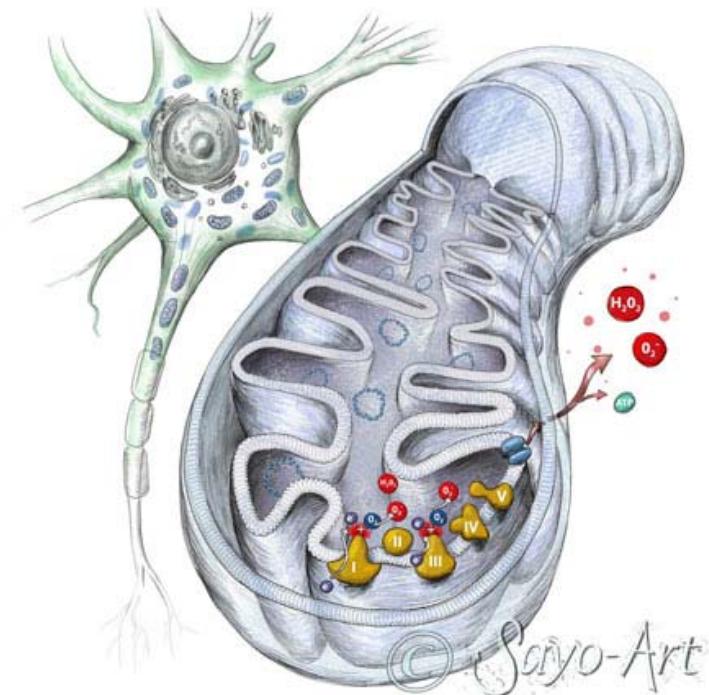
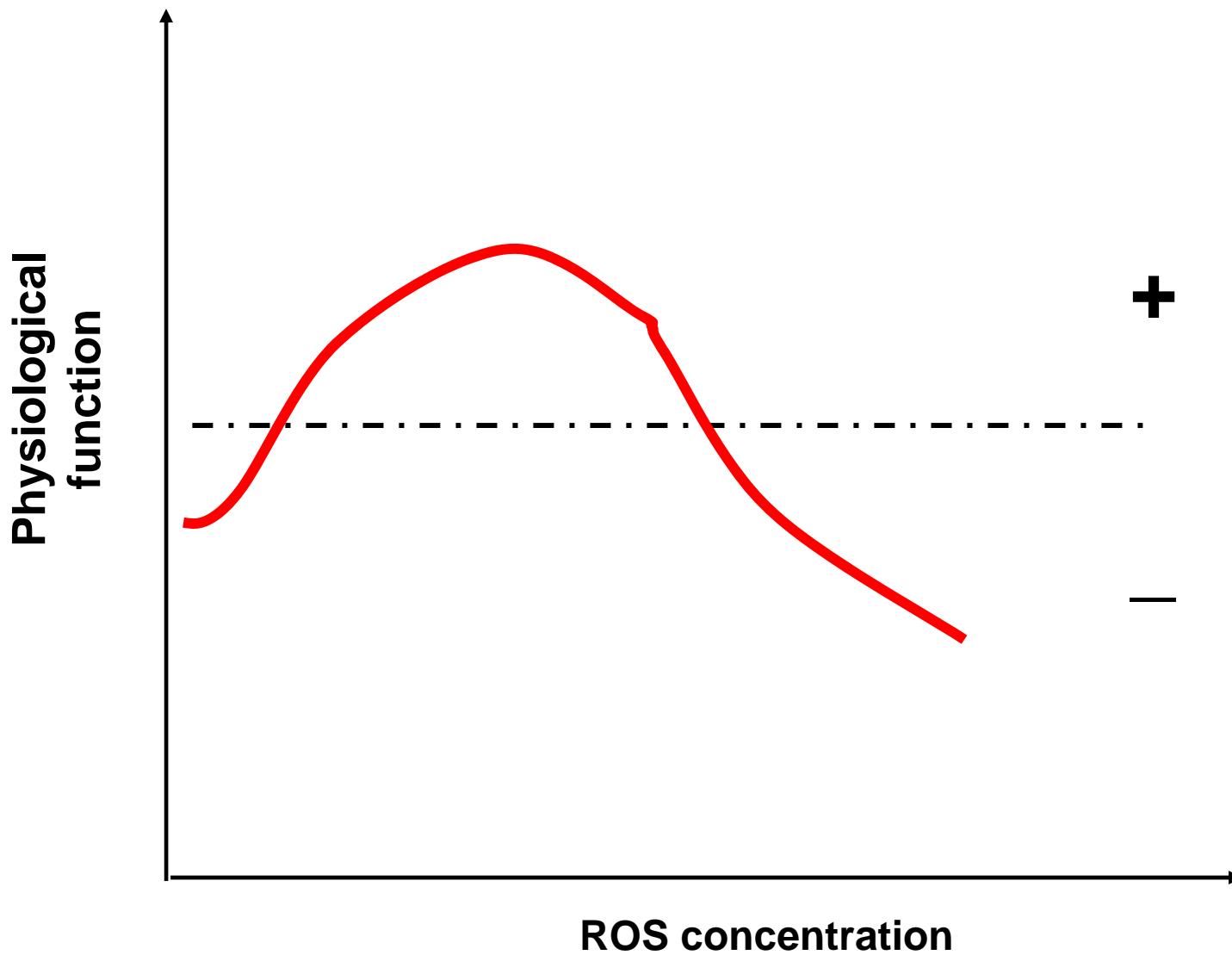


Oxidative damage: Is damage a correct term?

