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Characterization of high-affinity complexes of Parkinsonism protein DJ-1 with nitrilotriacetic acid-transition metal moieties

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Mutations in human protein DJ-1 cause an early onset of Parkinson's disease. Reactive Cysteine (Cys106) is crucial for the protective function of DJ-1, although the underlying mechanisms are unclear. We have found that a fraction of bacterially expressed hexahistidine tagged human DJ-1 eluted very slowly from Ni-NTA column with an apparent first order rate constant of ~10-4 s-1. This unusually tight binding was accompanied by the appearance of blue-violet color on Ni-NTA column. We demonstrate that Cys106 is carboxy methylated in a fraction of DJ-1 that binds tightly to Ni-NTA. However, when eluted protein was re-applied onto Ni-NTA column no tight binding has been observed indicating that the formation of high affinity complex with Ni-NTA depends on a transient modification of Cys106 residue that transforms into Cys106-carboxymethyl adduct upon elution from Ni-NTA. The formation of high affinity complexes and the appearance of blue color were also observed when Ni was replaced with Co, Cu or Zn. However, high affinity complexes were not formed when other affinity media such as iminodiacetic acid or carboxy methyl aspartate have been used instead of NTA. We conclude that an unknown metabolite reacts with Cys106 of DJ-1 to result in a relatively stable post-translational modification. This modification allows high affinity and high specificity interaction of DJ-1 with complexes of NTA with transition metals.

Biography

Timur Baizhumanov has completed his PhD from College of Nanoscience and Nanotechnology at Pusan National University. He has worked as a Research Professor at Pusan National University and Seoul National University. He has authored and co-authored over 40 peer-reviewed papers, two book chapters and has one patent. His research interests are mainly focused on the synthesis and characterization of multifunctional inorganic nanostructures for biomedical, optical, energy and sensors applications.

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