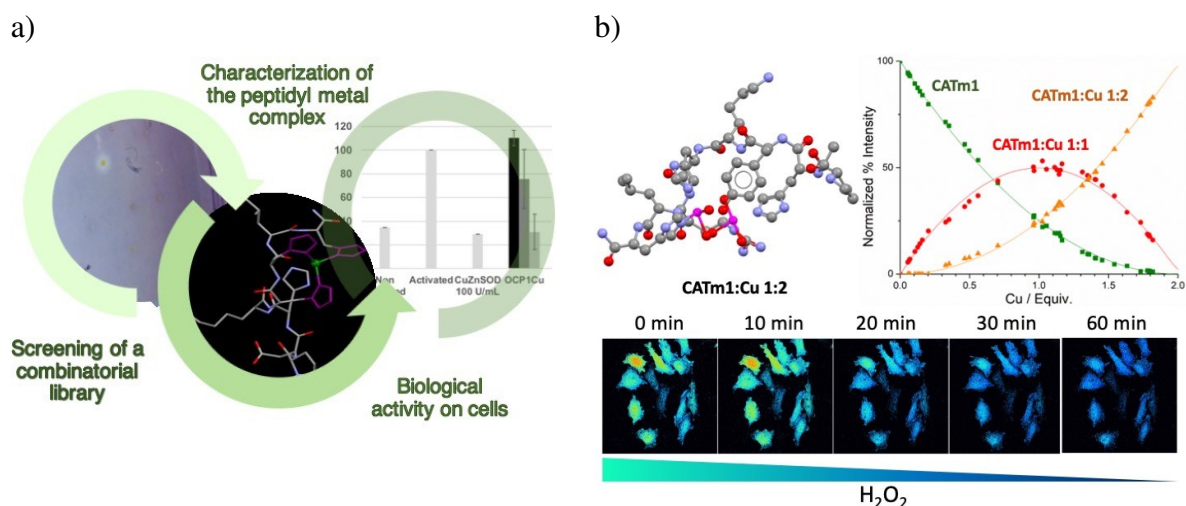


## Combinatorial approaches for the discovery of peptidyl metal complexes mimicking antioxidant metalloenzymes

Peptides are of great interest as ligands for the synthesis of redox-based catalysts since their synthesis is highly versatile, they are biocompatible and provide a great variety of coordination environments. However, the rational design of a peptide that binds a specific metal center with high affinity and that leads to a complex with the required redox potential is very tedious. To overcome this difficulty, we have set up a combinatorial approach combined with an activity-based screening to discover efficient and stable peptidyl complexes mimicking metalloenzymes such as superoxide dismutase (SOD) and catalase (CAT).<sup>1,2</sup> These new catalysts have been characterized using a range of analytical techniques and their activity have been assessed in test tubes and in cells. These enzymes being implicated in the redox homeostasis of cells, such SOD and CAT mimics represent a new interesting class of catalytic drugs.



**Figure 1.** Two examples of studies performed on a SOD (a) and a CAT mimic (b) possessing a peptide as ligand.

- (1) Vincent, A.; Fores, J. R.; Tauziet, E.; Quévrain, E.; Dancs, Á.; Conte-Daban, A.; Bernard, A.-S.; Pelupessy, P.; Coulibaly, K.; Seksik, P.; Hureau, C.; Selmeczi, K.; Policar, C.; Delsuc, N. An Easy-to-Implement Combinatorial Approach Involving an Activity-Based Assay for the Discovery of a Peptidyl Copper Complex Mimicking Superoxide Dismutase. *Chem. Commun.* **2020**, 56 (3), 399–402. <https://doi.org/10.1039/C9CC07920C>.
- (2) Coulibaly, K.; Thauvin, M.; Melenbacher, A.; Testard, C.; Trigoni, E.; Vincent, A.; Stillman, M.J.; Vríz, S.; Policar, C.; Delsuc, N. A Di copper Peptidyl Complex Mimics the Activity of Catalase, a Key Antioxidant Metalloenzyme. *Inorg. Chem.* **2021**, accepted. <https://doi.org/10.1021/acs.inorgchem.0c03718>.