**Zsolt RADA
K, D.Sc.**
Semmelweis University
Budapest, Hungary

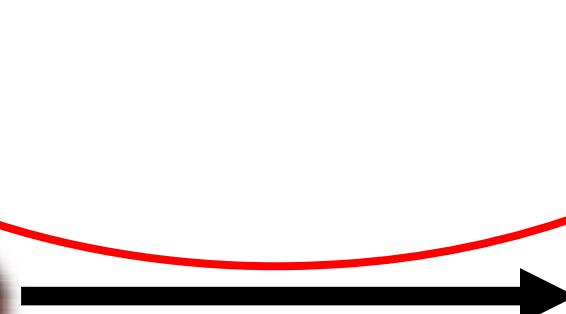


Hormetic response to ROS





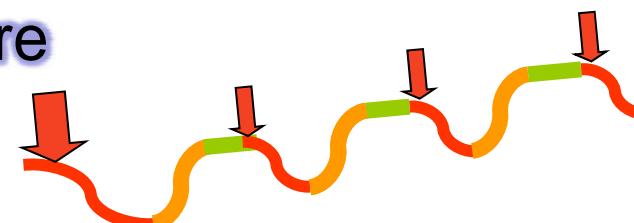
**Chronic exposure
(aging)**



Oxidative stress

**Oxidative
damage**

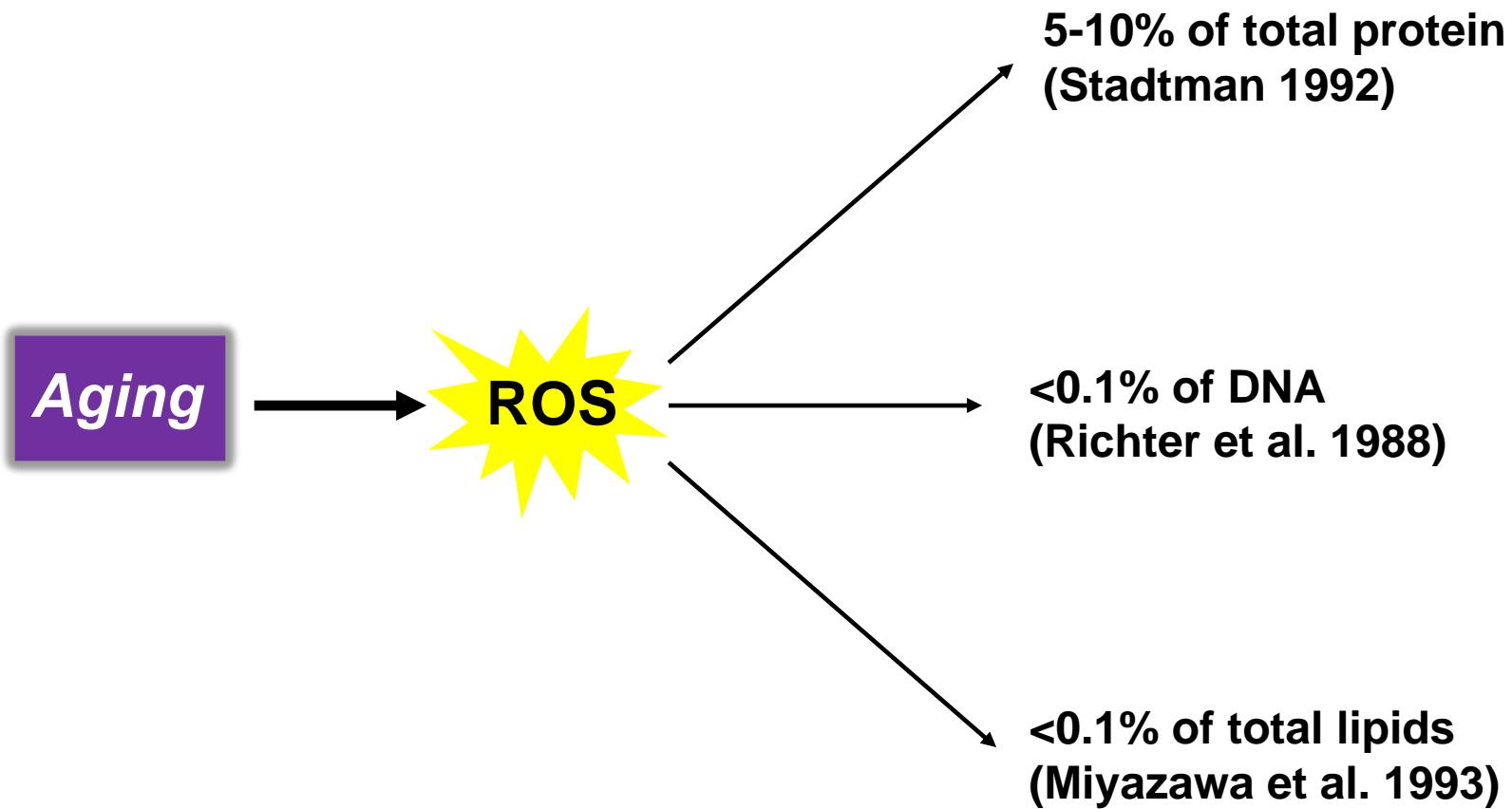
**Intermittent exposure
(exercise)**



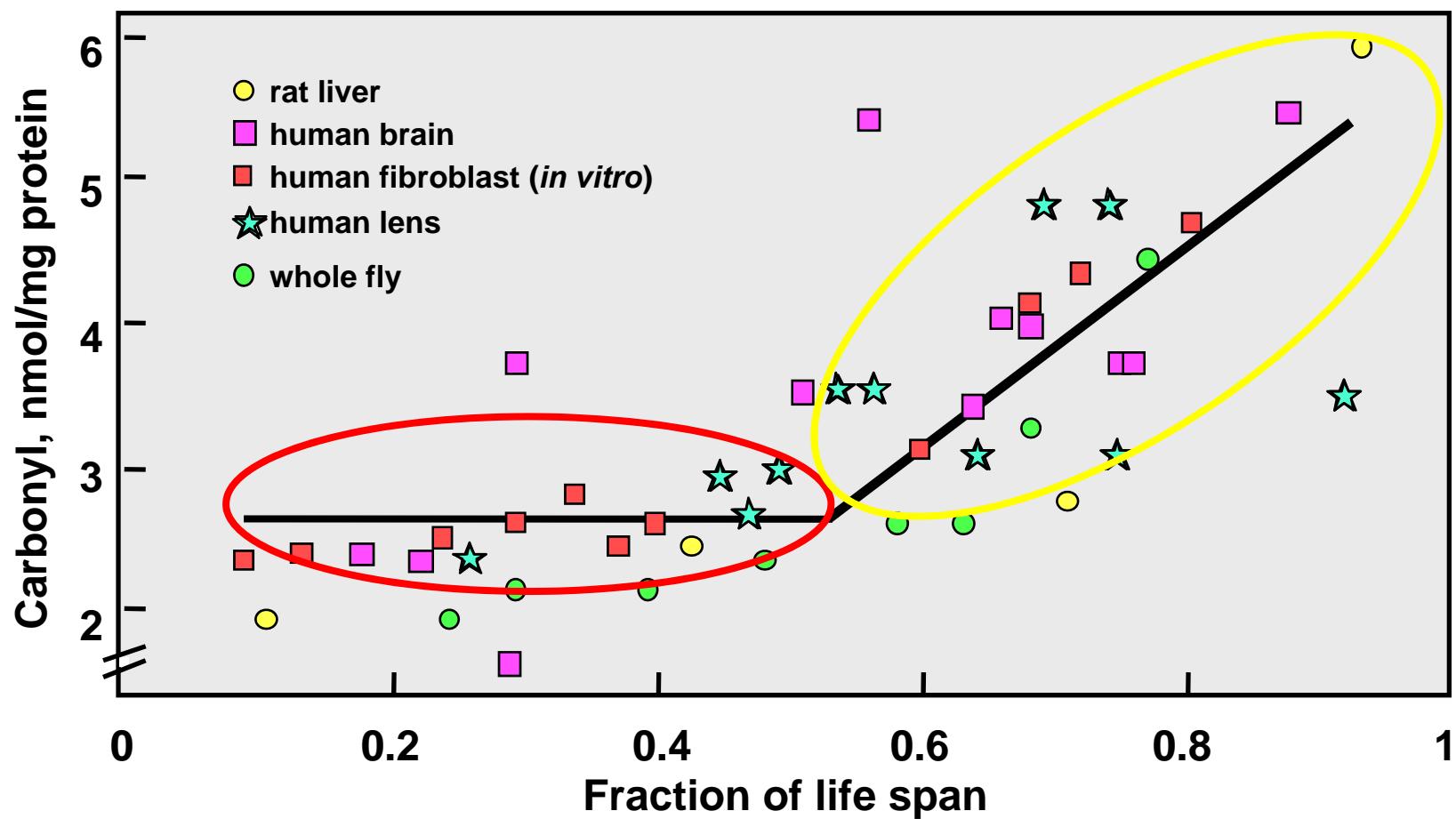
Adaptation



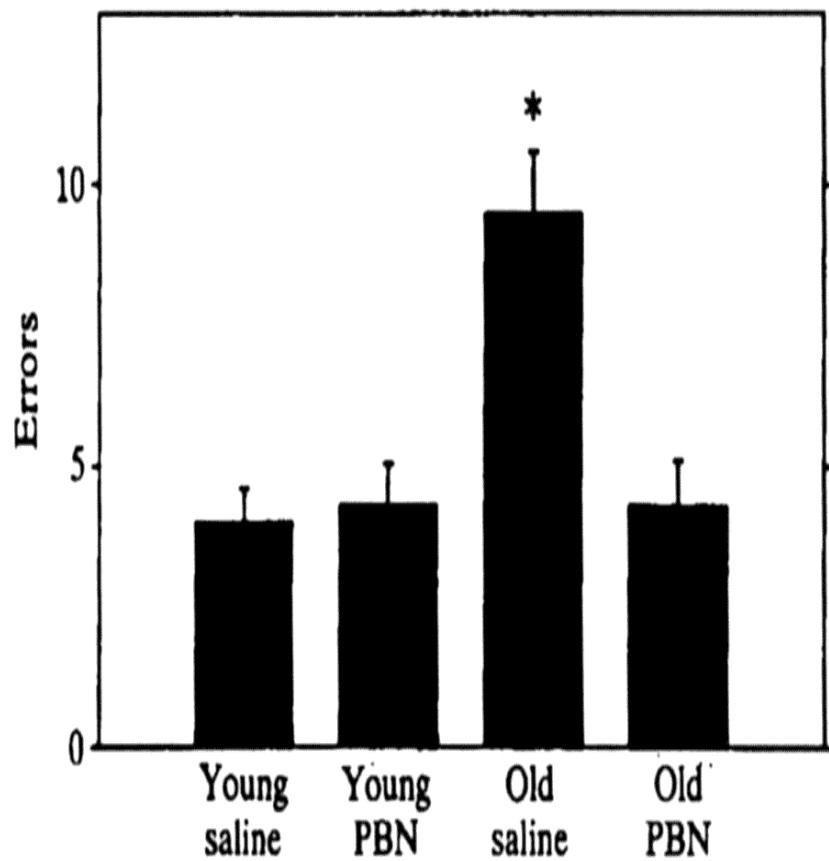
Oxidative modification of lipids, DNA and proteins as a result of aging



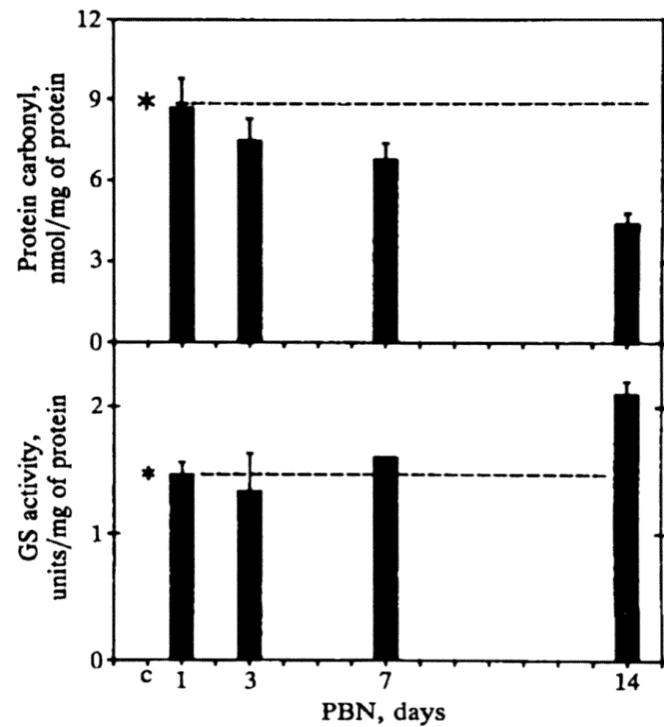
Change in Protein Carbonyl with Age in Various Animals



