Ghrelin Receptor Ligands, from Laboratory to Market

Jean Martinez[1]*

[1]Institut des Biomolécules Max Mousseron (IBMM), UMR 5247, CNRS - Université Montpellier - ENSCM, Faculté de Pharmacie, 15 avenue Charles Flahault, 34093 Montpellier Cedex 5, France
*Jean.martinez@umontpellier.fr

Biography

Jean Martinez received both his PhD in 1972 from the University of Montpellier 2, at the National School of Chemistry and his Dr Sciences Degree in 1976 from the same University, under the supervision of Professor F. Winternitz. The same year, he joined Dr E. Bricas group at Orsay, University of Paris Sud, as a post-doctorate fellow and in 1977 the laboratory of Professor M. Bodanszky at Case Western Reserve University in Cleveland, Ohio, USA, where he stayed till mid 1979.

Jean Martinez is a Full Professor at the University of Montpellier. In 2007, he created the « Institut des Biomolécules Max Mousseron » (IBMM), which he has been the Director until December 2014. He is actually Head of the department of Amino Acids, Peptides and Proteins at IBMM.

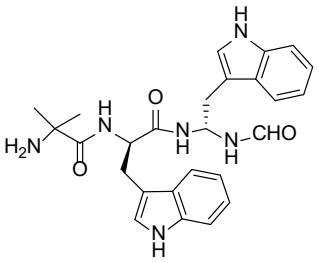
He served the University of Montpellier 1 as a Member of the Scientific Council for 8 years, and as Vice-President for 6 years (2009-2014).

Prof Martinez is recognized for his important contributions, at the interface of chemistry and biology, to the development of methodology in organic and peptide synthesis, design and synthesis of various potent and selective neuropeptide analogues, and biomaterials containing biomolecules.
He has published over 900 original papers, 50 patents, numerous review articles, and he has been editor of several books. In 2012, he was accepted into the « Académie Nationale de Pharmacie », France, and in 2014 into the « Real Academia Nacional de Farmacia », Spain. In 2015, he has been nominated Docteur Honoris causa of the Jagellonian University of Kracow, Poland. He has received various prizes including the Leonidas Zervas Award (Barcelona, Spain 1990), the Silver Medal CNRS (Paris, France 1996), The Labbe Award (Paris, France 1996), The Mentzer Award (Caen, France 1998), the Max Bergmann Medal (Munster, Germany 2004), the Cathay Award (Shanghai, China 2006), the Akabori Award (Tokohama, Japan 2006), the Ehrlich Award (Lyon, France 2011), the Roche « Johannes Meinhofer Award » (Boulder Co, USA 2011), the Léon Velluz Award (Paris, France 2015), the Rudinger Award (Leipzig, Germany 2016). He is « Chevalier dans l'Ordre des Palmes Académiques » (2010), and Chevalier dans l'Ordre de la Légion d'Honneur (2011).

Abstract

The Ghrelin receptor (GHS-R1a for Growth Hormone Secretagogue Receptor type 1a) is a G protein-coupled receptor (GPCR) that mediates in particular ghrelin-induced growth hormone secretion, food intake, and reward-seeking behaviours. Because of its probable involvement in several physiological disorders such as obesity and drugs/alcohol addictions, GHS-R1a represents a major target for the development of therapeutic molecules.

We have developed a series of selective potent Ghrelin receptor ligands [1-5] including agonists, antagonists, partial agonists and inverse agonists. The design, synthesis and pharmacological evaluations of these compounds will be detailed and discussed. Among the ghrelin receptor agonists we have developed in our laboratory, compound JMV1843 showed particular interesting properties. The story of compound JMV1843, an orally active ghrelin agonist that is today commercialized (Macimorelin®, Macrilen®) [1,6] for the diagnosis of adult growth hormone deficiency (AGHD) will be presented.



JMV 1843: Aib-(D)Trp-*g*-(D)Trp-CHO

References:

1. Guerlavais, D. B. et al. *J. Med. Chem.* **2003**, 14, 1191-1203
2. Demange et al., *J. Med. Chem.* **2007**, 50, 1939-1957
3. Moulin et al. *Amino Acids* **2013**, 44, 301-314
4. Damian et al. *Proc. Natl. Acad. Sci. U. S. A.* **2015**, 112, 1601-1606
5. M'Kadmi et al. *J. Biol. Chem.* **2015**, 290, 27021-27039
6. Martinez, J.; Fehrentz, J-A. *Aust. J. Chem.* **2020**, 73, 334-337.