

## Zn<sup>2+</sup> and Cu<sup>2+</sup> binding to the extramembrane loop of Zrt2, a zinc transporter of *Candida albicans*.

### Autorzy

Denise Bellotti

Adriana Miller

Magdalena Rowińska-Żyrek

Maurizio Remelli

### Rok wydania

2022

### Czasopismo

Biomolecules

### Numer woluminu

12

### Strony

121/1-121/16

### DOI

10.3390/biom12010121

### Kolekcja

Naukowa

### Język

Angielski

### Typ publikacji

Artykuł

### Streszczenie

Zrt2 is a zinc transporter of the ZIP family. It is predicted to be located in the plasma membrane and it is essential for *Candida albicans* zinc uptake and growth at acidic pH. Zrt2 from *C. albicans* is composed of 370 amino acids and contains eight putative transmembrane domains and an extra-membrane disordered loop, corresponding to the amino acid sequence 126–215. This protein region contains at least three possible metal binding motifs: HxHxHxxD (144–153), HxxHxxEHxD (181–193) and the Glu- and Asp- rich sequence DDEEEDxE (161–168). The corresponding model peptides, protected at their termini (Ac-GPHTSHFGD-NH<sub>2</sub>, Ac-DDEEEDLE-NH<sub>2</sub> and Ac-PSHFAHAQEHDQDP-NH<sub>2</sub>), have been investigated in order to elucidate the thermodynamic and coordination properties of their Zn<sup>2+</sup> and Cu<sup>2+</sup> complexes, with the further aim to identify the most effective metal binding site among the three fragments. Furthermore, we extended the investigation to the peptides Ac-GPHTHAHFGD-NH<sub>2</sub> and Ac-PAHFAHAQEHDQDP-NH<sub>2</sub>, where serine residues have been substituted by alanines in order to check if the presence of a serine residue may favor the displacement of amidic protons by Cu<sup>2+</sup>. In the native Zrt2 protein, the Ac-GPHTSHFGD-NH<sub>2</sub> region of the Zrt2 loop has the highest metal binding affinity, showing that three alternated histidines separated by only one residue (-HxHxH-) bind Zn<sup>2+</sup> and Cu<sup>2+</sup> more strongly than the region in which three histidines are separated by two and three His residues (-HxxHxxxH- in Ac-PSHFAHAQEHDQDP-NH<sub>2</sub>). All studied Zrt2 loop fragments have lower affinity towards Zn<sup>2+</sup> than the zinc(II) binding site on the Zrt1 transporter; also, all three Zrt2 regions bind Zn<sup>2+</sup> and Cu<sup>2+</sup> with comparable affinity below pH 5 and, therefore, may equally contribute to the metal acquisition under the most acidic conditions in which the Zrt2 transporter is expressed.

#### Słowa kluczowe

metal-binding protein, zinc transporter, coordination chemistry, solution equilibria, zinc(II), copper(II), *Candida albicans*, Zrt2

#### Licencja otwartego dostępu

##### CC-BY

Licencja na prawach której można swobodnie kopiować, rozprowadzać, zmieniać i remiksować objęty prawem autorskim utwór (Utwór-przedmiot prawa autorskiego) pod warunkiem podania imienia i nazwiska autora utworu pierwotnego oraz źródła pochodzenia utworu.

Pełny tekst licencji:

<https://creativecommons.org/licenses/by/3.0/pl/legalcode>

#### Adres publiczny

<http://dx.doi.org/10.3390/biom12010121>

#### Strona internetowa wydawcy

<http://www.mdpi.com/journal/metals>