BolA proteins: roles in metal homeostasis

Thomas Roret[1], Pascale Tsan[1], Jean-Michel Girardet[2], Bo Zhang[3], Geneviève Alloing[4], Thomas Perrot[2], Jérémy Couturier[2], Pierre Frendo[4], Michael K. Johnson[3], Nicolas Rouhier[2] and Claude Didierjean[1]

[1] CRM2 (UMR UL-CNRS 7036), Faculté des Sciences et Technologies, Université de Lorraine, 54506 Vandœuvre-lès-Nancy, France.

[2] Université de Lorraine-INRA, UMR 1136 Interactions Arbres/Microorganismes, 54506 Vandœuvre-lès-Nancy, France.

[3] Department of Chemistry and Center for Metalloenzyme Studies, University of Georgia, Athens, Georgia 30602, USA.

[4] INRA, Université Côte d'Azur, CNRS, UMR 1355-7254, Institut Sophia Agrobiotech, Sophia Antipolis, France.

In many biological processes, uptake of metal ions by cells is crucial for the function of certain molecules such as iron-sulfur clusters (ISC). Thus, for living organisms which cannot move around, heavy metal bioavailability and bioaccessibility in soil as well as ecosystem contamination by heavy metals raise the problem of cellular metal homeostasis and trafficking. This is reinforced by the fact that most free metals are relatively toxic even at low concentrations especially iron. Among the various cellular defense mechanisms and through support of these metals, it was shown in a soil metatranscriptomics study that a small protein named BolA confers cross metal tolerance to cobalt, cadmium, zinc and manganese by probably interfering with iron homeostasis in yeast [1]. BolAs were initially defined as stress-responsive transcriptional regulators whose overexpression in *Escherichia coli* modified bacterial shape and induced biofilm formation [2,3]. Currently, the BolA family is divided into two classes named BolA_H and BolA_C (due to the presence of a conserved histidine or cysteine residue, respectively) [4]. It was thus surprising that a BolA, referred to as Fra2 (Fe repressor of activation-2), and monothiol glutaredoxins 3/4 contributed to the regulation of iron homeostasis by forming stable [2Fe-2S] cluster-bridged heterodimers controlling the nuclear translocation of the *Saccharomyces cerevisiae* Aft1/Aft2 transcription factors in response to a mitochondrial signal [5,6,7]. On the other hand, we and others reported that Grx-BolA couples from various sources could also form apo-heterodimers [4,7,8]. This is consistent with the observation that an *in vivo* Grx3/4-Fra2 interaction is found both in iron-replete and iron-depleted yeast cells [5]. BolA proteins from *Arabidopsis thaliana* and *Sinorhizobium meliloti*, which have the capacity to interact with metal ions are presented.

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