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RESEARCH INTERESTS

- Biochemistry of metalloenzymes
- Cytochromes P450, Flavins
- Enzyme catalysis and mechanism
- Coenzyme Q biosynthesis
- Fe-S hydroxylating non O₂-dependent enzymatic system
- Phylogeny

SUMMARY

Coenzyme Q (CoQ) is an endogenous lipid soluble molecule found in bacterial plasmatic or mitochondrial inner membranes, where it works as an essential electron carrier in the respiratory chain. Today, several inactivating mutations in genes affecting the biosynthesis of CoQ have been identified in severe pathologies as myopathies, nephropathies, or cerebellar ataxia. CoQ biosynthesis is complex and requires no less than a dozen of proteins, but a clear assignment of catalytic or biological function for many participating proteins is still missing. We aim at getting a better knowledge at the fundamental level of the biosynthesis of CoQ in *E.coli*, using a judicious combination of molecular genetics, site-directed mutagenesis, biochemistry, molecular biophysics and structural biology. The aim of this project is to provide *in vitro* biochemical characterization of the proteins involved in the biosynthesis of CoQ in *E.coli*, to elucidate their exact function, to solve their structures, to study their molecular mechanism, and also to design and synthesize small molecules targeting the ubiquinone anaerobic pathway which could be potential antimicrobials.

I am also interested in RNA modifying enzymes, notably TrhP and RlhA, two Fe-S proteins that share biochemical and structural identity with UbiU and UbiV involved in anaerobic CoQ biosynthesis in *E.coli*.

PUBLICATIONS (last 12 years)

2024

- An organic O donor for biological hydroxylation reactions
Kazemzadeh, K, Simon, P, Pelosi, L, Séchet, E, Arulanandam, R, Hajj Chehade, M, Rey, M, Onal, D, Flandrin, L, Chreim, R, Faivre, B, Vo, CDT, Arias-Cartin, R, Barras, F, Fontecave, M, Bouveret, E, **LOMBARD, M**, Pierrel F
PNAS, 2024, 121(13):e2321242121, doi: 10.1073/pnas.2321242121.
- Activation of Coq6p, a FAD monooxygenase involved in coenzyme Q biosynthesis, by adrenodoxin reductase/ferredoxin
Gonzalez, L, Vo, CDT, Faivre, B, Pierrel, F, Fontecave, M, Hamdane, D, **LOMBARD, M**
Chembiochem, 2024, 25(5):e202300738, doi: 10.1002/cbic.202300738.

- Functional redundancy in tRNA dihydrouridylation
Sudol, C, Kilz, LM, Marchand, V, Thullier Q, Guérineau, V, Goyenvalle, C, Faivre, B, Toubdji, S, **LOMBARD, M**, Jean-Jean, O, de Crécy-Lagard, V, Helm, M, Motorin, Y, Brégeon, D, Hamdane, D
Nucleic Acids Res, 2024, 52(10):5880-5894, doi: 10.1093/nar/gkae325.

2022

- Evolutionary Diversity of Dus2 Enzymes Reveals Novel Structural and Functional Features among Members of the RNA Dihydrouridine Synthases Family
LOMBARD, M, Reed, CJ, Pecqueur, L, Faivre, B, Toubdji, S, Sudol, C, Brégeon, D, de Crécy-Lagard, V, Hamdane, D
Biomolecules. 2022, 12:1760, 10.3390/biom12121760, doi: 10.3390/biom12121760.
- Dihydrouridine in the transcriptome: New life for this ancient RNA chemical modification.
Brégeon, D, Pecqueur, L, Toubdji, S, Sudol, C, **LOMBARD, M**, Fontecave, M, De Crécy-Lagard, V, Motorin, Y, Helm, M, Hamdane, D
ACS Chem Biol. 2022, 17(7):1638-1657, doi: 10.1039/d1cp03379d.

2021

- Ultrafast dynamics of fully reduced Flavin in catalytic structures of thymidylate synthase ThyX
Dozova, N, Lacomat, F, **LOMBARD, M**, Hamdane, D, Plaza, P.
Phys Chem Chem Phys. 2021, 23(39):22692-22702, doi: 10.1039/d1cp03379d.
- An enzymatic activation of formaldehyde for nucleotide methylation.
Bou-Nader, C, Stull, FW, Pecqueur, L, Simon, P, Royant, F, Fontecave, M, **LOMBARD, M**, Palfey, BA, Hamdane, D.
Nature Comm. 2021, 12(1):4542, doi: 10.1038/s41467-021-24756-8.
- Dihydrouridine synthesis in tRNAs under reductive evolution
Faivre, B, **LOMBARD, M**, Fakroun, S, Vo, CDT, Goyenvalle, C, Guérineau, V, Pecqueur, L, Fontecave, M, de Crécy-Lagard, V, Brégeon, D, Hamdane, D.
RNA biol. 2021, doi: 10.1080/15476286.2021.1899653

2020

- The O₂-independent pathway of ubiquinone biosynthesis is essential for denitrification in *Pseudomonas aeruginosa*
Vo, CDT, Michaud, J, Elsen, S, Faivre, B, Bouveret, E, Barras, F, Fontecave, M, Pierrel, F, **LOMBARD, M***, Pelosi, L.
J Biol Chem. 2020, doi: 10.1074/jbc.RA120.013748
- Structural and functional characterization of 4-Hydroxyphenylacetate 3-hydroxylase from *Escherichia coli*.
Deng, Y, Faivre, B, Back, O, **LOMBARD, M**, Pecqueur, L, Fontecave, M.
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2019

- Ubiquinone Biosynthesis over the Entire O₂ Range: Characterization of a Conserved O₂-Independent Pathway.
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mBio. 2019, 10, e01319-19, doi: 10.1128/mBio.01319-19.
- A soluble metabolon synthesizes the isoprenoid lipid Ubiquinone.
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Cell Chem Biol. 2019, 26, 482-492. doi: 10.1016/j.chembiol.2018.12.001.

2017

- Power of protein/tRNA functional assembly against aberrant aggregation.
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Arch Biochem Biophys. 2017, 632:28-40. doi: 10.1016/j.abb.2017.06.011.
- The UbiK protein is an accessory factor necessary for bacterial ubiquinone (UQ) biosynthesis and forms a complex with the UQ biogenesis factor UbiJ.
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J Biol Chem. 2017, 292(28):11937-11950. doi: 10.1074/jbc.M117.789164.

2016

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Ismail, A, Leroux, V, Smadja, M, Gonzalez, L, **LOMBARD, M**, Pierrel, F, Mellot-Draznieks, C, Fontecave, M.
PLoS Comput Biol. 2016, 12(1): e1004690. doi: 10.1371/journal.pcbi.1004690.

2015

- Expression in yeast, new substrates, and construction of a first 3D model of human orphan cytochrome P450 2U1: Interpretation of substrate hydroxylation regioselectivity from docking studies.
Ducassou, L, Jonasson, G, Dhers, L, Pietrancosta, N, Ramassamy, B, Xu-Li, Y, Lorient, MA, Beaune, P, Bertho, G, **LOMBARD, M**, Mansuy, D, André, F, Boucher, JL.
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2014

- Biosynthesis and physiology of coenzyme Q in bacteria.

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2013

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