Elucidation of ligand binding and dimerization of NADPH:protochlorophyllide (Pchlide) oxidoreductase (POR) from pea (Pisum sativum L.) by structural analysis and simulations

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September 10, 2020

Abstract

NADPH:protochlorophyllide (Pchlide) oxidoreductase (POR) is a key enzyme of chlorophyll biosynthesis in angiosperms. It is one of few known photoenzymes, which catalyzes the light-activated trans-reduction of the C17-C18 double bond of Pchlide's porphyrin ring. Due to the light requirement, dark-grown angiosperms cannot synthesize chlorophyll. No crystal structure of POR is available, so to improve understanding of the protein's three-dimensional structure, its dimerization, and binding of ligands (both the cofactor NADPH and substrate Pchlide), we computationally investigated the sequence and structural relationships among homologous proteins identified through database searches. The results indicate that α4 and α7 helices of monomers form the interface of POR dimers. On the basis of conserved residues, we predicted 11 functionally important amino acids that play important roles in POR binding to NADPH. Structural comparison of available crystal structures revealed that they participate in formation of binding pockets that accommodate the Pchlide ligand, and that five atoms of the closed tetrapyrrole are involved in non-bonding interactions. However, we detected no clear pattern in the physico-chemical characteristics of the amino acids they interact with. Thus, we hypothesize that interactions of these atoms in the Pchlide porphyrin ring are important to hold the ligand within the POR binding site. Analysis of Pchlide binding in POR by molecular docking and PELE simulations revealed that the orientation of the nicotinamide group is important for Pchlide binding. These findings highlight the complexity of interactions of porphyrin-containing ligands with proteins, and we suggest that fit-inducing processes play important roles in POR-Pchlide interactions.

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