Mohamed Benchekroun, PhD MRSC
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Expertise and new technologies interests

Hands-on Organic Synthesis: synthesis of biologically active small molecules from milligram to multi-gram scale, methodology studies: multicomponent reactions, metal-catalysed cross coupling reactions, photochemistry, cycloaddition reactions, organocatalysis, asymmetric catalysis, PROTAC design.

Drug Discovery: SAR studies, and physico-chemical properties/DMPK assisted by data mining/vizualisation/prediction tools (Dotmatics® Suite 5.2, ChemAxon® Marvin, Schrödinger® Maestro), large dataset handling, integrated e lab-book, Computer-Aided Drug Design (Fragment- and Structure- Based Drug Design).

Analytical Chemistry: Characterization of small and macro molecules by modern spectroscopic and chromatographic techniques (1D/2D NMR, FT-IR, HPLC, UPLC, HR-MS, LC-MS, GC-MS), methodology development.

Education

2011-2014 PhD in Medicinal Chemistry, Université de Franche-Comté, Besançon, France.

2009-2010 MSc Organic Chemistry, Université Paris-Sud, Orsay, France.

2007-2008 BSc Organic Chemistry, Université Paris-Sud, Orsay, France.

Career history

Since Oct. 2019
Research Fellow in Medicinal Chemistry
Conservatoire National des Arts et Métiers, Paris, France.
Duties: Design, synthesis and pharmacological evaluation of new TNF-α modulators for the treatment of inflammatory diseases, SAR and ADME-tox studies.

Sept. 2018-Aug. 2019
Research Fellow in Medicinal Chemistry
CNRS, Institut de Chimie des Substances Naturelles, Gif-sur-Yvette, France.
Duties: Design, synthesis and pharmacological evaluation of new kinases inhibitors inspired from marine natural products for the treatment of inflammatory diseases, SAR studies.

Sept. 2016 – July 2018
Research Fellow in Medicinal Chemistry
Sussex Drug Discovery Centre, University of Sussex, Brighton, United Kingdom.
Duties: Hit-to-Lead and lead optimization of non-sedating $GABA_A$ receptors modulators for the potential treatment of anxiety without sedative effect, SAR and ADME studies, writing of scientific publications, visualisation and dataset DMPK analyses for the selection of lead molecules using data mining tools.

July 2015 – Aug. 2016
Postdoctoral Research Associate in Organic & Medicinal Chemistry
CNRS, Institut de Chimie des Substances Naturelles, Gif-sur-Yvette, France.
Duties: Discovery of novel β-lactamases inhibitors to fight multi-drug resistant Gram-negative bacteria, development of new [2+2] and [3+2] cycloaddition reactions, SAR studies, writing of scientific publications, search for new scientific collaborations.

May 2015 – July 2015 *Postdoctoral Research Associate in Organic Chemistry*
Université Paris-Sud, Faculté de Pharmacie de Chatenay-Malabry, France.
Methodology in Barluenga cross-coupling reactions: application in cancer research, writing of scientific publications.

Oct. 2011 – Oct. 2014 *PhD Researcher in Medicinal Chemistry*
Université de Franche-Comté, France.
Duties: Multicomponent synthesis and biological evaluation of new Ugi and Passerini adducts for the potential treatment of Alzheimer's disease (*Summa cum Laude*), SAR studies, writing of scientific publications, teachings in Organic & Medicinal Chemistry, supervision of two pharma student (2nd and 3rd year).

Teaching experience

2016-2018 Case studies in Medicinal Chemistry, Sussex Drug Discovery Centre, Brighton, U.K. (20h, 10 pers.).

2015 Case studies in total synthesis, Institut de Chimie des Substances Naturelles, CNRS, Gif-sur-Yvette (20h, 6 pers.).

2012 Teachings in Organic Chemistry (64h/year)
Practical work in Organic Chemsitry: 2nd and 3rd year of Pharmacy (36h) ;
Courses in Organic Chemistry: 1st year of Pharmacy (27h) ; lecture in Medicinal Chemistry : 3rd year of Pharmacy (4h) (Faculty of Pharmacy, Université de Franche-Comté).

Scientific and community contribution

1 patent, **17 publications in peer-reviewed journals** (*h*-index= 8, Clarivate Web of Science®), 3 oral communications, 5 posters, 1 workshop. Member of the French Société Chimique de France, member of the Royal Society of Chemistry.

