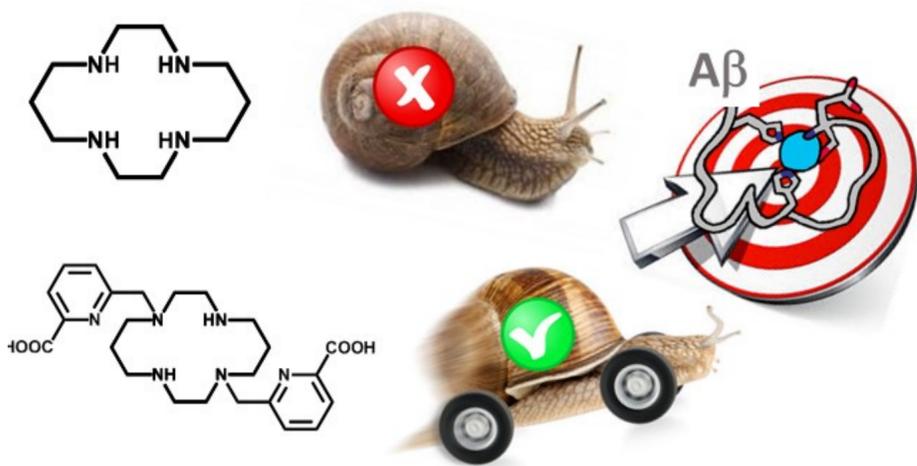


# OUR RESULTS FOR THE YEAR 2019

## Targeting copper ions to fight Alzheimer's



1. [Crédit photo : Christelle HUREAU / LCC toulouse](#)

Copper ions are implicated in the etiology of Alzheimer's disease, particularly through their ability to form highly toxic reactive oxygen species (ROS). Within the synaptic cleft, where the first elements of the disease develop, copper ions are bound to amyloid-beta peptide (Aβ) and the complex thus formed produces significant amounts of ROS participating in the overall oxidative stress detected in the disease. It is in order to target copper ions and render them inactive in ROS formation that many groups are working on the development of ligands for therapeutic purposes. In the team, the objective is more to highlight certain properties that these ligands must possess to be effective ligands (id est, leading to the cessation of ROS production by the Cu(Aβ) complex). In the article XXXX, we have demonstrated the importance of the rate of uptake of the copper(II) ion by the ligand. For this purpose we studied a family of macrocyclic ligands with identical thermodynamic properties, namely a better affinity of the ligands for Cu(II) ions than the Aβ peptide, and thus the ability to extract Cu(II) ions from the Aβ peptide as well as a resistance to the reduction of the Cu(II) complexes formed and thus not being able to participate in ROS production. Despite these identical properties shared by the different ligands studied, only some of them were able to stop the production of ROS by the Cu(Aβ) complex: those with sufficiently high Cu(II) ion uptake rates. We have thus been able to highlight the importance of kinetic parameters, which have been little (or not at all) discussed in the design of ligands against Alzheimer. These results illustrate the complexity of ligand design in the context of Alzheimer's disease, which was previously underestimated.

**Kinetic is crucial when targeting copper ions to fight Alzheimer's disease: an illustration with azamacrocyclic ligands.**

Conte-Daban, A.; Beyler, M.; Tripier, R.; Hureau, C., *Chem. Eur. J.*, 2018, 24, 8447-8452.

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