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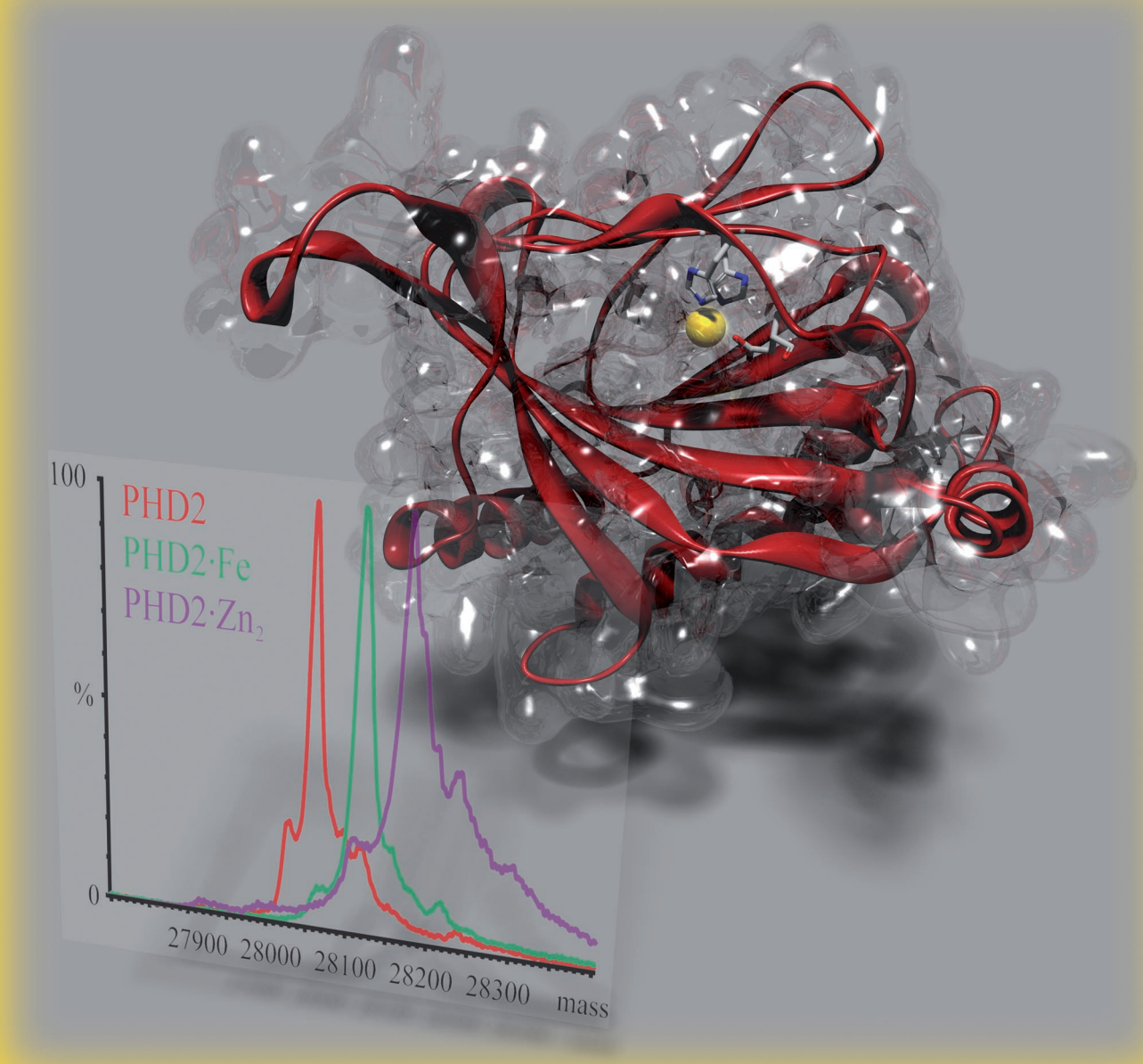
CHEMMEDCHEM

CHEMISTRY ENABLING DRUG DISCOVERY



4/2008

Minireview: Modeling hERG–Drug Interactions
(M. Recanatini)
Full Paper: Models of the APH-1–Presenilin Interface
(S. Filipek)

SPECIAL ISSUE
5th Joint Meeting on Medicinal Chemistry
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Cover Picture

Jasmin Mecinović, Rasheduzzaman Chowdhury, Benoît M. R. Liénard, Emily Flashman, Matthew R. G. Buck, Neil J. Oldham, and Christopher J. Schofield*

The cover picture shows a view from a crystal structure of prolyl hydroxylase domain 2 (PHD2), which is the major PHD that catalyses HIF-α hydroxylation under normoxic conditions. The hypoxic response in animals is mediated by the transcription factor hypoxia inducible factor (HIF). Levels of the HIF-α subunit are regulated by PHD-catalysed prolyl hydroxylation, which signals for the degradation of HIF-α under normoxic conditions. The requirement of the PHDs for molecular oxygen enables them to act as oxygen sensors. Inhibition of the PHDs in order to activate the hypoxic response is of interest for therapeutic benefit. Alongside the PHD2 structure are shown electrospray ionisation mass spectrometric data, described in the Communication by C. J. Schofield et al. on p. 569 ff., that reveal a second metal binding site on the enzyme.