Peer-reviewed publications/patent

(1) **Benchekroun, M.**; Ermolenko, L.; Tran, M. Q.; Vagneux, A.; Nedev, H.; Delehouzé, C.; Souab, M.; Baratte, B.; Josselin, B.; Iorga, B. I.; Ruchaud, S.; Bach, S.; Al-Mourabit, A. Discovery of Simplified Benzazole Fragments Derived From The Marine Benzosceptrin B as Necroptosis Inhibitors Involving The Receptor Interacting Protein Kinase-1. *Eur. J. Med. Chem.* **2020**. *under press*

(2) Romero, E.; Oueslati, S.; **Benchekroun, M.**; D'Hollander, A. C. A.; Ventre, S.; Vijayakumar, K.; Minard, C.; Exilie, C.; Tlili, L.; Retailleau, P.; Zavala, A.; Elisée, E.; Selwa, E.; Nguyen, L. A.; Pruvost, A.; Naas, T.; Iorga, B. I.; Dodd, R.; Cariou, K. Azetidinimines as a Novel Series of Non-Covalent Broad-Spectrum Inhibitors of β-Lactamases with Submicromolar Activities Against Carbapenemases of Classes A, B and D. **2020**. Preprint https://doi.org/10.26434/chemrxiv.11897157.v1. Submitted to *ACS Infect. Dis.*

(3) Maramai, S.; **Benchekroun, M.**; Ward, S. E.; Atack, J. R. Subtype Selective γ-Aminobutyric Acid Type A Receptor (GABAAR) Modulators Acting at the Benzodiazepine Binding Site: An Update. *J. Med. Chem.* **2019**. https://doi.org/10.1021/acs.jmedchem.9b01312.

(4) Malek, R.; Refouvelet, B.; **Benchekroun, M.**; Iriepa, I.; Moraled, I.; Andrys, R.; Musilek, K.; Ismaili*, J. M.-C. and L. Synthesis and Biological Evaluation of Novel Chromone+Donepezil Hybrids for Alzheimer's Disease Therapy. *Curr. Alzheimer Res.* **2019**, *16*, 815–820.

(5) **Benchekroun, M.**; Pachón-Angona, I.; Luzet, V.; Martin, H.; Oset-Gasque, M.-J.; Marco-Contelles, J.; Ismaili, L. Synthesis, Antioxidant and Aβ Anti-Aggregation Properties of New Ferulic, Caffeic and Lipoic Acid Derivatives Obtained by the Ugi Four-Component Reaction. *Bioorganic Chem.* **2019**, *85*, 221–228. https://doi.org/10.1016/j.bioorg.2018.12.029.

(6) **Benchekroun, M.**; Maramai, S. Multitarget-Directed Ligands for Neurodegenerative Diseases: Real Opportunity or Blurry Mirage? *Future Med. Chem.* **2019**, *11* (4), 261–263. https://doi.org/10.4155/fmc-2018-0249.

(7) **Benchekroun, M.** The Advent of Directed Protein Degraders in Drug Discovery. *Future Drug Discov.* **2019**. https://doi.org/10.4155/fdd-2019-0019.

(8) Naret, T.; Bignon, J.; Bernadat, G.; **Benchekroun, M.**; Levaique, H.; Lenoir, C.; Dubois, J.; Pruvost, A.; Saller, F.; Borgel, D.; Manoury, B.; Leblais, V.; Darrigrand, R.; Apcher, S.; Brion, J.-D.; Schmitt, E.; Leroux, F. R.; Alami, M.; Hamze, A. A Fluorine Scan of a Tubulin Polymerization Inhibitor Isocombretastatin A-4: Design, Synthesis, Molecular Modelling, and Biological Evaluation. *Eur. J. Med. Chem.* **2018**, *143*, 473–490. https://doi.org/10.1016/j.ejmech.2017.11.055.

(9) Cariou, K.; Dodd, R. H.; Romero, E.; **Benchekroun, M.**; Iorga, B.; Naas, T.; Oueslati, S. 2- or 3-Imidazolines as Carbapenemases Inhibitors. WO2018162670 (A1), September 13, 2018.

(10) Swager, T. M.; Kim, Y. Four-Membered Heterocycles from Ynamide. *Synfacts* **2017**, *13* (10), 1036. https://doi.org/10.1055/s-0036-1591242.

(11) Romero, E.; Minard, C.; **Benchekroun, M.**; Ventre, S.; Retailleau, P.; Dodd, R. H.; Cariou, K. Base-Mediated Generation of Ketenimines from Ynamides: Direct Access to Azetidinimines by an Imino-Staudinger Synthesis. *Chem. – Eur. J.* **2017**, *23* (53), 12991–12994. https://doi.org/10.1002/chem.201702545.