The beneficail effects of antioxidant treatment on maze test

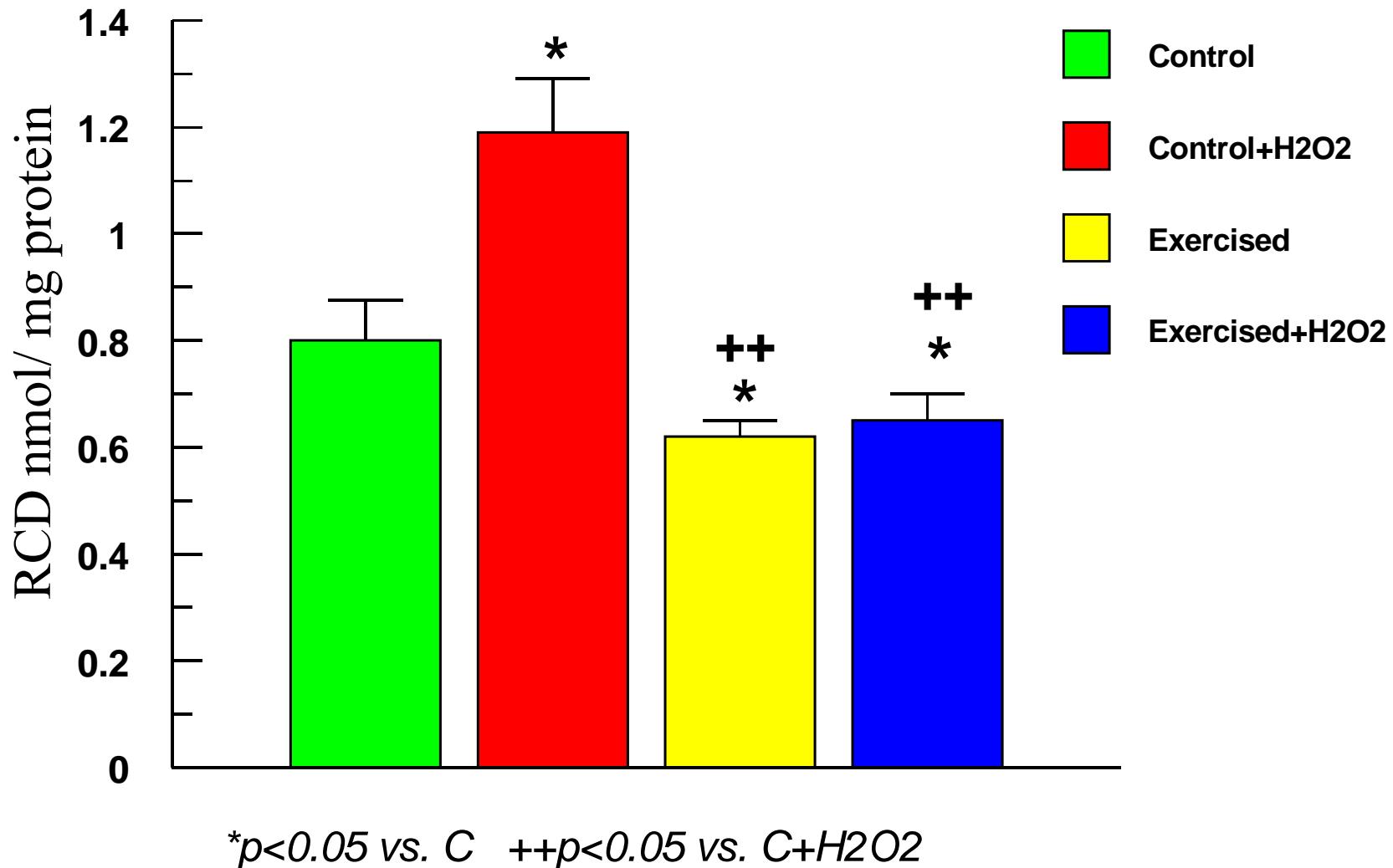


The effect of PBN administration on brain carbonyls and GS activity

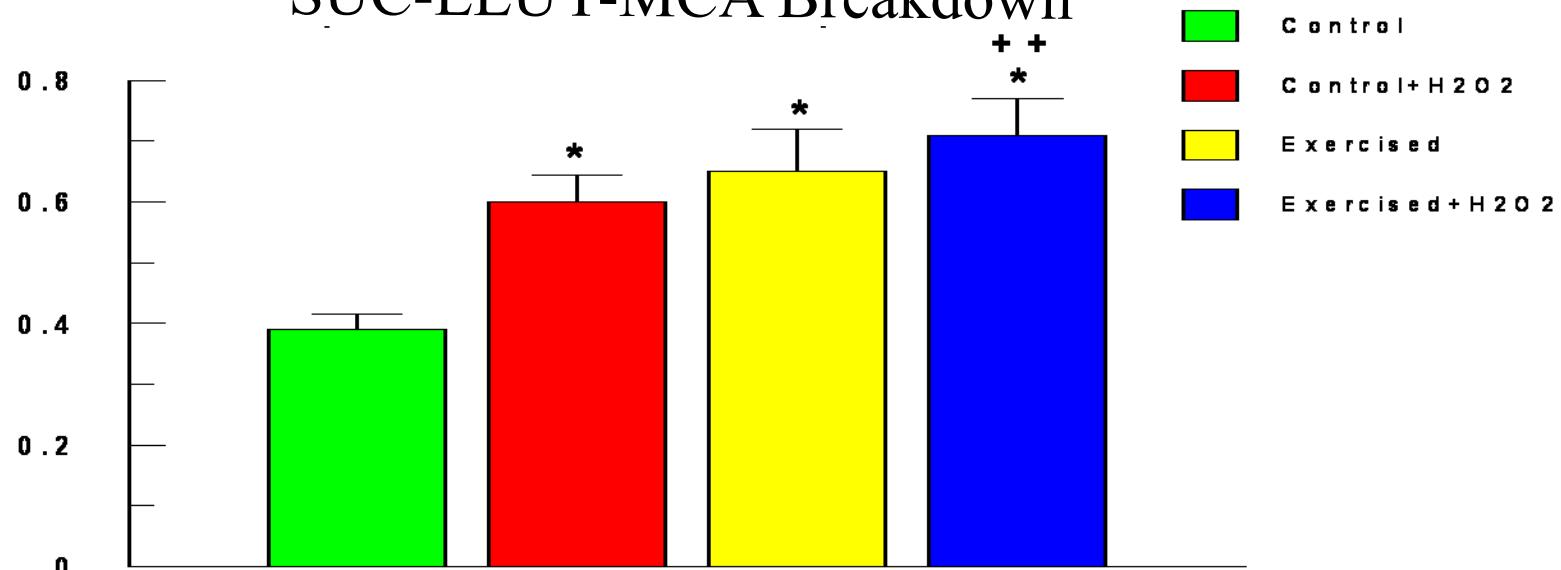


Carney et al. 1991

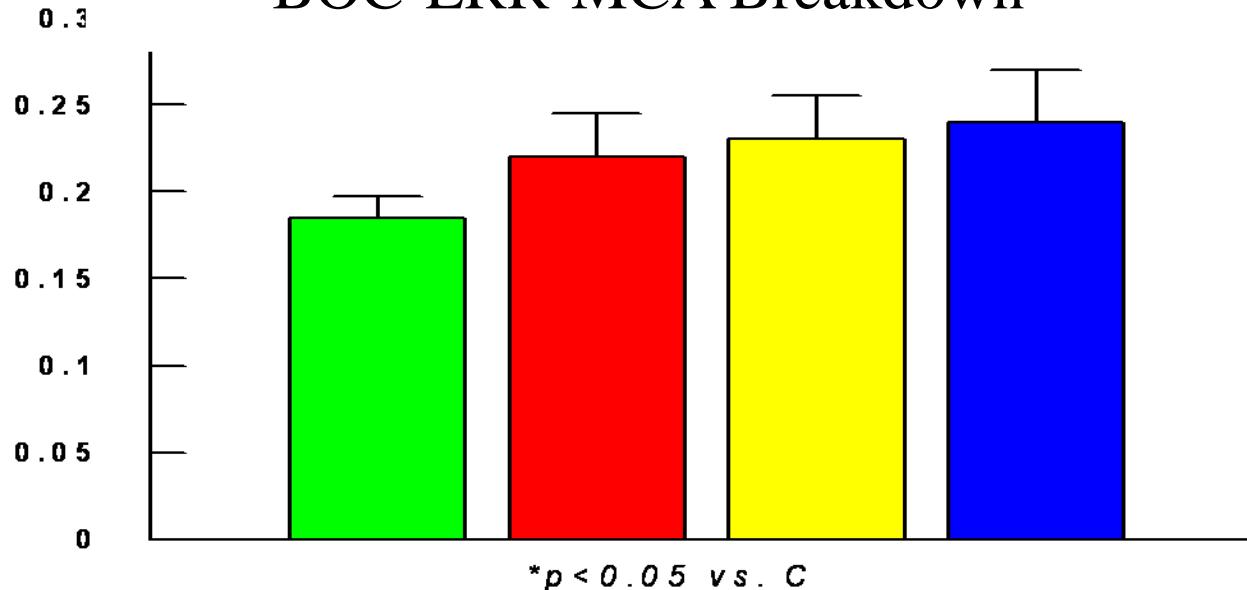
The accumulation of carbonylated proteins



SUC-LLUY-MCA Breakdown



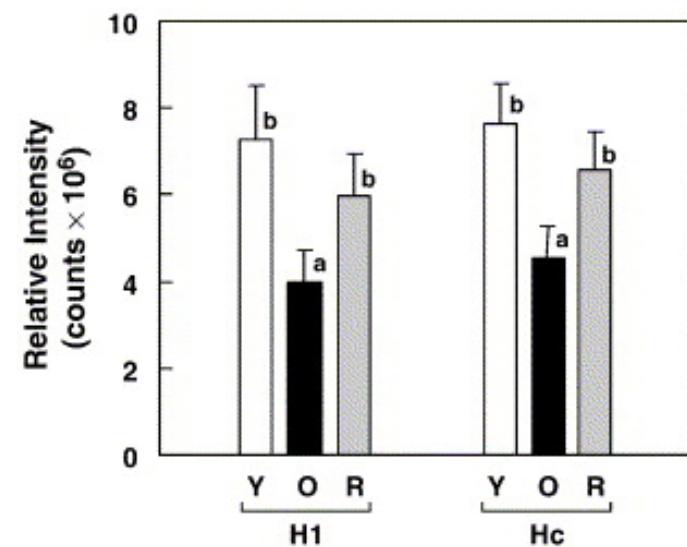
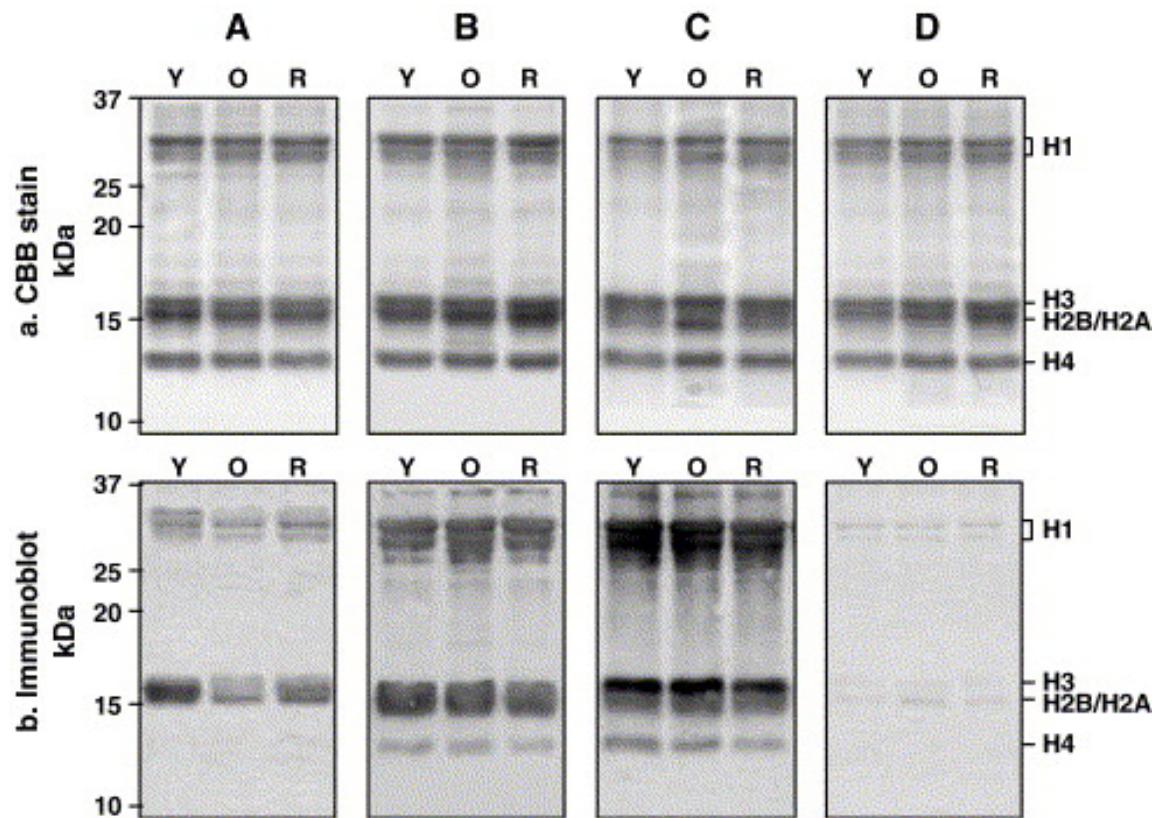
BOC-LRR-MCA Breakdown



* $p < 0.05$ vs. C



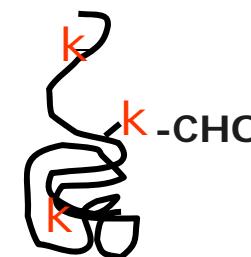
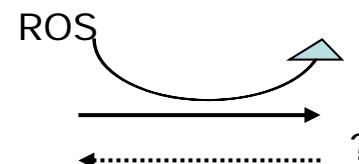
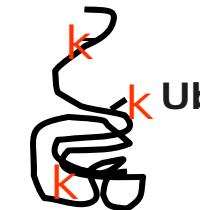
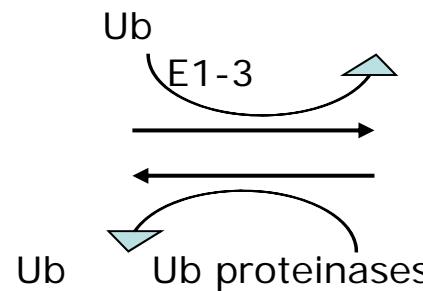
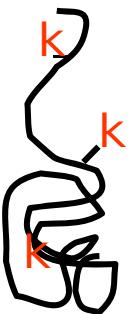
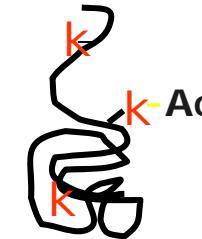
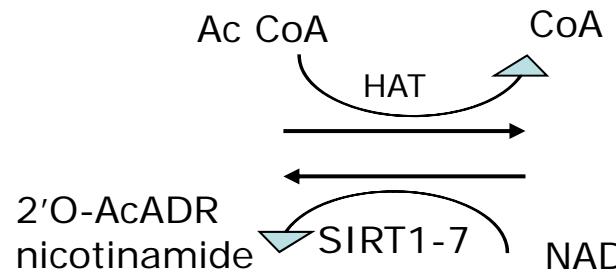
Representative patterns of carbonylation of histones from the liver of young (Y), old (O), and old dietary restricted (R) rats





