death.

Dysfunction of mitochondria is observed early in patients (and in experimental models for ALS) and causes the death of neurons, which underlies onset of paralysis and death of patients.
In this project, we propose to attempt rescue of correct mitochondrial function in mice models for familial ALS by genetic removal of p66Shc, a protein that controls oxidative stress and mitochondrial damage in cells.

Although this is a pre-clinical study, we believe that individuation of new strategies to intercept damage in mitochondria may allow devising new therapeutic approaches for ALS patients.

TO LEARN MORE ABOUT OXIDATIVE STRESS AND MITOCHONDRIAL DAMAGE IN ALS

TEAM

Maria Teresa Carrì (Principal Investigator-see picture below far left) is a Full Professor of Biochemistry at the University of Rome “Tor Vergata”, Italy. She is author of more than 40 publications on ALS in peer-reviewed international journals.

From left to right: M.T. Carri, M. Nencini-a graduate technician, A. Ferri-an assistant Professor, M. Cozzolino- a senior Post-Doc and I. Amori and M. Grazia Pesaresi – both Ph.D. students. All of these scientists are part of Professor Carri's team and working on the project.