Tandem repeat-like domain of "Similar to prion protein" (StPrP) of Japanese pufferfish binds Cu(II) as effectively as the mammalian protein.

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The main structural domains of prion proteins, in particular the N-terminal region containing characteristic amino acid repeats, are well conserved among different species, despite divergence in primary sequence. The repeat region seems to play an important role, as verified by pathogenicity only observed in organisms having repeats composed of eight residues. In this work three different peptides belonging to the tandem repeat region of StPrP-2 from the Japanese pufferfish *Takifugu rubripes* have been considered; the coordination modes and conformations of their complexes with Cu(II) have been investigated by using potentiometric titrations, spectroscopic data, and restrained molecular dynamics simulations. In all cases the histidine imidazole(s) provide the anchoring site for copper, with the further involvement of amide nitrogens depending on the peptide sequence and on pH. An increase in copper binding affinity has been observed going from the shortest peptide, corresponding to a single repeat and containing two histidines, to the longest one, encompassing three repeats with six histidines.

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