Characterization of Novel Metal Centers in Purple Acid Phosphatases and Related Model Complexes

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Purple acid phosphatases (PAPs) constitute a class of metalloenzymes that catalyze the hydrolysis of a variety of phosphoric acid esters and anhydrides within the pH range 3 to 8. PAP has been isolated from various mammalian and plant sources, and evidence has accumulated that suggests its presence in a limited number of micro-organisms. Animal PAPs contain redox active $Fe^{III}Fe^{II/III}$ binuclear active sites where only the reduced form is catalytically active. In contrast, plant PAPs purified from red kidney beans (rkbPAP) and sweet potatoes (spPAP) contain redox inactive $Fe^{III}Zn^{II}$ or $Fe^{III}Mn^{II}$ centers, respectively. Whilst the amino acids coordinated to the metal ions are identical in these PAPs, the protonation state of the bridging ligand (μ-OH (rkbPAP) vs. μ-oxo (spPAP)) and the binding mode (bidentate (rkbPAP) or tridentate (spPAP)) of the inhibitor/reaction product phosphate differ, reflecting their different reactivities.[1]

Whilst the precise biological role(s) for all PAPs is still contentious, there is a clear correlation between PAP activity and increased bone resorption in animals making this enzyme a major target for the synthesis of chemotherapeutics against bone-related disorders. Recently, we have characterized several hetero-dinuclear ($Fe^{III}Cu^{II}$,[2] $Fe^{III}Ni^{II}$, $Fe^{III}Zn^{II}$, $Fe^{III}Mn^{II}$) complexes with the unsymmetrical ligand 2-bis[{(2-pyridylmethyl)-aminomethyl}-6-{(2-hydroxybenzyl)(2-pyridylmethyl)}-aminomethyl]-4-methyl phenol. These complexes differ not only in their metal ion composition, but also in the identity of bridging ligands. Notably, the $Fe^{III}Cu^{II}$ derivative is significantly more reactive than its isostructural homologues with different divalent metal ions and is an efficient nuclease, cleaving double stranded DNA. Herein we will compare the electronic and geometric structures of the different metal centers in the plant PAPs and model complexes, and correlate the observed variations in reactivity.

[1] Schenk, G; Gahan, L.R.; Carrington, L.E.; Mitic, N.; Valizadeh, M.; Hamilton, S.E.; de Jersey, J; Guddat, L.W. *Proc. Natl. Acad. Sci. USA*, **2005**, *102,* 273-278.

[2] Lanznaster, M.; Neves, A.; Bortoluzzi, A.J.; Aires, V.V.E.; Szpoganicz, B.; Terenzi, H.; Cardoso Severino, P.; Fuller, J.M.; Drew, S.C.; Gahan, L.R.; Hanson, G.R.; Riley, M.J.; Schenk, G. *J. Biol. Inorg. Chem.*, **2005**, In Press.