PERSONAL INFORMATION

HUREAU-SABATER Christelle (08/27/1976 – 4 kids) **– Orcid :** 0000-0003-3339-0239
URL for web site: https://hureaulab.wixsite.com/equipeflcc/christelle-hureau-1

CURRENT POSITION (since 2015-)

Leader of the "ALzheimer, AMyloids and BioInorganic Chemistry (ALAMBIC)" team, in the Coordination Chemistry Laboratory (LCC), Toulouse. The team is made of 4 permanent researchers, Drs. C. Esmieu (new traceable Cu(I) chelators), E. Mathieu (peptide-based mimics of the Lanthanide-methanol dehydrogenase) and G. Pratviel (interactions of metal porphyrins with DNA or amyloid-forming peptides).

PREVIOUS POSITIONS

2016-20 Co-leader of the BIOMAPS "team-project", ITAV (Institute of advanced technology for life science) unit for a dedicated 4-years project (in parallel with regular team leader position at LCC).
"Synthesis and studies of amyloid-specific probes"

2007-15 CNRS researcher in the Biological Chemistry Group headed by Prof. P. Faller (LCC).
"Role of metal ions in the amyloid cascade linked to Alzheimer's disease"

2006-07 Post-doctoral researcher at the University Denis Diderot in Paris with Dr. B. Limoges
"Electrochemical studies of a Laccase immobilized on gold electrodes"

2004-06 Post-doctoral researcher at CEA Saclay with Dr. S. Un.
"HF-EPR studies of Manganese enzymes and of chemical models"

2004 Post-doctoral researcher at the University J. Fourier in Grenoble with Prof. L. Charlet.
"Copper binding site to the fifth site of the Prion protein"

2003 PhD - Inorganic Chemistry, University of Orsay with Drs. J.-J. Girerd, G. Blondin and E. Anxolabéhère.
"Investigations of new PSII structural models electrochemically generated"

EDUCATION

2012 *Habilitation* degree in bio-inorganic chemistry, University Paul Sabatier, Toulouse, France
2003 PhD in coordination chemistry, Paris-Sud University, Orsay, France
2000 Molecular physical chemistry Master degree - Paris-Sud University, Orsay, France
2000 MSc in molecular chemistry in the Ecole Polytechnique, Palaiseau, France

HONORS AND AWARDS

2022 Access to **research director grade** (DR1, CoNRS 16)
2022 Prize from the Gay-Lussac Fundation – French Academy of Sciences (chemistry for societal challenges)
2021 Coordinator of the SUPRAMY collaborative project (Funding from the French National Agency)
2017 Prize of excellence from the University P. Sabatier, Toulouse
2017 Access to **research director grade** (DR2, CoNRS 14)
2016 EuroBIC medal award (European medal for Bio-Inorganic Chemist)
2015 Fellowship USIAS (University of Strasbourg - Institute for advanced studies)
2014 **ERC "Starting Grant" aLzINK**
2013 "Prix Junior" of the Coordination Chemistry Division from the French Chemical Society.
2013 Award from France-Alzheimer Foundation
2012 **CNRS Bronze medal**
2012-23 CNRS Scientific Excellence Award (attributed three times for four years)
2011 Young Investigator Award from the Chemistry Institute of Toulouse

SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS

* Enthusiastic and committed mentor, I have supervised 12 post-doctoral associates, 13 doctoral fellows and more than 25 undergraduate students since 2007. Beyond my strong commitment for the promotion of young talented scientists, I also bring a special care to gender equality.

* I am highly proud and pleased that two of the PhD and two of the post-doctoral researchers (PD) now hold a permanent position in academia and that one PhD and one PD were granted a European MSCA fellowship. The other fellows have taken PD positions and/or are currently working in French education or industry.

ORGANISATION OF SCIENTIFIC MEETINGS

2024 **Chair of the 2nd MBP** (Metal Binding Peptides conference, Toulouse, France, 3 days, expected 150 participants), with E. Mathieu

2017 **Chair of the 14th ISABC** (International Symposium on Applied Bio-Inorganic Chemistry, Toulouse, France, 3 days, 300 participants), with P. Faller

2016 & 17 Chair of FrenchBic (French National Bio-Inorganic symposium, 2 days, 80 participants)

2016 Chair of the "Journées de chimie de coordination" (two days, 120 participants, Toulouse)

MAIN INSTITUTIONAL RESPONSIBILITIES

2021- 27 Vice-president (2021-23) and **president elected** (2023-27) **of French Bioinorganic Chemistry community** (300 members). Member of scientific board of FrenchBIC since 2010.