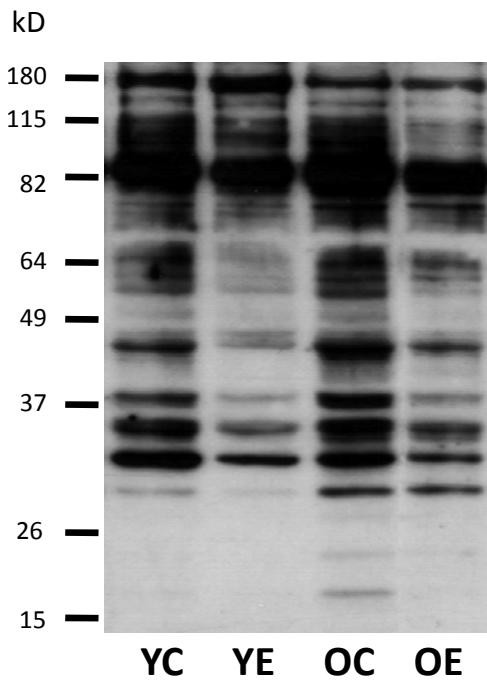
Posttranslational modifications

Activation/inhibition/stability/regulation

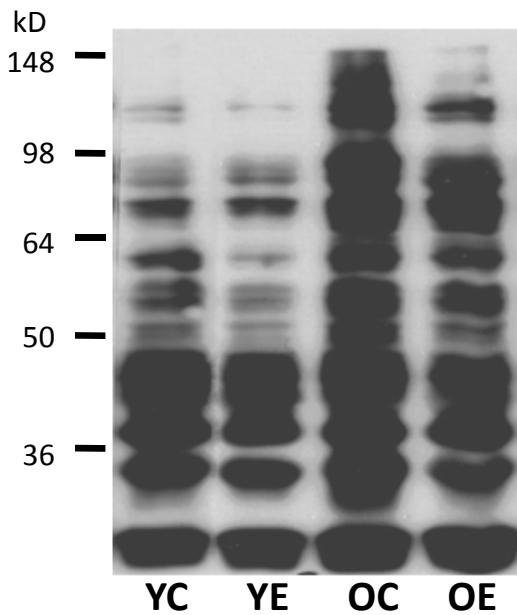


Posttranslational modifications of skeletal muscle with aging and exercise

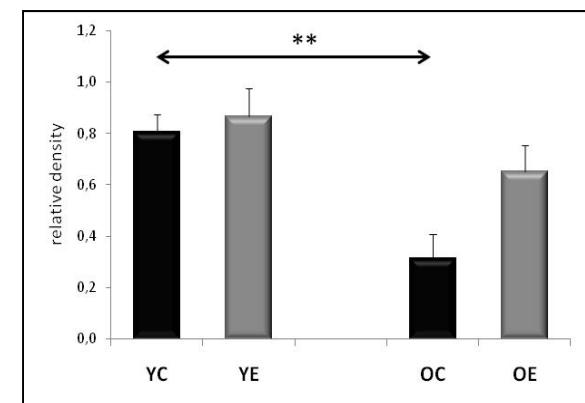
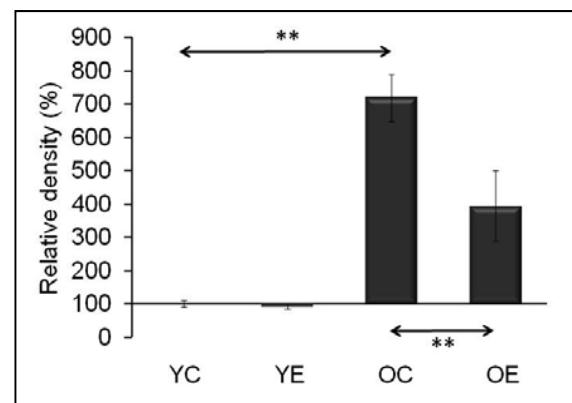
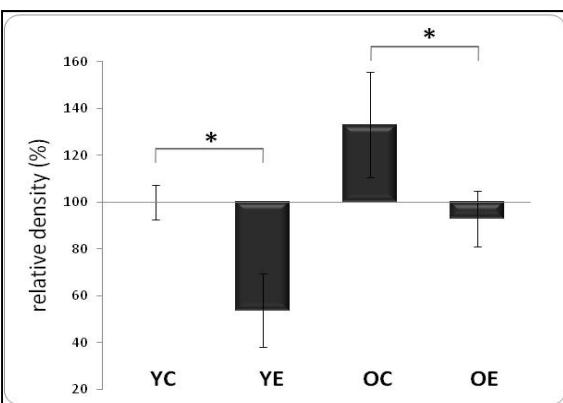
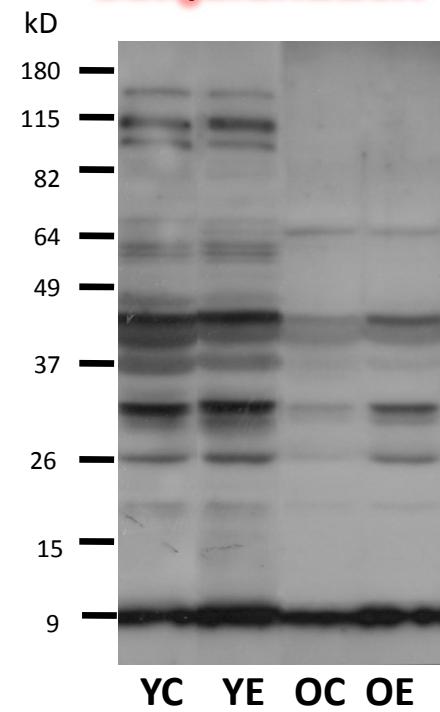
Acetylation



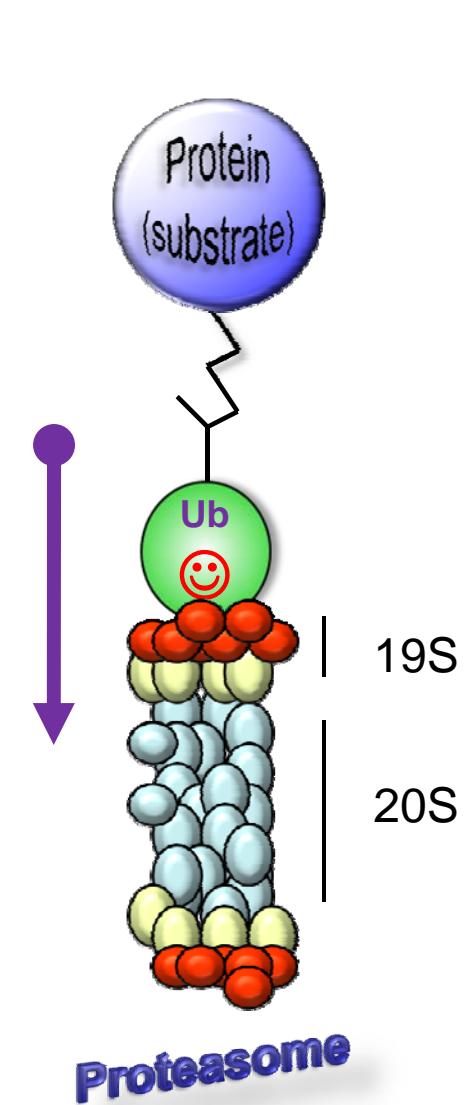
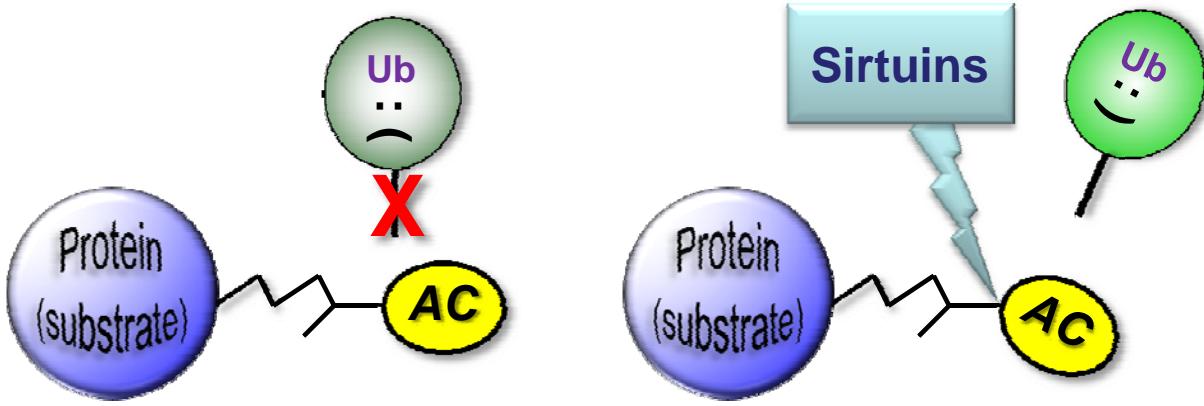
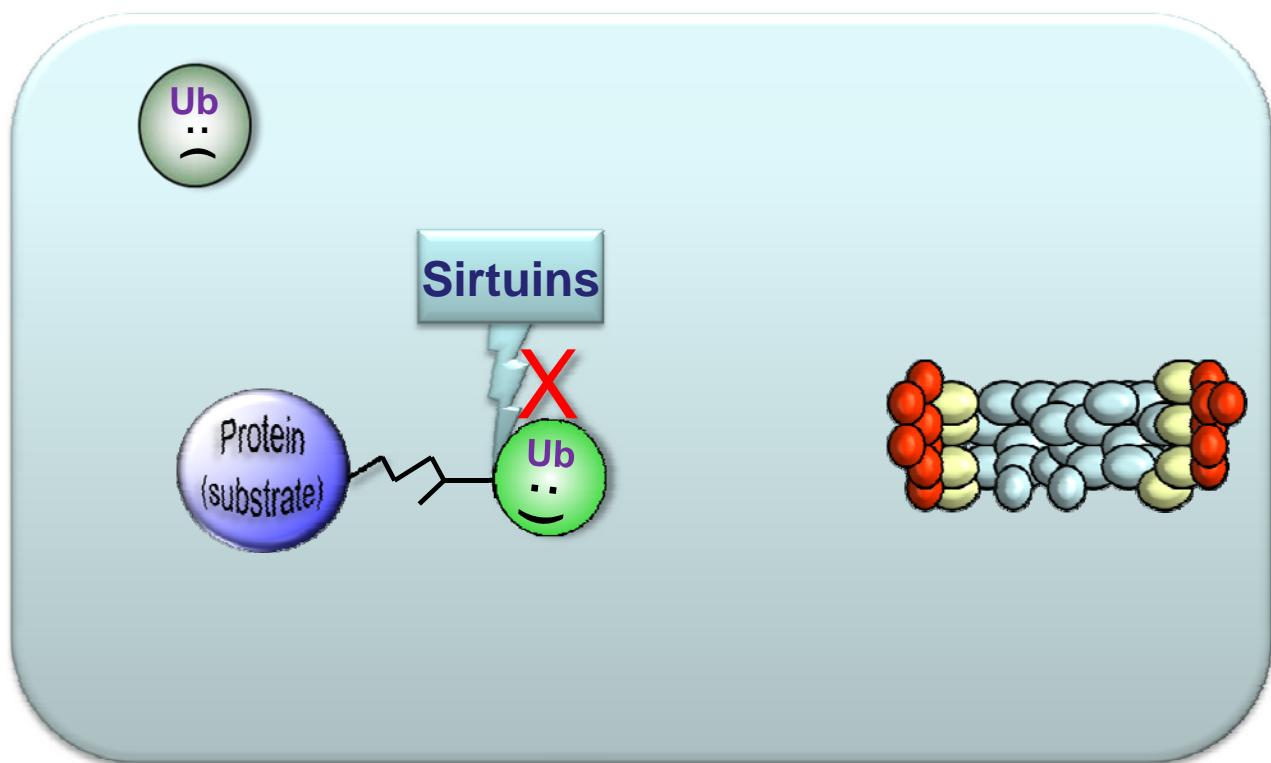
Carbonylation



