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Design and characterization of peptidic models of zinc finger sites. Insights into their reactivity in conditions of oxidative stress.

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Zinc fingers are small protein domains where a Zn^{2+} ion is bound to the protein by four cysteine or histidine side chains $(Zn(Cys)_{4-x}(His)_x$; x=0,1,2). Most of these sites have a structural role ensuring the correct fold of a protein but some of them are reactive toward electrophiles serving for instance as redox-switches in signalling events. Due to the presence of cysteines in these sites, there are likely targets of reactive oxygen species (ROS = H_2O_2, $O_2^{\cdot-}$, HOCl, ...) produced in cells in conditions of oxidative stress. However, little is known about the reactivity of zinc-bound thiolates with ROS. Our goal is to describe the reactivity of zinc fingers towards ROS in order to get a deeper insight into their involvement in oxidative stress. For this purpose, we use small peptides (< 26 amino-acids) to model the zinc finger sites of various proteins. These peptides are designed to mimic perfectly the structure (peptide folding, hydrogen bond network) of natural zinc finger sites.

We will describe the design and the characterizations of these model peptides and show how these robust and structurally meaningful models provide a better understanding of the coordination properties and the reactivity of zinc fingers in relation to biological considerations.

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