2021 Co-applicant for a MSCA - Doctoral Networks Grant "Metals and Health", on behalf of the LCC

Editorial & reviewing activity: Editorial member for Inorganics (2018-) & for Journal of Inorganic Biochemistry (2021-) ; Associate Editor, Chemical Biology Section, Front. Chem. (2022-) ; Guest Editor for Coord. Chem. Rev. (Metal ions in neurodegenerative diseases, 2012).

Active reviewer (since 2007) for scientific journals including Nature, Chem. Sci.; Chem. Eur. J. (~30 articles per year, top 5% reviewer for Angew. Chem. Int. Ed. in 2018)

Evaluation committees: Member of the French Research Agency (CE19, 2018-9); Evaluator for European Innovation Council (2023), for the Indo-French, American Alzheimer Association, British, Polish, French and regional research councils (about three projects per year since 2012) & of recruitment committees for (assistant) professor positions & EuroBIC medal, LOREAL-UNESCO grants.

Evaluations of PhD and "habilitation" degrees (about 6 per year, three as reviewers, since 2010)

Chairs: Co-chair of the Midi-Pyrénées Section of the French Chemical Society (2013-7) & of the Midi-Pyrénées Section of the "Chemistry and Society" association (since 2013)

MAIN FUNDINGS (ON-GOING IN THE LAST 5 YEARS)

Amyl-in-AD. 2023-26. MITI CNRS. ***Is amylin the real villain in Alzheimer's disease?*** PI (3 pm/y)

SUPRAMY. 2021-25. ANR PRC, CE06, ***Polyanions to tune the supramolecular assembly of amyloid-forming peptides***. PI (6 pm/y).

aLzINK. 2014-21. ERC StG, PE05. ***Alzheimer & Zinc: the missing link ?*** PI (8 pm/y).

LnZYME. 2023-27. ANR JCJC, CE07. **Lanthano-peptides as Ln-MDH mimics.** PI Dr. E. Mathieu (hired in 2021). Participant (2 pm/y).

MASAI. 2022-26. ANR PRC, CE44, ***Metal-based Agents for Selective Amyloid Imaging.*** PI partner UPR 8241 (3 pm/y). PI: Dr. E. Jakab-Toth (CBM, UPR 4301, Orléans).

DREAMY. 2022-26. ANR PRC, CE29. ***DecipheRing Early steps of self-assembly of AMYloid forming peptides.*** PI partner UPR 8241 (3 pm/y). PI: Dr. N. Giraud (Université de Paris).

COPPERATION. 2020-24. ANR JCJC, CE07. ***Copper fluorescent ligands: for a rational design of Cu-targeting drugs in Alzheimer context.*** PI Dr. C. Esmieu (hired in 2019). Participant (2 pm/y).

CatSAmy. 2019-23. ANR PRC, CE07. ***Catalytic Scaffolds based on Amyloid aggregates.*** PI partner UPR 8241 (2.5 pm/y). PI: Dr. E. Gras (LHFA, Toulouse).

DIVA. 2017-22. ANR PRC, CE18. ***Diabetes Imaging by Visualizing Amylin with Metal-based Probes.*** PI partner UPR 8241 (3 pm/y). PI: Dr. E. Jakab-Toth (CBM, Orléans).

PUBLICATIONS

In line with the CNRS recommendations and because there is no fair number to mirror the quality of research, I give below several indicators that, once gathered, might ease to evaluate my research activities.

>130 international peer-reviewed publications: 1 Acc. Chem. Res. ; 4 Anal. Chem.; 6 Angew. Chem. Int. Ed.; 5 Chem. Commun.; 3 Chem. Soc. Rev.; 2 Chem. Sci. ; 17 Chem. Eur. J.; 24 Inorg.Chem.; 1 Redox Biology; including **10** publications highlighted in covers

+ **6** book chapters & **18** international conference proceedings referenced in the WoS database.

64 publications as corresponding authors; **18** as first author & **51** at last author.

H-index: **43**, and average citations: **43**; citations: > **6500** (without self-citations: > 5500)

Brief description of my research profile. During my doctoral studies, I focused my interests on coordination chemistry of Manganese-based structural models of the water-oxidizing centre in the Photosystem. After the major expertise in bioinorganic chemistry and related spectroscopies acquired during my PhD, I have gained more experience in research fields at the frontier between chemistry, biochemistry and advanced spectroscopy. In 2007, I joined the Coordination Chemistry Laboratory (LCC) as a tenured CNRS researcher. Since then, I have developed a main research line on metal ions coordination to the amyloid-β peptide (Aβ) involved in the Alzheimer's Disease and on the associated deleterious processes: Catalysis of Reactive Oxygen Species production and triggering of Aβ self-assembly. Then, accordingly, I moved to the development of Cu-targeting selective ligands able to prevent Cu(Aβ) ROS formation and more recently to the design and evaluation of Aβ self-assembly inorganic modulators (such as polyoxometallates, porphyrines,…), with the will to delineate new therapeutic lines. During the two last years, I also started a new project on the co-assembly of the amylin involved in diabetes with Aβ based on the proven cross-talk of the pathologies.