Ubiquitination

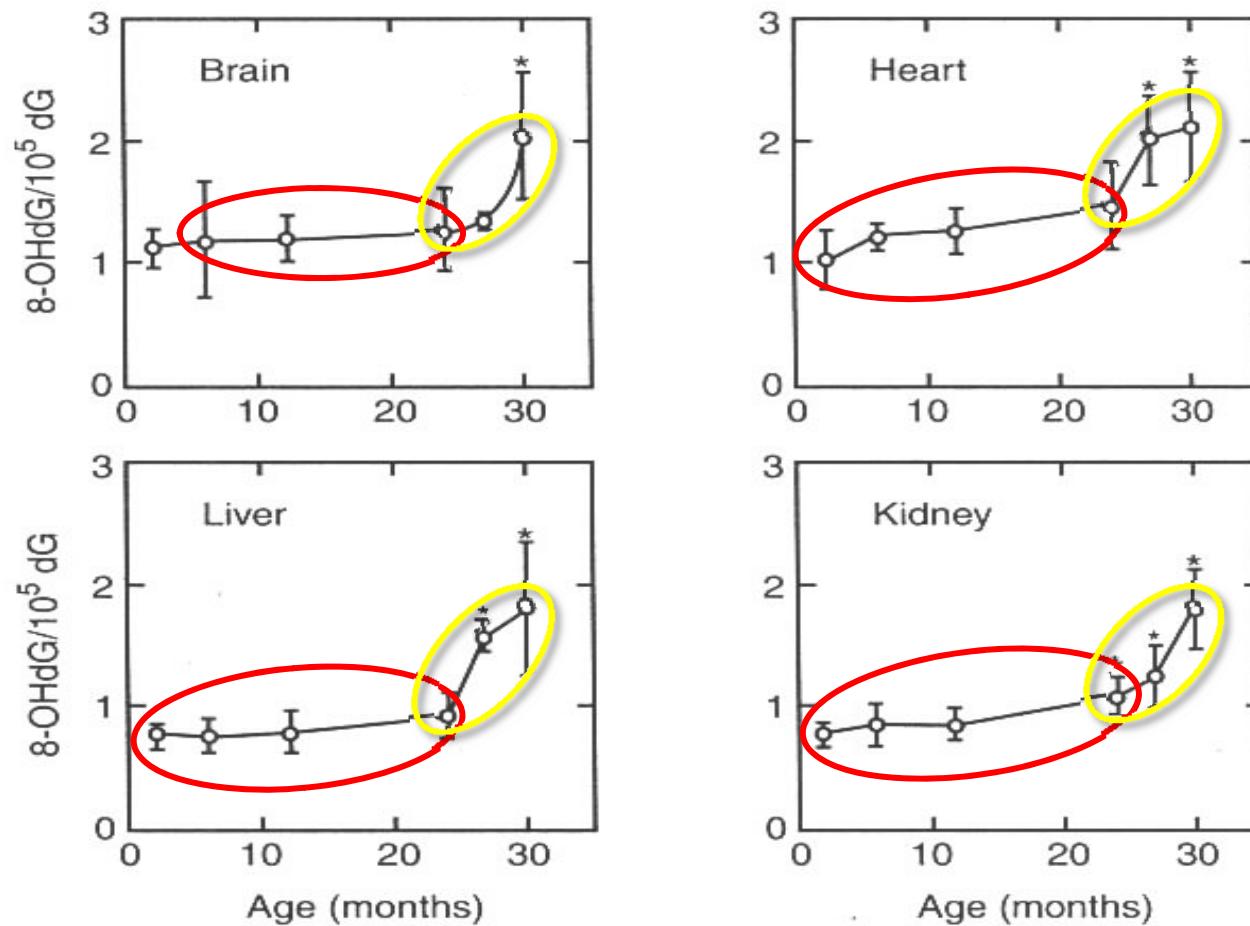


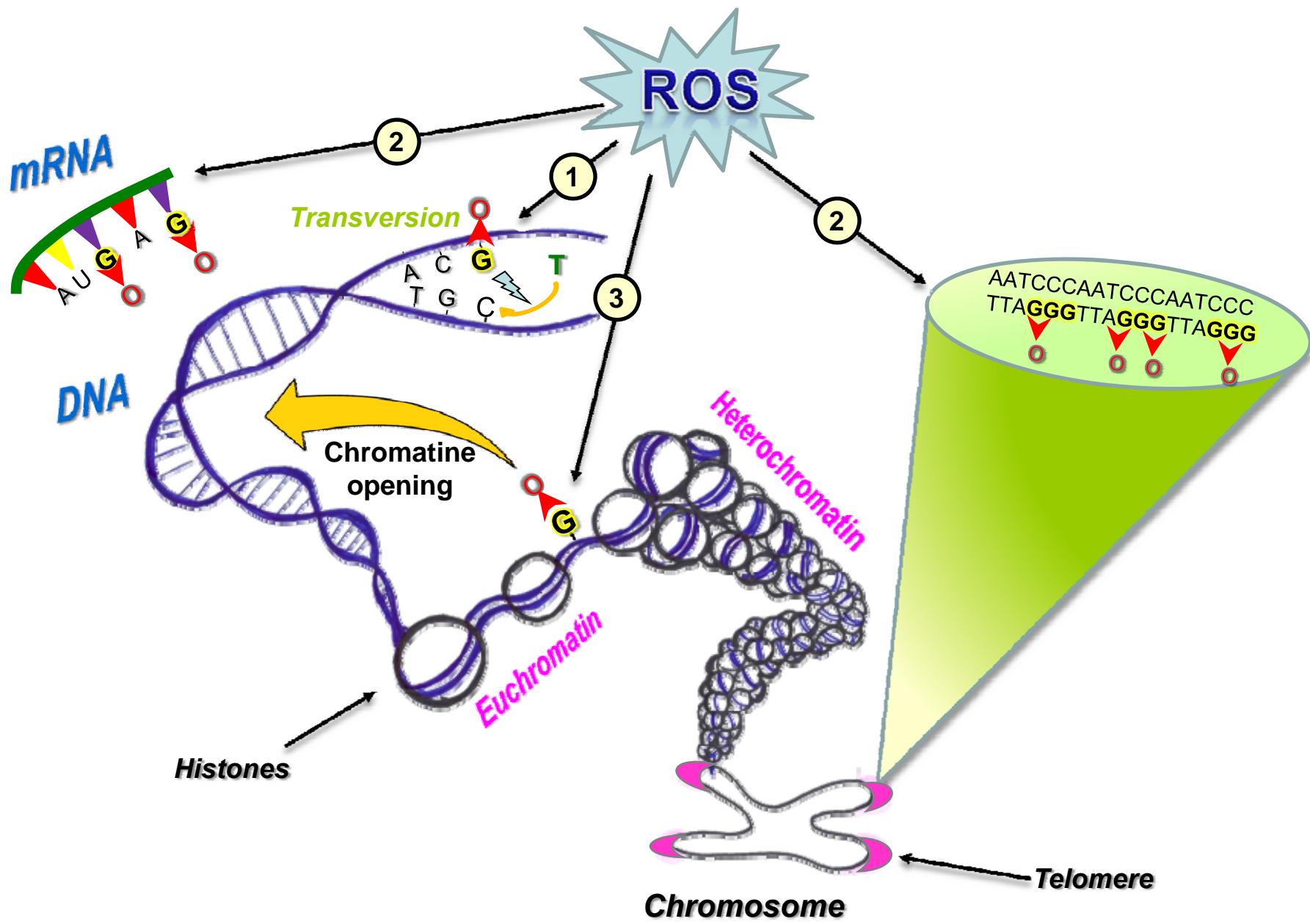
Sirtuins-ubiquitination-proteasome pathway

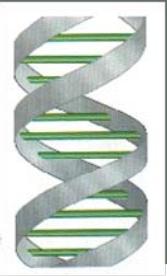




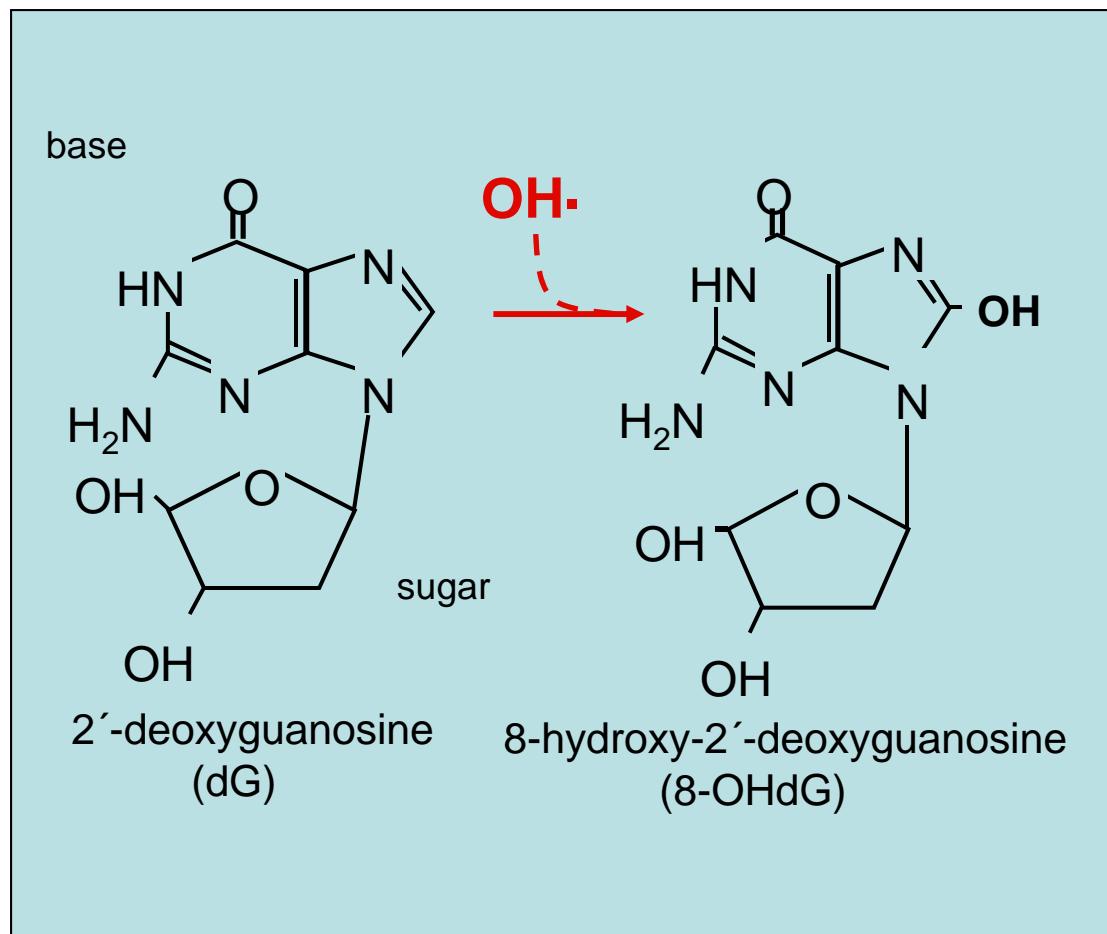
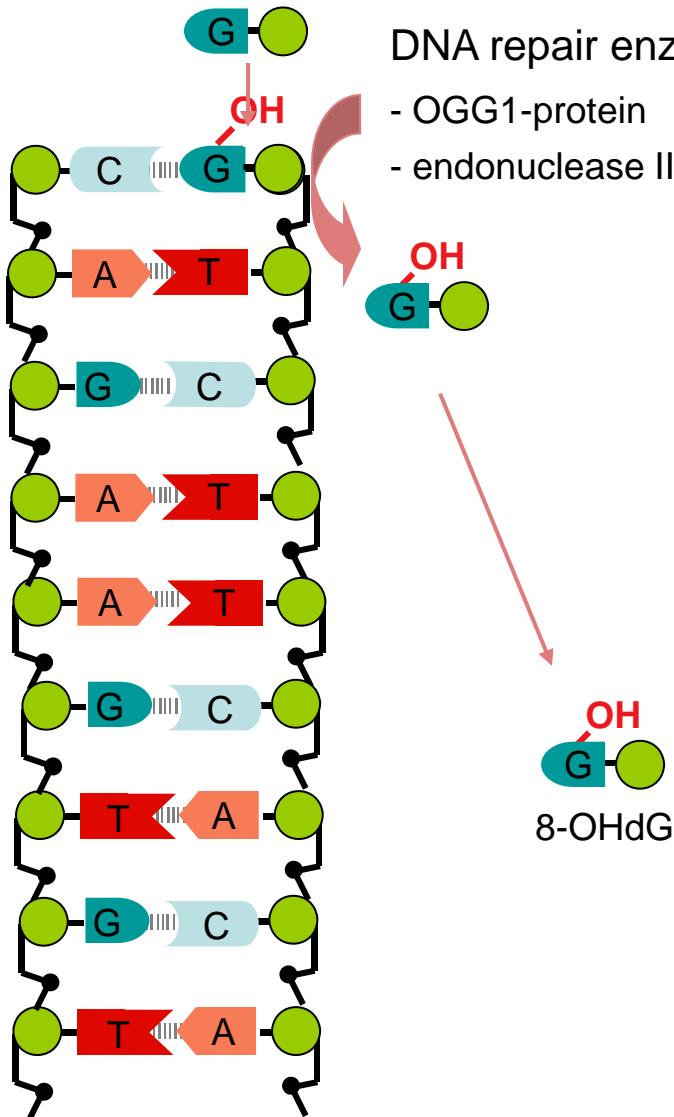
Age-related increase in 8-OH-dG content in different organs of rats







