UV Resonance Raman Spectroscopic Studies of Metal Ion Assisted Activation Mechanism of Human Hematopoietic Prostaglandin D_2 Synthase

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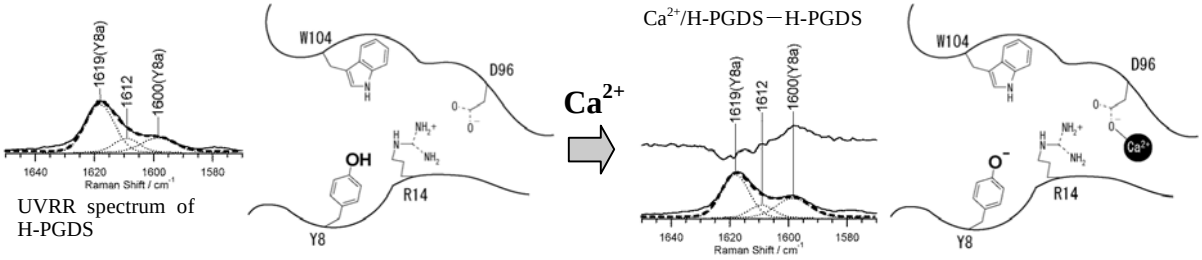
Prostaglandin (PG) D_2 is known to be a mediator of allergy, inflammation response, and sleep regulation in the variety of Human tissues. Hematopoietic PGD_2 synthase (H-PGDS) catalyzes the isomerization of PGH_2 to PGD_2. Very recently, the activation of human H-PGDS by Ca^{2+} and Mg^{2+} was reported [1].

Recent development of stable UV lasers and sensitive detectors has made it possible to utilize UV resonance Raman (UVRR) spectroscopy for the structural analysis of protein molecules. With those points in mind, we have studied the metal ion assisted activation mechanism of human H-PGDS by UVRR spectroscopy.

A new Raman band at 1600 cm^{-1} (characteristic for tyrosine phenolate) was detected for the Ca^{2+}-bound H-PGDS. The 1600 cm^{-1} Raman band is shifted to 1612 cm^{-1} by the addition of glutathione to the solution of Ca^{2+}-bound H-PGDS. The Raman bands at 1600 and 1612 cm^{-1} was assigned to Tyr8 from the comparison of the UVRR spectra of Y8F mutant. The higher frequency shift of the 1600 cm^{-1} Raman band to 1612 cm^{-1} suggests the re-protonation of the phenolate moiety of Tyr8.



UVRR spectrum of H-PGDS

Metal ion assisted activation mechanism of human hematopoietic prostaglandin D_2 synthase.

Reference.
[1] Inoue T., *et al.*, (2003) *Nat. Struct. Biol.*, **10**, 291-296.