Significant scientific achievements .

Metal ions interaction with Amyloid-β (Aβ): (1) Key contributions to the elucidation of the Cu(II), Cu(I), Zn(II) coordination sites in the Aβ peptide involved in AD to a point that the binding models are now widely accepted by the community (CoordChemRev2018). (2) Determination of the importance of (i) pH (refs. **8**-**10**; and InorgChem2011; Chemisty2018), (ii) Dynamic effects (ref. **10** and JBIC2009; InorgChem2012) and (iii) second sphere effects in the structure of the metal binding sites in such intrinsically disordered peptides (InorgChem2012). These were seminal studies that have inspired similar investigations by other groups, working with disordered peptides other than Aβ. (3) Development of analytical methods for the determination of Cu(II), Cu(I) and Zn(II) affinity for Aβ (AnalChem2013; AnalChem2017; Metallomics2014; ChemEurJ2012). The values thus determined made consensus (while they were highly debated before) and the tools set up have been used further by other groups. (4) Implementation of straightforward NMR methodology and advanced EPR for characterization of Cu(II)-Aβ interactions (refs. **9**-**10**) that are currently used by my peers.

New concepts for Cu targeting in AD: Demonstration of several key concepts for the rationale design of Cu-targeting molecules (partly reviewed in InorgChem2019), illustrating overlooked principles such as the key interference with Zn(II) (refs. **5** and ChemEurJ2018; DaltonTrans 2017 and 2016; InorgChem2021; Molecules2021), the importance of kinetic (beyond only thermodynamic consideration) (ChemEurJ 2023 and 2018; Biomolecules2022) and to target Cu(I) (ref. ChemEurJ 2021 and 2017; Metallomics 2015 and 2019). Such researches have opened the route to better rationale in ligand design in the context of AD.

Metal ions interaction with Aβ in link with oxidative properties: (1) Highlight of a complex redox mechanism for the Cu-Aβ species (ref. **1**, Metallomics2016; PNAS2010) with direct implication for reactive oxygen species (ROS) production, one of the deleterious events in AD (DaltonTrans2016); Intervention of Zn(II) in such process (ChemComm2013). (2) Description at the molecular level of the species responsible for ROS formation and of the mechanism at play (ref. **7** and AnalChem2018). The mechanism at play can be enlarged to any other flexible peptide binding redox-active ions. (ref. **1**)

Assembly and co-assembly process of amyloid-forming peptides. (1) The most recent breakthrough is the discovery of key principles in the co-assembly process of amyloid-forming peptides as illustrated in ref. **3** and **6**. (2) In addition, recent results on tuning and probing the self-assembly of peptides have been obtained (ref. **4**, CEJ2021, ChemFront2021).

My recognition in these research fields is demonstrated by the high number of invited contributions (highly cited reviews: RedoxBiol2018; ChemSocRev 2013 and 2017; AccChemRes2014, CoordChemRev2018, regular papers and book chapters: AD2022), and invitations in internationally conferences as keynote or plenary speaker and regularly as session chairs.

Ten main publications as corresponding author

1 Falcone, E.; **Hureau, C.*** "Redox processes in Cu-binding proteins: the "in-between"states in intrinsically disordered peptides" **Chem. Soc. Rev.** (viewpoint), in press, 10.1039/D3CS00443K

2 Malikidogo, K. P.; Drommi, M.; Atrián-Blasco, E.; Hormann, J.; Kulak, N.; Esmieu, C.*; **Hureau, C.*** "Ability of Azathiacyclen Ligands To Stop Cu(Aβ)-Induced Production of Reactive Oxygen Species: [3N1S] Is the Right Donor Set" **Chem. Eur. J.** **2023**, 29, e202203667 (cover picture), 10.1002/chem.202203667

3 Cheignon, C., Collin, F.; Sabater, L.; **Hureau, C.*** " Oxidative Damages on the Alzheimer's Related-Aβ Peptide Alters Its Ability to Assemble" **Antioxydants 2023**, 12, 472, 10.3390/antiox12020472

4 Atrián-Blasco, E.; de Cremoux, L.; Lin, X.; Mitchell-Heggs, R.; Sabater, L.; Blanchard, S.*; **Hureau, C.*** "Keggin-type polyoxometalates as Cu(II) chelators in the context of Alzheimer's disease" **Chem. Commun. 2022**, 58, 2367-70, 10.1039/D1CC05792H

5 Behar, A. E.; Sabater, L.; Baskin, M.; **Hureau, C.***; Maayan, G.* "A Water-Soluble Peptoid Chelator that Can Remove Cu(II) from Amyloid-β Peptides and Stop the Formation of Reactive Oxygen Species Associated with Alzheimer's Disease" **Angew. Chem. Int. Ed**, 2021, 60, 24588-97, 10.1002/anie.202109758

