

Guillaume PONCET-MONTANGE

Pharm.D. and Ph.D.

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EDUCATION AND DEGREES

- July-2007 : **Ph.D. in Structural Biology.** School of Pharmacy, University of Montpellier I, France.
- 2002-2003 : **M.S. in Biological Chemistry:** specialization in structural biology, School of Pharmacy, University of Montpellier I, France.
- 1996-2002 : **Pharm.D.,** School of Pharmacy, Paul-Sabatier University, Toulouse, France.
- 1995-1996 : High School Diploma (Sciences).

PROFESSIONAL EXPERIENCES

- 2008-present: **Postdoctoral Scholar** in the laboratory of Pr. S.B. Prusiner, Institute for Neurodegenerative Diseases, University of California, San Francisco, USA.
Supervised by Dr. Sina Ghaemmaghami and Pr S.B. Prusiner.
Subject: Drug design and therapeutics of prion diseases.
- 2006-2007 : **Postdoctoral Scholar** in the laboratory of Dr. J.M. Verdier, Molecular Mechanisms of Neurodegenerative Diseases, INSERM U710, Montpellier, France.
Supervised by Pr. J.M. Verdier and Dr. V. Perrier.
Subject: Drug design and therapeutics of prion diseases.
Teaching: Chemo and Bio-informatics, University of Montpellier II, France.
- 2003-2007 : **Doctoral training** in the laboratory of Dr. C.A. Royer, Center for Structural Biochemistry, CNRS UMR5048 - INSERM U554, Montpellier, France.
Subject: Crystal structures of *L. monocytogenes* NAD kinase complexes: towards structure based drug design using a fragment approach.
Supervised by Dr. G. Labesse.
Teaching: Analytical chemistry of a natural drug, School of Pharmacy, University of Montpellier I, France.
- 2002-2003 : **M.S. training** in the laboratory of Dr. C.A. Royer, Center for Structural Biochemistry, Montpellier, France.
Supervised by Dr. G. Labesse and Dr. D. Douguet.
Subject: Rational drug design of MabA, a beta keto-acyl-ACP reductase of *M. tuberculosis*.
- 2001-2002 : **European exchange students** at the Huddinge Karolinska Institute, Huddinge University, Stockholm, Sweden.
Supervised by Pr. P. Hartvig.
Training periods in **Toulouse University hospital**, France.
- 2000-2001 : **Training period** in the laboratory of Dr. B. Meunier, Chemical and Coordination Laboratory, Paul-Sabatier University, Toulouse, France.
Supervised by Pr. J. Bernadou.
Subject: Investigation of a new synthesis way of a nearby isoniazide drug.

COMPETENCES

Technical skills

X-ray crystallography : crystallogenesi s, European X-ray crystallography data collection (European Synchrotron Radiation Facility, Grenoble, France), data processing and refinement using CCP4 suite and COOT/ ONO software, nucleotides fragment-based drug design.

Other Biophysical studies : general biochemistry, circular dichroism, diffusion light scattering, Small Angles X-ray Scattering data collection (Deutsches Elektronen Synchrotron, Hambourg, Germany), biophysical ligand-binding assay.

Chemo and Bio-informatics : Virtual screening (FlexX and Surflex softwares), comparative modelling of protein structures.

Languages

French (mother tongue), English.

THESIS AND POST DOCTORAL RESEARCH ABSTRACT

Guillaume Poncet-Montange thesis focused on structural and functional characterizations of NAD Kinases enzymes with the goal of developing a fragment-based drug design approach using X-ray crystallography. This study has been carried out at the Center for Structural Biochemistry (Montpellier, France) in tight connection with biologist and chemist from the Pasteur Institute (Paris, France). Structures of the NAD Kinase from *L. monocytogenes* (LmNADK1) solved by Guillaume Poncet-Montange, provided with : 1) a refined structure of the active site and a better knowledge of the recognition of NAD, 2) a description of the enzymatic mechanism which involves a substrate assisted catalysis, 3) the first complex of a NAD Kinase with a non natural inhibitor which has been discovered by combining a focused combinatorial chemistry and X-ray crystallography, 4) the allosteric mechanism for this kinase, 5) the formation of a novel hyperphosphorylated nucleotide compound.

Then, he completed a postdoctoral position at the University of Montpellier, which focused on molecular mechanisms in neurodegenerative dementia. His work was dedicated to prion therapeutics, especially the identification of small molecules by virtual screening and their structure-activity relationships with the prion protein.

As a member of the Prusiner lab (Institute for Neurodegenerative Diseases, UCSF, USA), Guillaume Poncet-Montange will be involved in discovering new ligands that directly bind and stabilize the soluble form of the human prion protein (PrP^c), inhibiting its conversion into the oligomeric, disease-causing form (PrP^{Sc}). New specific PrP^c ligands will be useful to investigate the protein's biological function and as leads for drug discovery. To do so, his research will be achieved in collaboration with the Shoichet lab (Dept. of Pharmaceutical Chemistry, UCSF, USA).

PROTEIN DATA BANK DEPOSITIONS AND RELATED ARTICLES

MabA triple mutant	PDB2NTN. <u>Poncet-Montange G.</u> , Ducasse-Cabanot S., Quemard A., Labesse G. and Cohen-Gonsaud M. "The lack of dynamic in the active site of MabA kills the enzyme activity. Practical consequences for drug-design studies", <i>Acta Cryst.</i> (2007). D63, 923-925.
LmNAD kinase 1	PDB2I1W, PDB2I29, PDB2I2A, PDB2I2B, PDB2I2C, PDB2I2D, PDB2I2E, PDB2I2F and PDB2Q5F. <u>Poncet-Montange G.</u> , Assairi L., Arold S., Pochet S., Labesse G. "NAD kinases use substrate-assisted catalysis for specific recognition of NAD". <i>Journal of Biological Chemistry</i> (2007). 282(47):33925-34
LmNAD kinase 1	Four new crystal structures of LmNADK1 mutants in a refined state, will be soon deposited in the Protein Data Bank. <u>Poncet-Montange G.</u> , Assairi L., Labesse G. "Allosteric mechanism of NAD Kinases from Gram (+) bacteria". (<i>In preparation</i>).
Conferences:	Seminar at the pharmaceutical department, Pr. B.K. Shoichet laboratory, University of California, San Francisco, USA. Seminar at the biochemical and biophysical department, Pr. R.J. Fletterick laboratory, University of California, San Francisco, USA. Seminar at the biomolecular and cellular department, Pr. J.K. Kuriyan laboratory, Howard Hughes Medical Institut, University of California, Berkeley, USA.