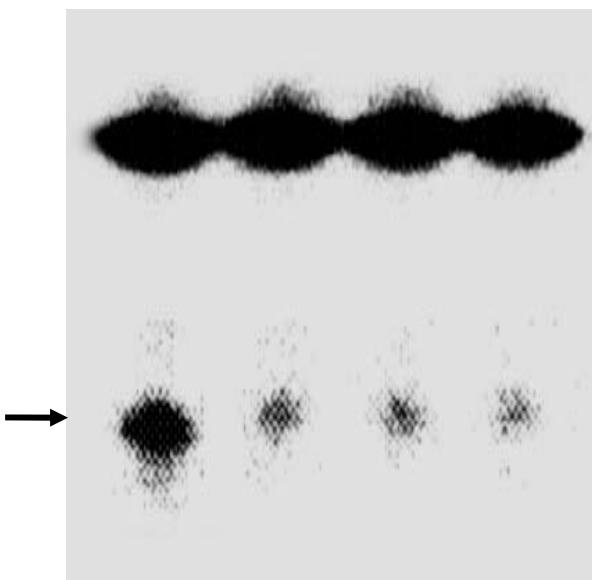
Oxidative DNA damage and repair



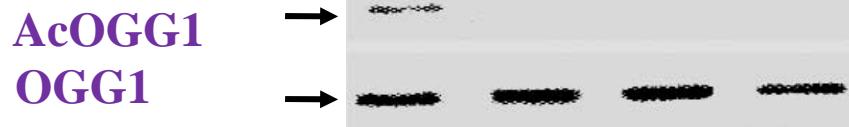
Acetylation of OGG1 induces the activity

A

	1	2	3	4
AcCoA	+	--	+	--
p300/CBP	+	+	--	--
OGG1	+	+	+	+

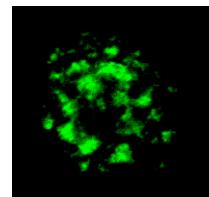


B



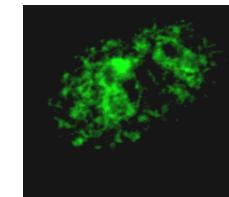
C

8-oxoG

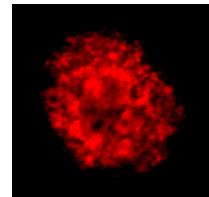


D

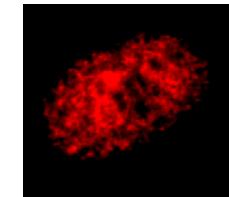
timidin-glikoziláz



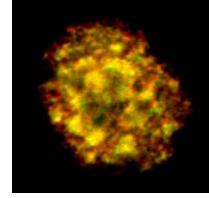
Ac-OGG1



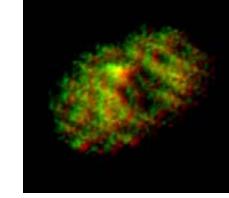
Ac-OGG1



8-oxoG+
Ac-OGG1

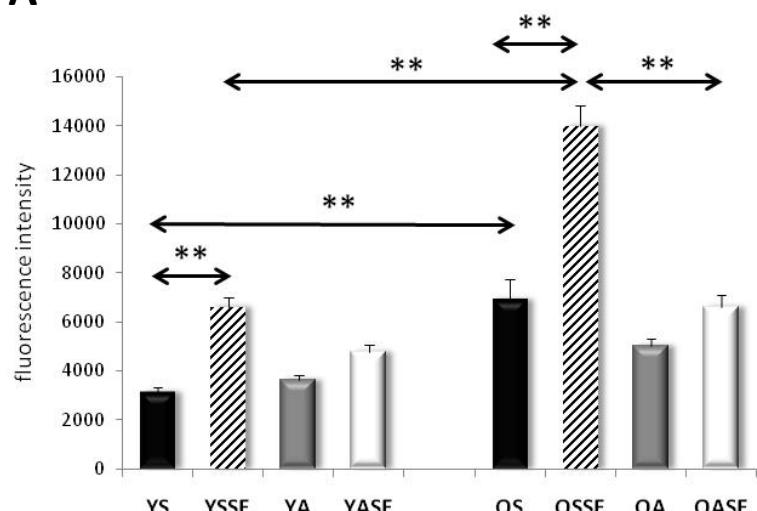


tim.-glik.+
Ac-OGG1

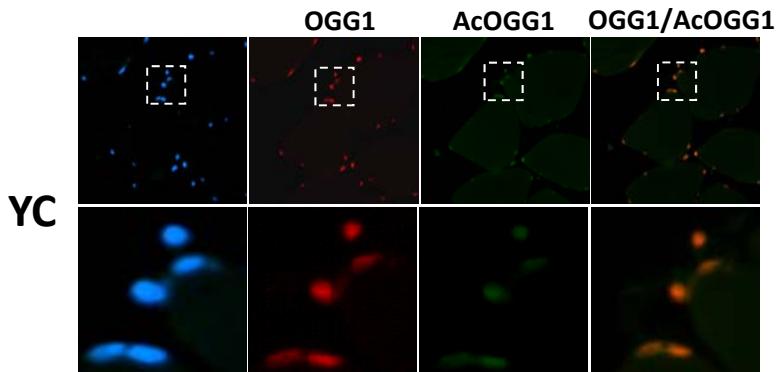


8-oxoG (A), OGG1 (B), OGG1 acetylation (C), OGG1 non-acetylation (D), AcOGG1 (E)

