Cadmium effect on superoxide dismutase 1: a three models approach

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Human superoxide dismutase 1 (SOD1) is a 32 kDa protein responsible for superoxide anions dismutation. It is a homodimeric metalloenzyme with each monomer binding one copper and zinc ions. Zinc plays roles in stabilizing SOD1 structure, while the copper ion is responsible for the catalytic activity. Mutated SOD1 in amyotrophic lateral sclerosis is implicated in the formation of toxic aggregates; recent studies suggested that SOD1 demetallation or aberrant metallation could be key factors for aggregation.
Cadmium (Cd) is a widespread toxic environmental contaminant, due to anthropogenic activities. It interferes with essential metal ions homeostasis and affects proteins structures and functions by its substitution with zinc, copper and iron.

In this study the effect of Cd on SOD1 has been investigated using three different approaches. Firstly we evaluated the effect of this metal combined with Cu and/or Zn on the recombinant GST-SOD1, expressed in *E. coli* BL21. After setting the optimal Cu and Zn concentrations for SOD1 activity, the enzyme activity and expression were investigated in the presence of fixed Cu and/or Zn doses and different Cd concentration. Cd causes a dose-dependent reduction in SOD1 activity, while the expression remains constant.
Similar results are obtained on the second model used, which is represented by the human SH-SY5Y cell line. These cells were treated with Cd for 24h and 48h and SOD1 enzymatic activity decreases in a dose- and time-dependent way, while the protein expression remains constant.
The last approach is the nematode *C. elegans*, in which Cd 16h treatment caused a 25% reduction of CuZn-SOD activity.
Taken together these results showed a Cd negative effect on the SOD1 enzymatic activity, but no alteration in the protein expression levels.