6 Stefaniak, E.; Atrian-Blasco, E.; Goch, W.; Sabater, L.; **Hureau, C.***; Bal, W.* "The Aggregation Pattern of Aβ1-40 is Altered by the Presence of N-Truncated Aβ4-40 and/or Cu(II) in a Similar Way through Ionic Interactions" Chem. Eur. J. 2021, 27, 2798-09, 10.1002/chem.202004484

7 Cheignon, C.; Jones, M.; Atrian-Blasco, E.; Kieffer, I.; Faller, P.; Collin, F.; **Hureau, C.*** "Identification of key structural features of the elusive Cu-Aβ complex that generates ROS in Alzheimer's disease" **Chem. Sci. 2017**, 8, 5107-18, 10.1039/c7sc00809k

8 Alies, B.; Sasaki, I.; Proux, O.; Sayen, S.; Guillon, E.; Faller, P.; **Hureau, C.*** "Zn impacts Cu coordination to amyloid-beta, the Alzheimer's peptide, but not the ROS production and the associated cell toxicity" **Chem. Commun. 2013**, 49, 1214-6, 10.1039/c2cc38236a

9 Eury, H.; Bijani, C.; Faller, P.; **Hureau, C.*** "Copper(II) coordination to amyloid beta: murine versus human peptide" **Angew. Chem. Int. Ed. 2011**, 50, 901-5, 10.1002/anie.201005838

10 **Hureau, C.***; Coppel, Y.; Dorlet, P.; Solari, P.-L.; Sayen, S.; Guillon, E.; Sabater, L.; Faller, P.* "Deprotonation of the Asp1-Ala2 peptide bond induces modification of the dynamic copper(II) environment in the Aβ peptide near physiological pH" **Angew. Chem. Int. Ed. 2009**, 48, 9522-5, 10.1002/anie.200904512

Invited conferences in international and national conferences

22 invitations in international conferences (including **4** as plenary & **10** as keynotes)
20 in national conferences as plenary and **24** in universities

Selected invited lectures in international conferences (in the last 5 last years)

#"Bioinorganic chemistry and oxidative stress", SCF meeting 2023, Nantes (France) (**plenary**); #"Inorganic modulators of Aβ self-assembly", 5th International Symposium on Pathomechanisms of *Amyloid* Diseases, Bordeaux (France) (**lecture**); **#**"Tuning the self-assembly of amyloid-β peptides with inorganic chaperones", ICCC, 2022, Rimini (Italy) (**lecture**); **#**"Polyanions to counteract the detrimental interaction between Cu(II)/Zn(II) and the Alzheimer's-related amyloid-β peptide", EuChems 8th, 2022, Lisbon, Portugal (**keynote**); **#**"Metal-modulated self-assembly of Aβ & effects of Polyphosphates", EuroBIC16, 2022, Grenoble (**keynote**); **#**" Macrocylic-based ligands to target Cu(II/I)-bound to the Alzheimer-related amyloid-β peptide" 51st KAIST Symposium, Corea, 2022 (**keynote**); **#** "Targeting copper(II/I) ions with short ATCUN-like peptides in the context of Alzheimer's disease", Metal Binding Conference, 2022, Nancy (**lecture**); **#**"Probes of amyloids' formation and amyloid fibrils" IMBG 8th, 2019, France (**keynote**); **#**"POMs to counteract the effect of CuAβ interactions in the context of Alzheimer's disease" ICBIC19, 2019, Interlaken, Switzerland (**keynote**); **#**"Kinetics are crucial for designing efficient Copper chelators to fight against Alzheimer's disease" SCF Meeting, 2018, Montpellier, France (**keynote**); **#**"Therapeutic approaches targeting Copper ions against Alzheimer's disease" ISMEC, 2018, Firenze, Italy (**plenary**);

Selected invited PLENARY lectures in national conferences

#"Strategies to target Cu(Aβ)-catalyzed ROS production and Aβ self-assembly in Alzheimer's disease", Days of the IMBG, 2023 (Grenoble); **#**"A short trip to the role of metal ions in Alzheimer's disease", Days of the ChemBio GDR, Toulouse, 2022; **#**"Cu-targeting ligands and chemical chaperones of the Aβ aggregation" Coordination Chemistry days, Marseilles, 2020; **#**"Therapeutic approaches that target Cu ions and associated oxidative stress to combat Alzheimer's disease" Gecom-Concoord, Longeville-sur-Mer, 2018; **#**"Cu and Zn in Alzheimer's: with a little help from coordination chemistry." Gecom-Concoord, Strasbourg, 2016.