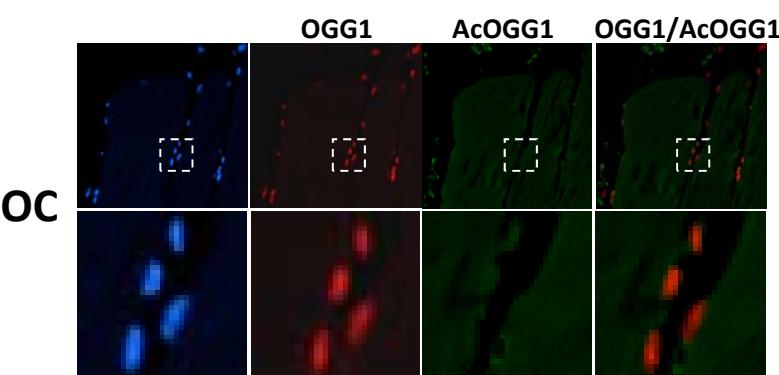
A



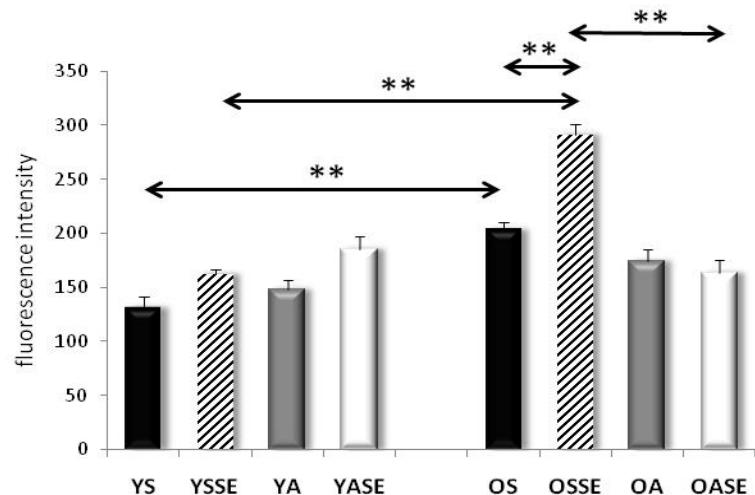
C



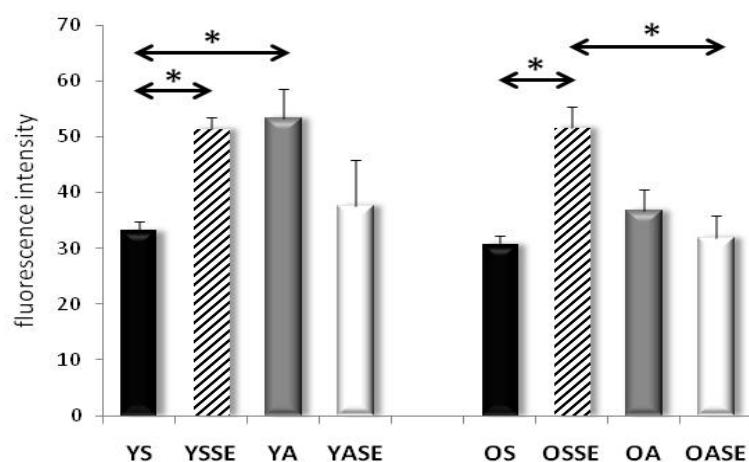
D



B

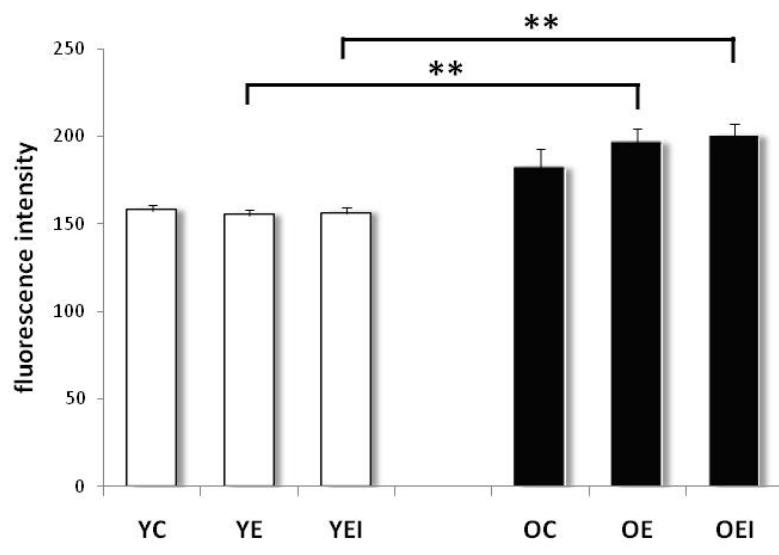


E

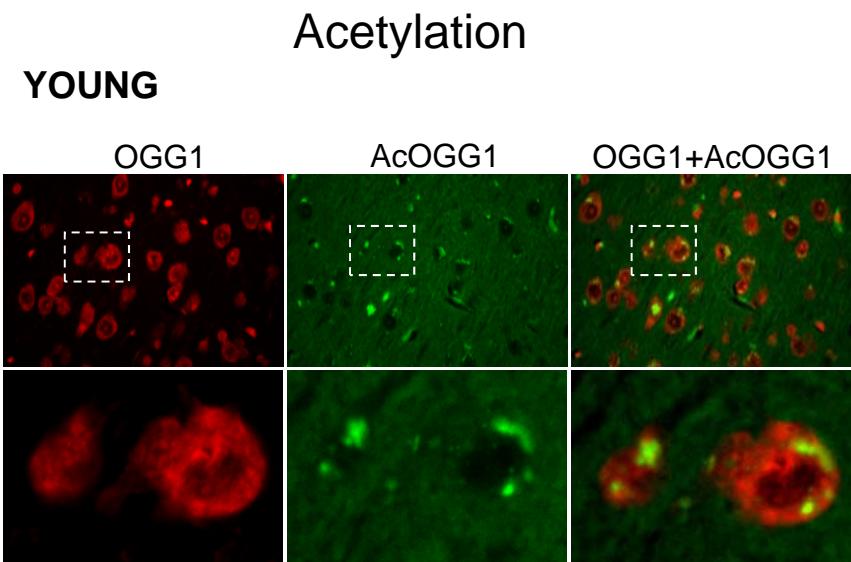


OGG1 and AcOGG1 levels in hippocampus

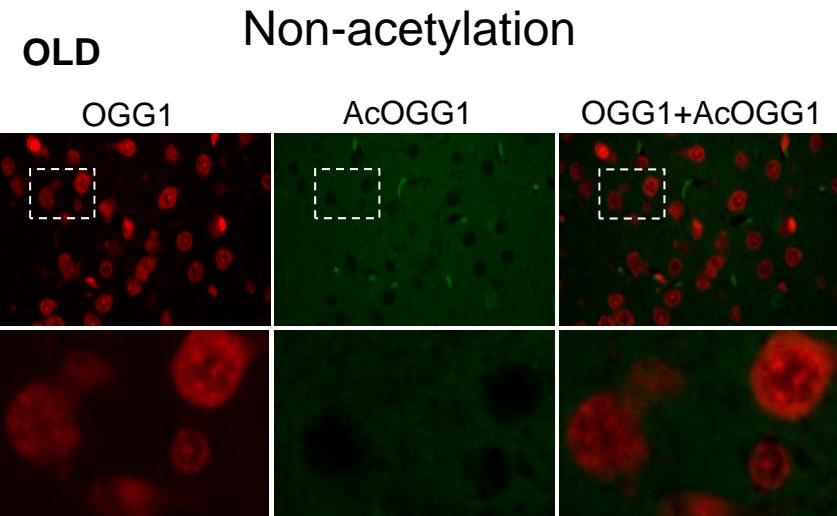
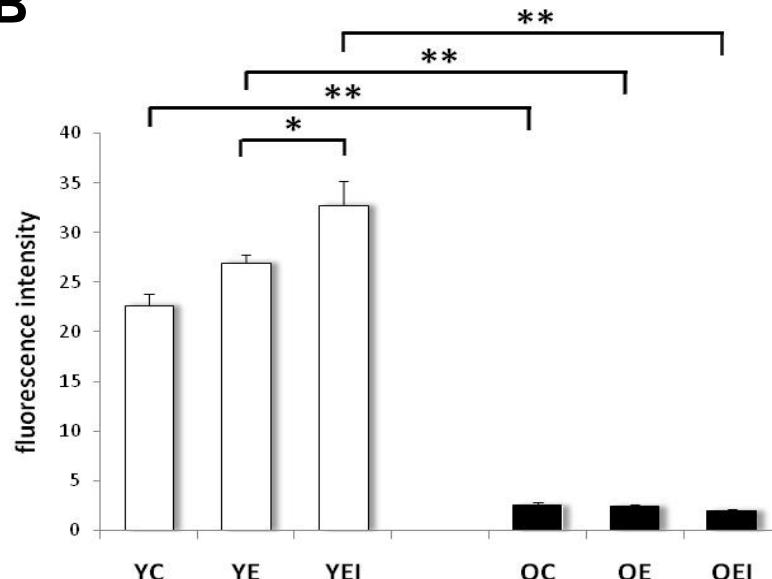
A



