Relation between the higher order structural changes of protein and function abnormarity of abnormal hemoglobin

1997 Fiscal Year Final Research Report Summary

RELATION BETWEEN THE HIGHER ORDER STRUCTURAL CHANGES OF PROTEIN AND FUNCTION ABNORMARITY OF ABNORMAL HEMOGLOBIN

Research Project

Project/Area Number

07670140

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

General medical chemistry

Research Institution

KANAZAWA UNIVERSITY

Principal Investigator

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Keywords

Hemoglobin / Abnormal hemoglobin / Functinal abnormarity / UV resonance Raman / Circular dichroism / Higher order structure / Phosphotyrosine

Research Abstract

It has been recently reported that resonance Raman spectra excited in the UV region at 200-240 can explore the environmental and hydrogen bonding changes of tryptophan (Trp) and tyrosine (Tyr) residues of proteins. we have demonstrated here the quaternary-structural dependent features for Tyr and Trp residues in alpha_1beta_2 interface of hemoglobin (Hb) from 235-nm excited UV resonance Raman (UVRR) spectra. Deoxy Hb A (T-form) showd a UVRR spectrum distinctly different from those of the ligated Hbs (R-form) including osyHb, COHb and NOHb.
To characterize the spectral changes of Trp-beta37 at alpha_1beta_2 interface due to the quaternary structure transition, the UVRR spectra of Hb A were compared with the corresponding spectra of Hb Hirose (Trp-beta37->Ser). Comparison of the Hb A - Hb Hirose difference spectra in oxy and deoxy states revealed that the oxygenation- induced changes of Trp RR bands arose mostly from Trp-beta37.
The UVRR spectral contribution of alpha42Tyr, Which is located in the "swhitch" region of the alpha_1beta_2 interface and forms an H-bond with the carboxylate side chain of beta99 Asp only in the T-state, was deduced for each of the deoxy- and CO-forms by subtracting the spectra of Hb alpha Y42H from those of Hb A.This suggested that alpha42Tyr is responsible for the frequency shift of Y8a (1617cm^<-1>) and Y9a (1179cm^<-1>) of the Tyr RR bands of Hb alphaY42H upon quaternary structure change are alike.
The extent of the oxidation of Hb M Sakatoon and Hb M Boston in the patients blood was determined by measurement of the intensity of EPR signal at g=6.0 for the normal subunits, g=6.7for the mutant subunit of Hb M Saskatoon, and g=6.3 for those of Hb M Boston. About 50% and 76% of mutant subunits in Hb M Boston and Hb M Sakatoon remained reduced in the fresh blood, respectively.

Research Products (8 results)

All | Other

All | Publications (8 results)

[Publications] Nagai, M: "Ultraviolet resonance Raman studies of quaternary structure of hemoglobin using a trytophan β37 mutant." Journal of Biological Chemistry. 270(4). 1636-1642 (1995)

[Publications] Nagai, M.: "Studies of the oxidation states of Hb M Boston and Hb M Saskatoon inblood by EPR spectroscopy" Biochemical Biophysical Reseach Communication. 210(2). 483-490 (1995)

[Publications] Nagai, M.: "Ultraviolet resonance Raman studies of hemoglobin quaternary structure using a tyrosine-α42 mutant." Journal of Molecular Structure. 379. 65-75 (1996)

[Publications] Nagai, M.: "Tyrosine phosphorylation-induced changes in absorption and UV resonance Raman spectra of Src-peptides." Journal of Raman Spectroscopy. 29. 31-39 (1998)

[Publications] Nagai, M.: "Ultraviolet resonance Raman studies of quaternary structure of hemoglobin using a tryptophan beta37 mutant." J.Biol.Chem.270. 1636-1642 (1995)

[Publications] Nagai, M.: "Studies of the oxidation states of Hb M Boston and Hb M Saskatoon in blood by EPR spectroscopy." Biochem.Biophys.Res.Comumun.210. 483-490 (1995)

[Publications] Nagai, M.: "Ultraviolet resonance Raman studies of hemoglobin quaternary structure using a tyrosine alpha42 mutant." J.Mol.Struct.379. 65-75 (1996)

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