Speaker information

General Information

Name	Patricia MELNYK	
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Affiliation	University of Lille, France	
Education Background	Engineer in Chemistry (ENSCP, Paris, Fr) PhD in organic chemistry (Univ P&M Curie, Paris, Fr)	
Professional Appointment	Professor in Chemistry	
Research Interest	Medicinal chemistry, chemical biology, neurodegenerative disorders, drug development	
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Recent Publications

1. Sergeant N, Vingtdeux V, Eddarkaoui S, Gay M, Evrard C, Lefur N, Laurent C, Caillierez R, Obriot H, Larchanché PE, Farce A, Coevoet M, Carato P, Kouach M, Descat A, Dallemagne P, Buée-Scherrer V, Blum D, Hamdane M, Buée L, Melnyk P. New piperazine multi-action drugs prevent neurofibrillary degeneration and amyloid deposition, and preserve memory in animal models of Alzheimer's disease. Neurobiol Dis, 2019, S0969-9961, 30327-9. Doi :10.1016/j.nbd.2019.03.028
2. Bolteau R, Descamps F, Ettaoussi M, Caignard D-H, Delagrange P, Melnyk P, Yous S. Quinalozine and Phtalazine Derivatives as Novel Melantonin Receptor Ligands Analogues of Agomelatine. Eur J Med Chem, 2020, 189, 112078. doi: 10.1016/j.ejmech.2020.112078
3. Liberelle M, Jonckheere N, Melnyk P, Van Seuningen I, Lebegue N. EGF-containing membrane-bound Mucins : a hidden ErbB2 signaling pathway ? J Med Chem, 2020, 63 (10), 5074-5088. doi: 10.1021/acs.jmedchem.9b02001
4. Tautou M, Eddarkaoui S, Descamps F, Larchanché PE, El Bakali J, Goveas LM, Dumoulin M, Lamarre C, Blum D, Buée L, Melnyk P, Sergeant N. A β-secretase modulator decreases Tau

pathology and preserves short-term memory in a mouse model of neurofibrillary degeneration. Front Pharmacol, 2021,12, 679335. doi: 10.3389/fphar.2021.679335

5. Sturbaut M, Bailly F, Coevoet M, Pugniere M, Liberelle M, Magnez R, Thuru X, Melnyk P, Gelin M, Allemand F, Guichou JF, Cotelle P. Discovery of a cryptic site at the interface 2 of TEAD – Toward new anti-cancer compounds. Eur J Med Chem, 2021, 226, 113835-849. doi : 10.1016/j.ejmech.2021.113835
6. Liberelle M, Toulotte F, Renault N, Gelin M, Allemand F, Melnyk P, Guichou JF, Cotelle P. Towards the design of selective ligands of TEADs C-terminal domain. J Med Chem, 2022, 65(8), 5926-40.
7. Bolteau R, Duroux R, Laversin A, Vreulz B, Shiriaeva A, Stauch B, Han GW, Cherezov V, Renault N, Barczyk A, Ravez S, Coevoet M, Melnyk P, Liberelle M, Yous S. High ligand efficiency quinazoline compounds as novel A2A adenosine receptor antagonists. Eur J Med Chem, 2022, 241, 114620.
8. Oxombre B, Madouri F, Journé A-S, Ravez S, Woitrain E, Odou P, Duhal N, Ninni S, Montaigne D, Delhem N, Vermersch P, Melnyk P. Safe and efficient sigma1 ligand: a potential drug candidate for Multiple Sclerosis. Int J Mol Sci, 2022, 23(19), 11893. doi: 10.3390/ijms231911893.
   Special Issue “The Intriguing Sigma-1 and Sigma-2 Receptors and Their Potential Therapeutic Roles 2.0”
9. Mésangeau C, Carato P, Renault N, Coevoet M, Barczyk A, Buée L, Sergeant N, Melnyk P. Discovery of Compounds that Selectively Repress the Amyloidogenic Processing of the Amyloid Precursor Protein : Design, Synthesis and Pharmacological Evaluation of Diphenylpyrazoles. Int J Mol Sci, 2022, 23(21), 13111. doi: 10.3390/ijms232113111.
   Special Issue "Advances in Alzheimer's Disease Drug Research and Development"
10. Tautou M, Descamps F, Larchanché PE, Buée L, El Bakali J, Melnyk P, Sergeant N. A polyaminobiaryl-based β-secretase modulator alleviates cognitive impairments, amyloid load, astrogliosis, and neuroinflammation in $APP^{Swe}/PSEN1^{\Delta E9}$ mice model of amyloid pathology. Int J Mol Sci, 2023, 24(6):5285. doi: 10.3390/ijms24065285
    Special Issue "New Trends in Alzheimer's Disease Research: From Molecular Mechanisms to Therapeutics".

Speaker information

Speech Topic and Abstract

Title:
A ligand-based approach for the design of multi-action anti-Alzheimer compounds

Abstract:
Alzheimer's disease (AD) is a multifactorial slow and progressive dementing disease that combines two pathophysiological mechanisms: the amyloid pathology and the Tau pathology. In parallel with these hallmarks, several dysfunctions are observed such as neuroinflammation, cellular death, altered proteostasis, lysosome dysfunctions, damaged mitochondria and altered synaptic transmission. Disease-modifying small molecules currently in clinical trials only act on either one of these processes or even on symptoms.

In the past years, thanks to a phenotypic screening and the identification of the two first active families, we developed a ligand-based approach and built a pharmacophoric model. From this model, we succeeded in identifying several families of compounds able to modulate the APP metabolism, reduce the Tau pathology development *in vivo* and improve the cognitive deficits in transgenic mouse models of hippocampal Tau pathology and amyloid pathology. We also highlighted the effect of some compounds on neuroinflammation and protein homeostasis.

The presentation will focus on the design, synthesis and activities of one of these compounds.