Artificial Iron Proteins: Modeling the Active Sites in Non-Heme Dioxygenases

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Author(s) Miller, Kelsey R.; Paretsky, Jonathan D.; Follmer, Alec H.; Heinisch, Tillmann; Mittra, Kaustuv; Gul, Sheraz; Kim, In-Sik; Fuller, Franklin D.; Batyuk, Alexander; Sutherlin, Kyle D.; Brewster, Aaron S.; Bhowmick, Asmit; Sauter, Nicholas K.; Kern, Jan; Yano, Junko; Green, Michael T.; Ward, Thomas R.; Borovik, A. S.
Author(s) at UniBasel Ward, Thomas R. ;
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An important class of non-heme dioxygenases contains a conserved Fe binding site that consists of a 2-His-1-carboxylate facial triad. Results from structural biology show that, in the resting state, these proteins are six-coordinate with aqua ligands occupying the remaining three coordination sites. We have utilized biotin-streptavidin (Sav) technology to design new artificial Fe proteins (ArMs) that have many of the same structural features found within active sites of these non-heme dioxygenases. An Sav variant was isolated that contains the S; 112; E mutation, which installed a carboxylate side chain in the appropriate position to bind to a synthetic Fe; II; complex confined within Sav. Structural studies using X-ray diffraction (XRD) methods revealed a facial triad binding site that is composed of two N donors from the biotinylated ligand and the monodentate coordination of the carboxylate from S; 112; E. Two aqua ligands complete the primary coordination sphere of the Fe; II; center with both involved in hydrogen bond networks within Sav. The corresponding Fe; III; protein was also prepared and structurally characterized to show a six-coordinate complex with two exogenous acetato ligands. The Fe; III; protein was further shown to bind an exogenous azido ligand through replacement of one acetato ligand. Spectroscopic studies of the ArMs in solution support the results found by XRD.
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