C

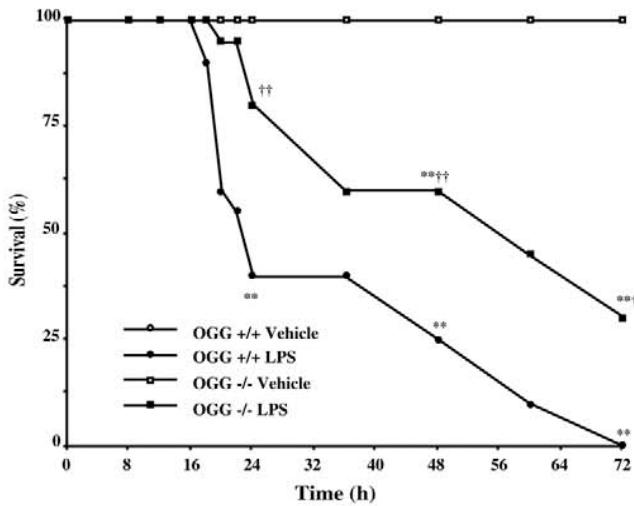


B

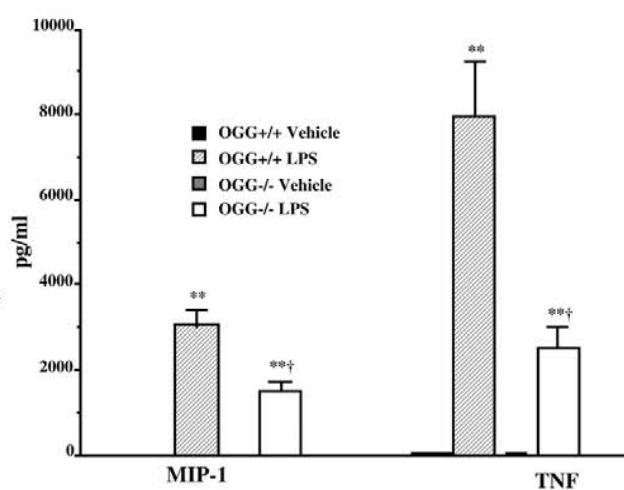


The role OGG1 knockout in lipopolysaccharide shock

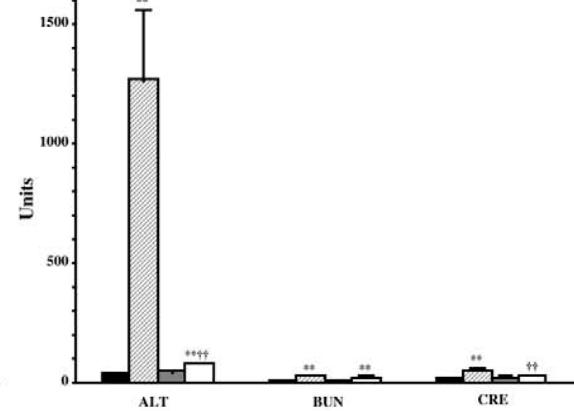
A



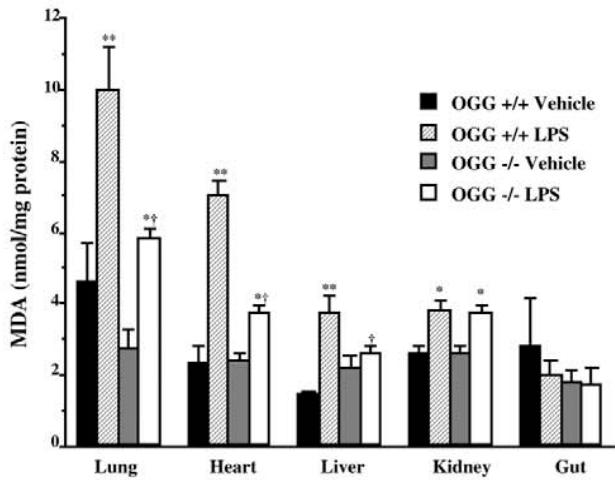
B



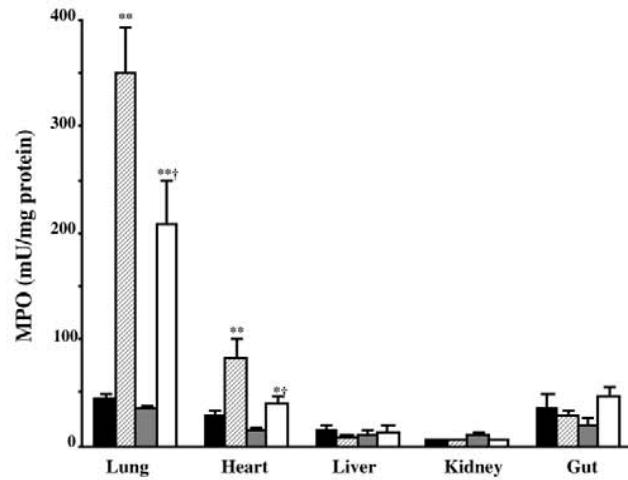
C



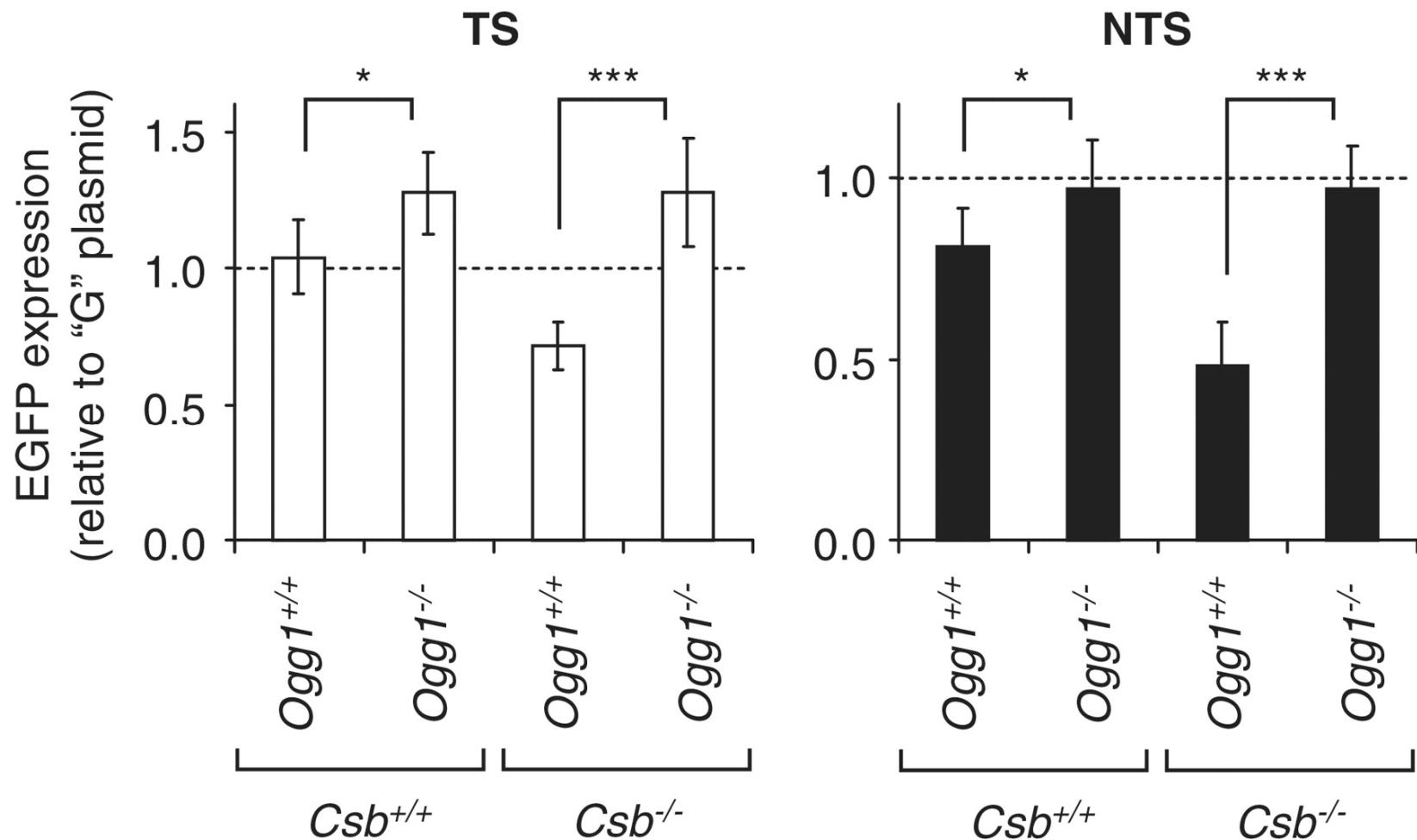
D



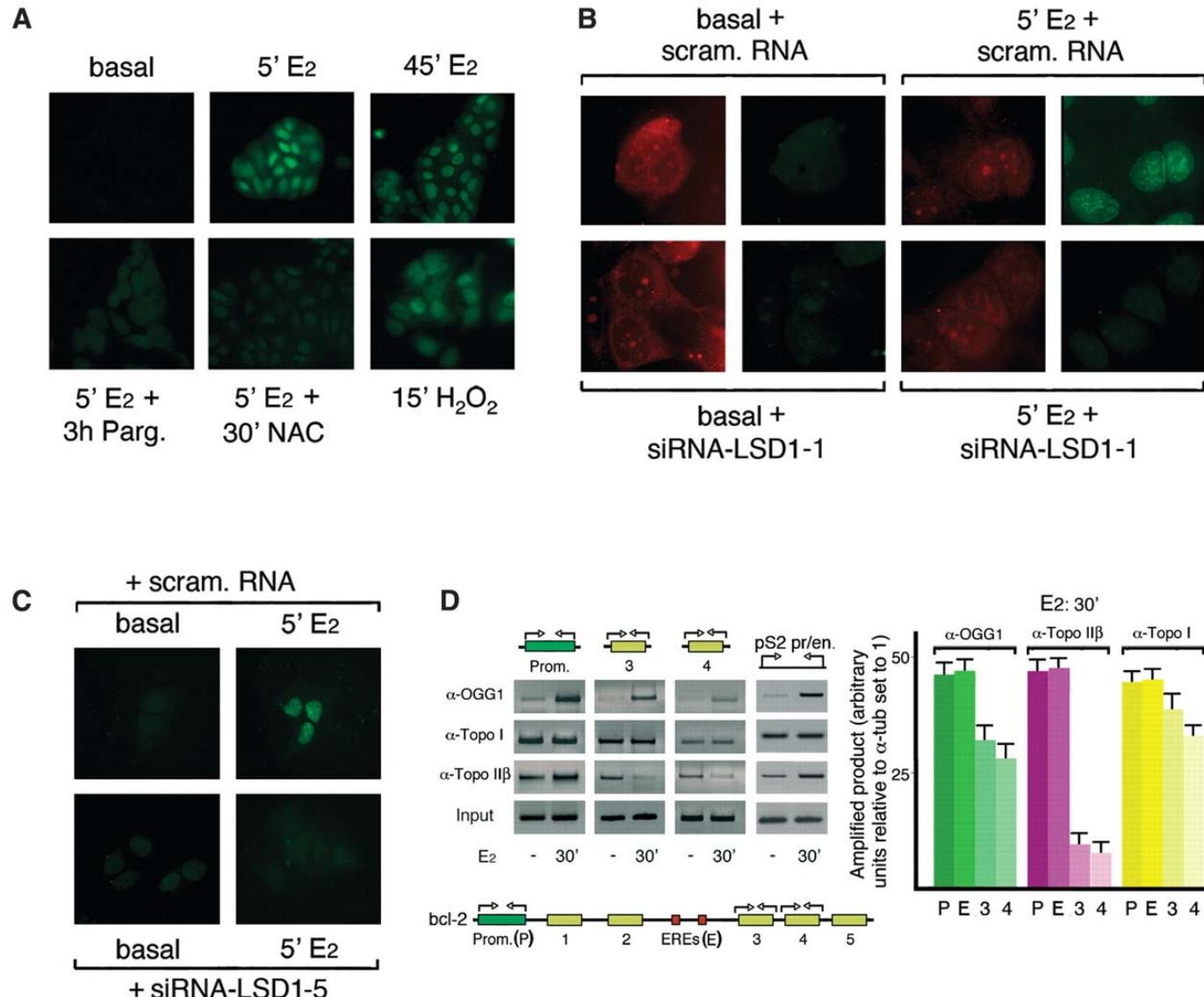
E



Effects of a single 8-oxo-G on EGFP expression in mouse embryonic fibroblasts of the indicated genotypes.

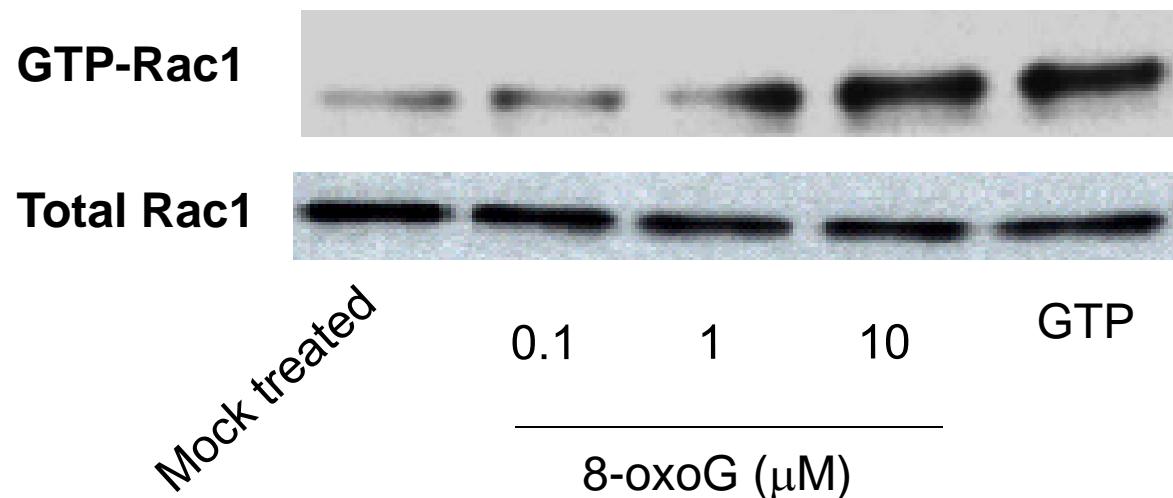


Estrogens induce a burst of nuclear 8-oxo-Gs and recruitment of OGG1 and topoisomerase II β (Topo II β) to the promoter and ERE region of E2-responsive genes

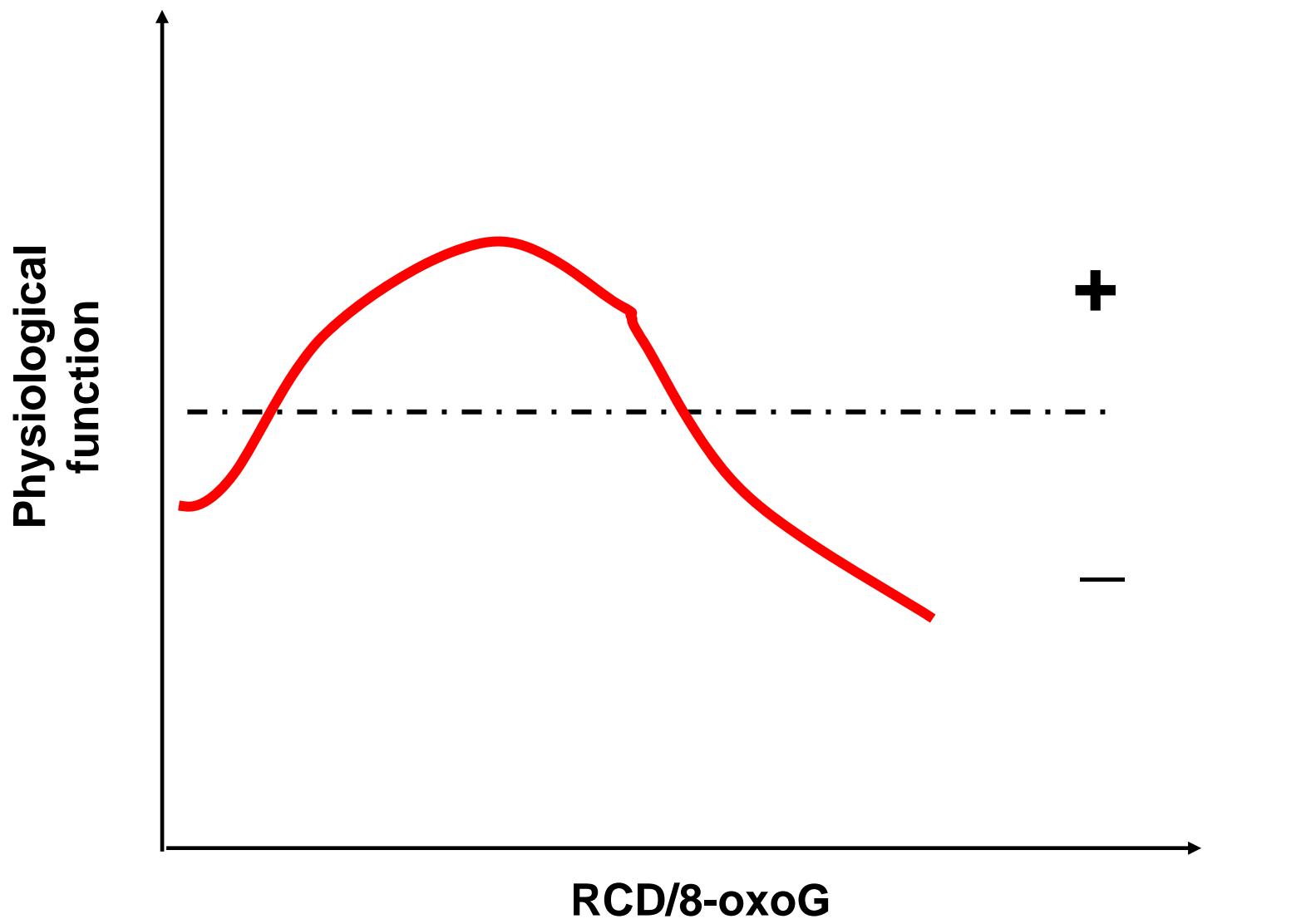




8-oxoG dose dependent increase in GTP-Rac1 level



Dose response of „oxidative damage”



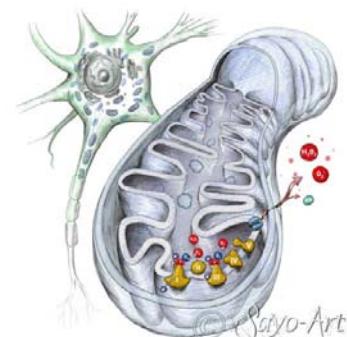
Summary

Carbonylation of amino acid residues could have controlling role on the stability of proteins and chromatin structure.

8-oxoG not always harmful for the cells, moreover it might be even important to transcription. Therefore, the removal of 8-oxoG by OGG1 could be even dangerous in certain conditions.

Sirtuins could be a negative regulators of OGG1, and the removal of 8-oxoG.

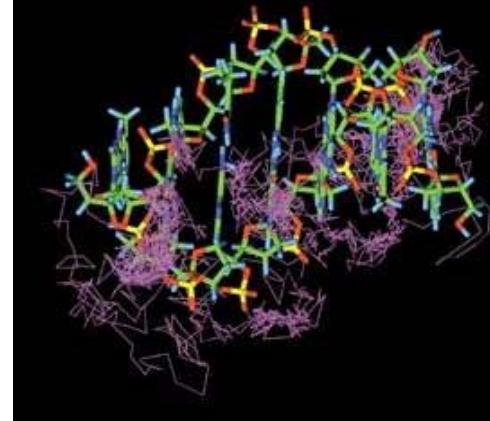
Overall, the dose response of carbonylation and 8-oxoG fits to the hormesis theory, hence certain degree of oxidative modifications of proteins and DNA might be even beneficial for the cells.





Acknowledgements

- **Sataro Goto**
- **Hisashi Naito**
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BUDAPEST