# Metal Ion Binding to the Unique Histidine-Rich Sequence. Pro(HisGly)$_4$Pro, of the Iron-Regulated Transport Protein IRT-1 from *Arabidopsis thaliana*

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The iron-regulated membrane protein, IRT-1, is a high affinity metal transporter found in the root epidermis cells of *Arabidopsis thaliana*, where it transports $Fe^{+2}$ into the cell under conditions of iron deprivation. IRT-1 also transports other metal ions ($Zn^{+2}$, $Mn^{+2}$, $Co^{+2}$, $Cd^{+2}$) and $Fe^{+2}$ transport is competitively inhibited by certain metal ions ($Fe^{+2}$, $Co^{+2}$, $Cu^{+2}$, $Cd^{+2}$). IRT-1 was the first identified member of a growing class of metal transport proteins known as the ZIP (ZRT- and IRT-like Proteins) family, all members of which have a characteristic His-rich sequence on the intracellular loop between helices III and IV. The function of these sequences is unknown, but it has been hypothesized that they may detect rising intracellular metal concentrations and thereby play a role in regulating metal transport.

To begin to address the functional role of these His-rich sequences, a peptide corresponding to the IRT-1 sequence, -PHGHGHGHGP-, has been synthesized and its metal-binding properties have been studied. The thermodynamics of metal binding have been quantified by isothermal titration calorimetry (ITC), as shown by the data below for $Zn^{+2}$ binding to IRT-1. These data allow correlations to be made between affinity of the sequence for metal ions and metal transport activity of IRT-1 or its inhibition. In addition, spectroscopic methods have been used to investigate the structure of metal coordination to this sequence for correlations between the metal-peptide structure and the biological activity.