Phytochromes of plants, fungi, algae and bacteria are the photoreceptors that bind linear tetrapyrroles and show reversible photoconversion between red-absorbing form (Pr) and far-red-absorbing form. Cyanobacteriochromes with various spectral properties are the recently emerged photoreceptors that are distinctive relative of the phytochromes. Among them, AnPixJ-GAF2 from cyanobacterium Anabaena sp. PCC 7120 is a novel photoreceptor that covalently binds phycocyanobilin and shows green/red reversible photoconversion. It is suggested that the Pr form of AnPixJ-GAF2, which corresponds to that of phytochrome, is photoconverted to unusual blue-shifted green-absorbing form (Pg) via phytocrome-like intermediate states. To get structural insights into this unique photoconversion mechanism, we tried to crystallize AnPixJ-GAF2 in both forms. As a result, we obtained blue crystals of the Pr form by hanging-drop vapor diffusion method. The crystals belong to space group P4_2_2_2 and contain one monomer in an asymmetric unit. The crystal structure was solved at 1.8 Å resolution by iodide-SAD method. The overall structure and the chromophore structure of the Pr form are very similar to those of the Pr forms of bacterial phytochromes, although relative position of the chromophore to the apoprotein is significantly deviated. In correspondence with the deviation, amino acid residues surrounding the chromophore are quite diverged. Nevertheless, we can point out a common structural feature conserved between the two Pr forms. Moreover, some residues unique to AnPixJ-GAF2 are suggested to be crucial for the formation of the unusual Pg form. These results shed light on the universal and unique aspects of photosensory mechanism of phytochromes and cyanobacteriochromes.

Keywords: cyanobacteria, photoreceptor, phytocrome

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Development of superagonist ligands for the vitamin D nuclear receptor, AMCR277A, -B and 2MeAMCR

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Vitamin D Receptor (VDR), a ligand-dependent transcriptional regulator, is an important target for multiple clinical applications like osteoporosis and cancer. However, high level of the natural ligand, 1alpha,25-(OH)2D3 (Fig. a), induces hypercalcemia. In order to minimize this side effect, chemical modifications have been made on the natural ligand. Based on the crystal structures of human VDR (hVDR) bound to 1alpha,25-(OH)2D3, superagonist KH1060, 2alpha-methyl vitamin D, we designed three new vitamin D analogues, AMCR277A, AMCR277B and 2MeAMCR (Fig. b, c and d, respectively). The crystal structures of hVDR bound to AMCR277A, -B and 2MeAMCR were solved at 2.0, 1.8 and 1.9 angstrom, respectively. Compared to the natural ligand, the three compounds make additional van der Waals (VDW) contacts with Val300 of hVDR. These contacts have also been found in the other superagonist-hVDR structures. The modified methyl group of 2MeAMCR at position C-2alpha of the A-ring makes additional VDW contacts. Therefore, the 2MeAMCR inherits structural features of both AMCR277A and 2alpha-methyl vitamin D. In addition, in vitro assays showed that AMCR277A and 2MeAMCR exhibit superagonist activity.

Keywords: nuclear receptors, vitamin D, drug discovery and biological crystallography