(12) Ismaili, L.; Refouvelet, B.; **Benchekroun, M.**; Brogi, S.; Brindisi, M.; Gemma, S.; Campiani, G.; Filipic, S.; Agbaba, D.; Esteban, G.; Unzeta, M.; Nikolic, K.; Butini, S.; Marco-Contelles, J. Multitarget Compounds Bearing Tacrine- and Donepezil-like Structural and Functional Motifs for the Potential Treatment of Alzheimer's Disease. *Prog. Neurobiol.* **2017**, *151*, 4–34. https://doi.org/10.1016/j.pneurobio.2015.12.003.

(13) Tomassoli, I.; Herlem, G.; Picaud, F.; **Benchekroun, M.**; Bautista-Aguilera, O. M.; Luzet, V.; Jimeno, M.-L.; Gharbi, T.; Refouvelet, B.; Ismaili, L. Synthesis, Regioselectivity, and DFT Analysis of New Antioxidant Pyrazolo[4,3-c]Quinoline-3,4-Diones. *Monatshefte Für Chem. - Chem. Mon.* **2016**, *147* (6), 1069–1079. https://doi.org/10.1007/s00706-016-1660-7.

(14) Dgachi, Y.; Ismaili, L.; Knez, D.; **Benchekroun, M.**; Martin, H.; Szałaj, N.; Wehle, S.; Bautista-Aguilera, O. M.; Luzet, V.; Bonnet, A.; Malawska, B.; Gobec, S.; Chioua, M.; Decker, M.; Chabchoub, F.; Marco-Contelles, J. Synthesis and Biological Assessment of Racemic Benzochromenopyrimidinimines as Antioxidant, Cholinesterase, and Aβ1−42 Aggregation Inhibitors for Alzheimer's Disease Therapy. *ChemMedChem* **2016**, *11* (12), 1318–1327. https://doi.org/10.1002/cmdc.201500539.

(15) Dgachi, Y.; Bautista-Aguilera, O. M.; **Benchekroun, M.**; Martin, H.; Bonet, A.; Knez, D.; Godyń, J.; Malawska, B.; Gobec, S.; Chioua, M.; Janockova, J.; Soukup, O.; Chabchoub, F.; Marco-Contelles, J.; Ismaili, L. Synthesis and Biological Evaluation of Benzochromenopyrimidinones as Cholinesterase Inhibitors and Potent Antioxidant, Non-Hepatotoxic Agents for Alzheimer's Disease. *Molecules* **2016**, *21* (5), 634. https://doi.org/10.3390/molecules21050634.

(16) **Benchekroun, M.**; Romero, A.; Egea, J.; León, R.; Michalska, P.; Buendía, I.; Jimeno, M. L.; Jun, D.; Janockova, J.; Sepsova, V.; Soukup, O.; Bautista-Aguilera, O. M.; Refouvelet, B.; Ouari, O.; Marco-Contelles, J.; Ismaili, L. The Antioxidant Additive Approach for Alzheimer's Disease Therapy: New Ferulic (Lipoic) Acid Plus Melatonin Modified Tacrines as Cholinesterases Inhibitors, Direct Antioxidants, and Nuclear Factor (Erythroid-Derived 2)-Like 2 Activators. *J. Med. Chem.* **2016**, *59* (21), 9967–9973. https://doi.org/10.1021/acs.jmedchem.6b01178.

(17) **Benchekroun, M.**; Ismaili, L.; Pudlo, M.; Luzet, V.; Gharbi, T.; Refouvelet, B.; Marco-Contelles, J. Donepezil–Ferulic Acid Hybrids as Anti-Alzheimer Drugs. *Future Med. Chem.* **2015**, *7* (1), 15–21. https://doi.org/10.4155/fmc.14.148.

(18) **Benchekroun, M.**; Bartolini, M.; Egea, J.; Romero, A.; Soriano, E.; Pudlo, M.; Luzet, V.; Andrisano, V.; Jimeno, M.-L.; López, M. G.; Wehle, S.; Gharbi, T.; Refouvelet, B.; de Andrés, L.; Herrera-Arozamena, C.; Monti, B.; Bolognesi, M. L.; Rodríguez-Franco, M. I.; Decker, M.; Marco-Contelles, J.; Ismaili, L. Novel Tacrine-Grafted Ugi Adducts as Multipotent Anti-Alzheimer Drugs: A Synthetic Renewal in Tacrine–Ferulic Acid Hybrids. *ChemMedChem* **2015**, *10* (3), 523–539. https://doi.org/10.1002/cmdc.201402409.

(19) Barroca-Aubry, N.; **Benchekroun, M.**; Gomes, F.; Bonnaffé, D. P-Methoxybenzyl-N-Phenyl-2,2,2-Trifluoroacetimidate: A Versatile Reagent for Mild Acid Catalyzed Etherification. *Tetrahedron Lett.* **2013**, *54* (37), 5118–5121. https://doi.org/10.1016/j.tetlet.2013.07.066.