Designed copper metalloenzymes for the production of value-added chemicals

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In the recent years, waste materials have attracted academic and industrial communities aiming to identify strategies to convert waste to value-added materials and chemicals.[1] The reutilization of vegetable and industrial waste is therefore one of the main global challenges in mitigating environmental impact.
The exploitation of such waste chemicals (e.g. lignin, chitin, cellulose, phenol-like species) for value-added products is considered of remarkable scientific and social impact. In particular, the oxidative degradation of recalcitrant polymeric substrates for the conversion into second-generation biofuels, as catalyzed by bacterial Lytic Polysaccharide MonoOxygenases (LPMOs), and the conversion of toxic phenol-like species into value-added products, as performed by Polyphenol Oxidases (PPOs), may represent the first step for the valorization of waste chemicals.
Structural motif of the active site of LPMOs and PPOs, which both catalyzes the oxidation of exceedingly strong C-H bonds, are copper binding sites.[2] Reproducing the catalytic features of these enzymes in de novo designed protein scaffolds[3] can be important for structure-function relationship studies, but also for the development of efficient enzymes useful in waste treatment.
To this end, we adopted helix-bundle scaffolds to accommodate these copper binding sites. These simple models represent a milestone in the development of synthetic metalloenzymes for the degradation and conversion of biomass into second generation fuels.

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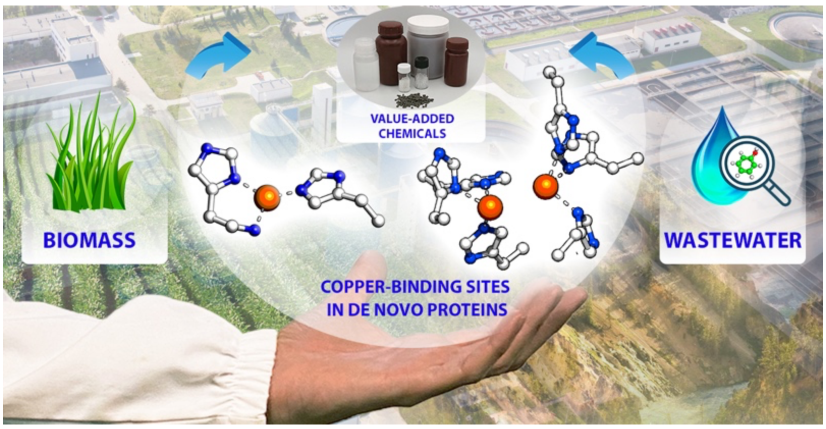

Figure 1. Engineered copper-binding sites involved in waste treatment.

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3. Nastri, F. *et al.* Engineering Metalloprotein Functions in Designed and Native Scaffolds. *Trends Biochem. Sci.* **44**, 1022–1040 (2019).