

# Redox-changes associated with the glutathione-dependent ability of the Cu(II)-GSSG complex to generate superoxide

Aliaga, Margarita E.

López-Alarcón, Camilo

García-Río, Luis

Martín-Pastor, Manuel

Speisky, Hernán

The intracellularly-occurring Cu(I)-glutathione complex (Cu(I)-[GSH]<sub>2</sub>) has the ability to reduce molecular oxygen into superoxide. Removal of such radicals leads to the irreversible conversion of Cu(I)-[GSH]<sub>2</sub> into the redox-inactive Cu(II)-GSSG complex. The present study addressed the potential of reduced glutathione, ascorbate and superoxide to reductively regenerate Cu(I)-[GSH]<sub>2</sub> from Cu(II)-GSSG, and investigated the redox changes involved in such process. Results show that: (i) among the three tested reductants, only GSH is able to reduce the Cu(II) bound to GSSG; (ii) during the reduction of Cu(II)-GSSG, a Cu(I)-GSSG intermediate would be formed (supported here by Cu(I) and GSSG recovery data and by NMR studies); (iii) when GSH is present in a molar excess equal or greater than 1:3, the reduction of Cu(II)-GSSG into Cu(I)-[GSH]<sub>2</sub> is quantitative and complete. Under such conditions, the Cu(II)-GSSG complex acquires a superoxide-generating capacity which is identical to that seen