Crystal structures of HIV-1 RT, either unliganded or complexed with different nonnucleoside RT inhibitors (NNRTI) or a double-stranded DNA, have been reported. There are significant differences between different HIV-1 RT structures; this serves to illustrate the high flexibility of this enzyme.

Comparison of various RT structures with or without bound ligand or substrate reveals that the p66 thumb subdomain can occupied at least three different positions that depend on whether RT interacts with or without substrate or various ligands. In contrast to the "thumb down" position found in the unliganded form, when HIV-1 RT binds a DNA substrate the p66 thumb is rotated open at the thumb's "knuckle", which is near residues Trp239 and Val317. This knuckle movement of the p66 thumb affects only the position of the p66 thumb, not other subdomains. The binding of an NNRTI, however, induces a hinge-like movement at the base of the p66 thumb subdomain, between the β6-β10-β9 and β12-β13-β14 ("primer grip") sheets. Associated with this hinge-like movement, the p66 thumb subdomain is further extended to a wide open position. The p66 connection subdomain, RNase H domain, and the subdomains in the p51 subunit are displaced by this hinge-like movement as well.

The polymerase active site is composed of structural elements from both protein and nucleic acid. NNRTI binding to HIV-1 RT leads to altered positions of both the p66 thumb and the primer grip, which consequently would alter the position of template-primer relative to both the polymerase and the RNase H active sites. Those conformational changes could account for the inhibition activity of NNRTIs, and explain the alteration of cleavage specificity of RNase H by NNRTI binding.

PS04.17.18 CYSTALLIZATION AND CRYSTALLOGRAPHIC STUDIES OF BAR-HEADED GOOSE DEOXYHAEMOGLOBIN. Ziqian Hua*, Yiling Fang, Xiaoxi Zhou, Qian Xu, Bao Kuang, Xincheng Wei, Guangying Lu, Xiaocheng Gu, College of Life Sciences,Peking University, Beijing 100871 China

Bar-headed goose (Anser indicus) live and hatch their young at the west China's Qinhai lake, but at the end of autumn they migrate to the plains of northwest India. Flocks has been observed flying over the Himalayan Mountains at altitudes of about 9000 m where ambient pO_2 only have about 50 mmHg which accounts to 20% of pO_2 at sea level (Swan, L. A. 1970, Nat. Hist., 79, 68).

The Hbs from bar-headed goose shows more high oxygen affinity compared to closely related lowland species of goose, such as grelag goose. There are only four amino acid differences between the major Hb types of these two species, only one of which appears likely to effect oxygen affinity, the α119 Pro matutes to Ala at $\alpha_1\beta_1$ interface(Oberthür, W., et al 1982, Hoppe-seyler's Z. Physiol. Chem.,363, 581)

We have determined the X-ray crystallographic structure of bar-headed goose haemogloblin in the Oxy form to a resolution of 0.2 nm, Now we have got the crystals of deoxyHb and done the preliminary crystallographic studies in order to elucidate high oxygen affinity mechanism. DeoxyHb of bar-headed goose was prepared with $Na_2S_2O_4$ as reducing agent. The single crystals suitable for X-ray analysis have been grown from PEG 6000 at pH 7.2, protein 20 mg/ml with the hanging drop vappor diffusion method. DeoxyHb crystallizes in a Pl space group with lattice constants a=7.09 nm, b=9.54 nm, c=5.87 nm, the asymmetric unit has two molecules, Vm=0.256 nm^3/Dal. The crystals diffract to about 0.23 nm resolution and 60% of X-ray diffraction data has been collected to 0.28 nm on X-200B Area Detector. A total of reflections is 30654, Rm=5.14% The determination of deoxyHb structure using the moleculer replacement method is in progress.

PS04.17.19 CRYSTALLIZATION AND PRELIMINARY X-RAY STUDIES OF PLASTOCYANIN FROM *SILENE* EXPRESSED IN *E. COLI*. T. Inoue*, M. Gotowda*, K. Hamada*, T. Takabe** & Y. Kai*.*Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan, **Department of Chemistry, Faculty of Science and Technology, Meijo University, Tenpaku-ku, Nogoya 468, Japan.

Plastocyanins are type I copper proteins with a single polypeptide chain (10.5KDa). They have been found in a variety of higher plants and algae where they function in photosynthetic electron transport (Sykes, A. G., *et al.*, 1993). Plastocyanins are unique proteins among the blue copper proteins showing the two different electron transfer (ET) sites (Sykes, A. G., 1991, Qin, L. & Kostic, N. M., 1993). However, it still remains necessary to understand further the precise specificities of the two sites, the nature of the binding, and the intramolecular ET to and from in particular the remote site with different redox partners. In order to make clear the reletionships between their functions and structures, we have carried out the study on Crystallization and Preliminary X-ray Studies of Plastocyanin from *Silene* expressed in *E. Coli* (PCSIL). PCSIL has been crystallized in a form suitable for X-ray diffraction analysis by macroseeding method using ammonium sulfate as a precipitant in acetate buffer (P^H=5.5). These crystals belong to space group $P3_221$ with lattice parameters $a=b$=76.6 Å and c=65.5 Å, indicating an asymmetric unit containing two plastocyanin molecules. The crystals diffract up to at least 2.0 Å resolution. 44196 diffraction data were observed, from which 11515 were unique, in the resolution range 15.0-2.0 Å, with an *R*merge of 6.0%. Molecular replacement method was applied to solve the crystal structure with *AMoRe* in *CCP4*. Rigid-body refinement of the model and subsequent refinement using molecular dynamics were carried out with *XPLOR*, leading to a current R factor of 17.6%, for the diffraction intensities up to 2.5 Å resolution.

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PS04.17.20 PRELIMINARY CRYSTALLIZATION OF A CYCLIN-DEPENDENT KINASE INHIBITOR: P18. Shannon Jarchow and Hengming Ke Department of Biochemistry and Biophysics, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA

Eukaryotic cell-cycle progression is regulated by a family of serine/threonine protein kinases, cyclin-dependent kinases (CDK's). CDK activity is regulated by subunit phosphorylation, activation via cyclin binding, and inhibition via binding of small regulatory proteins. Currently, these small inhibitor proteins can be classified into two families: the universal inhibitors of the p21/p27 family and the more specific inhibitors p16INK4 (p16)/p14INK4 (p14) family. A member of the p16/p14 family, p18 binds and inhibits CDK6 and CDK4, halting cell cycle progression.

Recombinant human p18 has been purified to homogeneity and diffraction quality crystals have been obtained by dialysis. Crystals have a typical size of 0.1 x 0.1 x 0.2 mm and can diffract to 2Å resolution. The space group has been determined to be P1 with unit cell dimensions of: a=60.3, b=40.2, c=28.4 Å, α=90.6°, ß=92.1°, γ=95.8°. Diffraction data have been collected on a RIGAKU R-AXIS image phosphate system. A data set of 16,785 measurements has been reduced to 11,595 independent reflection with an R-merge of 0.089. This data set is 70.5% complete to 2.06Å resolution. Heavy atom derivative preparation and structural analysis is in progress.