Figure S1. Structural and functional key residues conserved in the CDF family (PF01545). Transmembrane domains (TM1-6), residues of metal binding sites A, B, and C (red, blue and green dots) respectively, as well as the interlocked $(Lys^{77}\text{-}Asp^{207})_2$ salt-bridges (black dots) were located by comparison with the reported structure of YiiP[5]. The consensus sequence region reported for the CDF protein family[9] is black underlined (in TM2-3). The amino acid positions involved in protein function/activity as well as substrate selectivity (yellow highlighted) were located by comparison with previous works [4,23,25,26,36,38]. The CDF conserved regions were obtained from the Pfam HMM-domain and aligned with ClustalO. This 11-sequences alignment is a sample of the alignment of 318 CDF sequences used to infer the phylogeny.

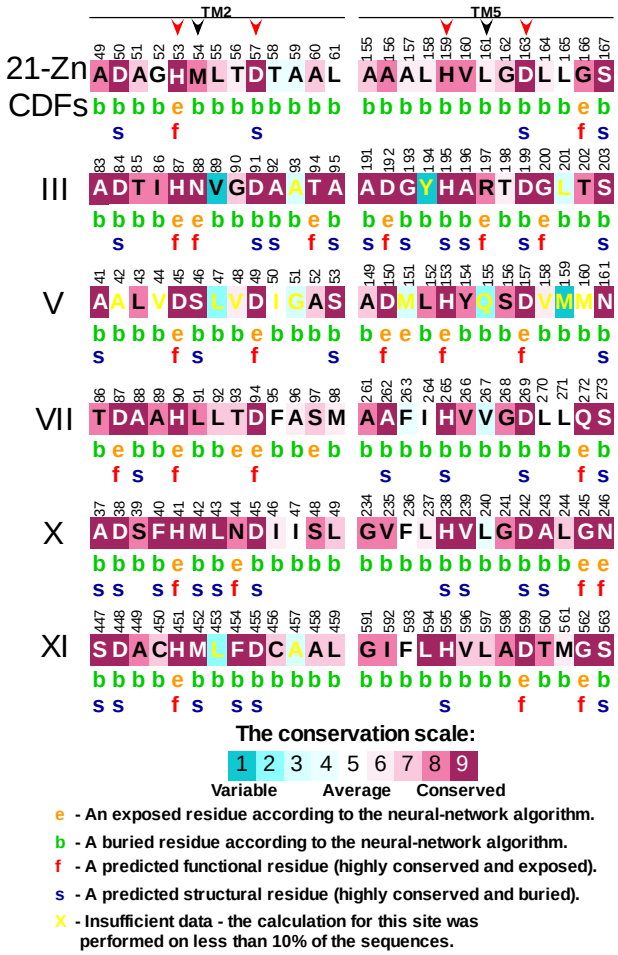

Figure S2. Comparison of conserved residues carrying potential N- ligand donors present in CDF proteins of clade III (Ni^{2+}/Co^{2+}), Zn^{2+}-transporting CDF (clades III, V, XI, VII,VIII) and 21 sole Zn-CDF proteins contained in the Table S1. The putative metal binding site A among the different groups is indicated by red arrows. The conserved and group specific Asn and Arg residues (black arrows) in group III proteins were present and functionally analyzed in NepA. Numbering corresponds to *R. etli* NepA, *E. coli* YiiP, *A. thaliana* AtMTP1, *S.cerevisiae* ZRC1 and *H. sapiens* ZnT5 proteins from III, V, VII, X and XI clades, respectively. For the 21 sole Zn CDF proteins the numbering of *E. coli* ZitB was used. Logos were built using Consurf (see methods).

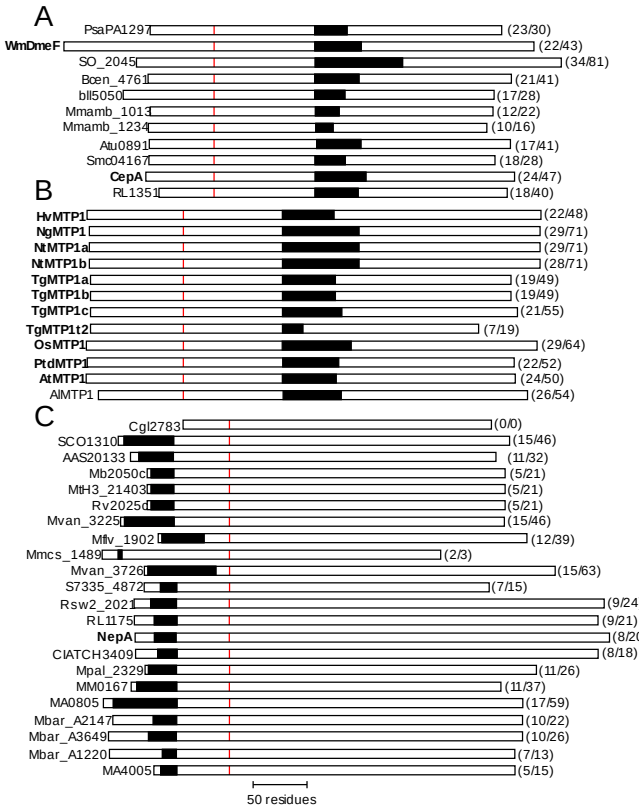

Figure S3. Group-specific His-rich stretches present in Co^{2+}, Zn^{2+} and Ni^{2+} transporters grouped in clades XII (A), VII (B) and III (C), respectively. In HvMTP1[38] or AtMTP1[40] proteins of group VII middle His-rich tracts are required for proper protein function and substrate selectivity. The role of equivalent regions in group III and XII proteins is unknown. The number of His-residues over the complete stretch-length is shown in parenthesis. Characterized CDF proteins are shown in black bold. The red line indicates the position of the first residue (TM2) of the putative metal binding site A.