

Diagnostic and therapeutic use of a novel protein-unfolding activity, oligomeric actin-interacting protein 2 (Aip2p), for neurodegenerative diseases

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We have found and purified a robust ATP-dependent protein-unfolding activity from *S.cerevisiae*. The purified factor in monomeric form is identical to the actin interacting protein 2 (Aip2p), but it has a novel tiara-like structure of 10–12 subunits with an ATP-dependent opening. ATP regulates the opening and closing of the “gate” that forms the opening within oligomeric Aip2p, where binding to the substrate occurs while in the open form with broad specificity *in vitro*. Of note, the activity could modify even the conformation of pathogenic highly aggregated polypeptides, such as recombinant prion protein in beta-sheet form, alpha-synuclein, and amyloid beta peptide (A β 1-42). With oligomeric Aip2p, we established a novel combinatorial method of laser microdissection system (LMD) and immunoblot analysis that enables us to examine the molecular profile of proteins in the microscopic regions of interest; pretreatment with oligomeric Aip2p enhances the immunoblot sensitivity by more than 1,000 fold. Oligomeric Aip2p at the log phase possessed higher activity than that at the stationary phase in yeast cells, suggesting the presence of cofactor/s *in vivo*. Identification of such cofactor/s is crucial for the future development of potential diagnostic and therapeutic use of oligomeric Aip2p since the activity as is destroys host cells.

Biography

Dr.Hachiya is Professor of Department of Neurophysiology in Tokyo Medical University. She has completed her Ph.D. from the Department of Molecular Biology at Kyushu University and postdoctoral studies from the University of California Berkeley. She represented Japan at the meeting of Japan-America Frontiers of Engineering Symposium in 2005. She has received international awards such as Keystone Symposia Scholarship Award, Journal of Biochemistry Award, The First Prize in the International Symposium of Prion Disease, GTC BIO outstanding abstract award.

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