

WG3 GROUP: Progress Report 2010

COST Working Group Meetings

A meeting of WG3 group members was held in Amsterdam (July 5, 2010) “Pharmacological properties of new selective histaminergic compounds targeting the H4 receptor”

A joint WG1-WG4 meeting was held in Durham, UK (13-16 July, 2010) during the 39th EHRS meeting (Progress Report by Paul Chazot)

Organized Meetings

Symposium organized by Paul Chazot and Rob Leurs “Histaminergic system and pain. Therapeutic opportunities for H3 and H4 receptor antagonists”, held during the Forum of European Neuroscience (FENS), Amsterdam, The Netherlands (July 5, 2010)

About 50 people (scientists, researchers, students attended the symposium. Three lectures on H4 receptors were presented (see the attached program) by University and Drug Company Researchers. In particular, Pfizer and Palau Pharma were involved). New people signed up to the COST action

The organizers regret that no EU support was provided.

Lectures at COST Meetings

R Leurs. From fragments to new histamine H4R antagonists. COST workshop: Histamine H4 receptor. Where we are and where we are going...”, Florence January 29-30, 2010

G Coruzzi. Histamine and the stomach: damage or protection? COST workshop: Histamine H4 receptor. Where we are and where we are going...”, Florence January 29-30, 2010

R Leurs. Medicinal Chemistry & receptor modeling. COST Action BM0806 Training School. Durham, UK, July 13, 2010

Publications

Coruzzi G, Leurs R, Stark H, Adami M. Histamine H3 receptors are involved in the protective effect of ghrelin against HCl-induced gastric damage in rats. *Pharmacology* 86: 259-266 (2010)

Coruzzi G, Pozzoli C, Adami M. The role of histamine H4 receptors in the gastrointestinal tract. *Front Biosci (Special Issue)*, in press 2011

Igel P, Dove S, Buschauer A. Histamine H4 Receptor agonists. *Bioorg Med Chem Lett* 20: 7191-7199 (2010)

Lim HD, de Graaf C, Jiang W, Sadek P, McGovern PM, Istyastono EP, Bakker RA, de Esch IJ, Thurmond RL, Leurs R. Molecular determinants of ligand binding to H4R species variants. *Mol Pharmacol* 77: 734-743 (2010)

Lazewska D, Kiec-Kononowicz K. Recent advances in histamine H3 receptor antagonists/inverse agonists. *Exp Opin Ther Pat* 20: 1147-1169 (2010)

Neumann D, Beermann S, Seifert R. Does the histamine H4 receptor have a pro- or anti-inflammatory role in murine bronchial asthma? *Pharmacology* 85: 217-223 (2010)

Smits RA, Adami M, Istyastono EP, Zuiderveld OP, van Dam CM, de Kanter FJ, Jongejan A, Coruzzi G, Leurs R, de Esch IJ. Synthesis and QSAR of quinazoline sulfonamides as highly potent human histamine H4 receptor inverse agonists. *J Med Chem* 25: 2390-2400 (2010)

Presentations at international Meetings

Adami M, Smits R, de Esch IJP, Leurs R, Coruzzi G. Effects of histamine H4 receptor ligands on rodent models of acute inflammation. 39th EHRS meeting, Durham, UK, July 13-16, 2010

Coruzzi G, Adami M, Pozzoli C, Smits R, Leurs R. Effects of histamine H3 and H4 receptor ligands in the rodent gastric mucosa. *Gut* 59 (Suppl III) A331, 2010) (presented at the 18th meeting of the United European Gastroenterology Week, Barcellona, Spain, October 2010)

Coruzzi G, Leurs R, Stark H, Adami M. Involvement of histamine H3 receptors in the gastroprotection induced by ghrelin in the conscious rat. 39th EHRS meeting, Durham, UK, July 13-16, 2010

De Kruijf P, Koelink P, Zheng B, Folkerts G, Leurs R, Chazot P, Lethbridge NL, Kraneveld AD, Smit MJ. Expression profiling of chemotactic receptors in inflammatory diseases. 39th EHRS meeting, Durham, UK, July 13-16, 2010

Geyer R, Igel P, Bernhardt G, Buschauer A. Synthesis and structure-activity relationships of conformationally constrained cyanoguanidines: potent and selective histamine H4 receptor agonists. 39th EHRS meeting, Durham, UK, July 13-16, 2010

Leurs R, Adami M, Smits R, Lim H, Zuiderveld O, de Esch I, Coruzzi G. Fragment optimization leading to H4 receptor ligands with differential pharmacology. 39th EHRS meeting, Durham, UK, July 13-16, 2010

Nijmeijer S, Vischer HF, Chazot P, Smit MJ, Leurs R. Protein fragment complementation, a new way to look at human H4 receptor oligomerization. 39th EHRS meeting, Durham, UK, July 13-16, 2010

Patent Applications

Rob Leurs is a member of the Management board of Griffin Discoveries (a privately owned, research-based drug discovery company) which focuses on the development of drugs targeting the H4R among other G-protein-coupled receptors.

Comments

Research of the WG3 group is focusing on the synthesis of new H4R ligands, molecular pharmacology of the H4 receptor and pharmacological characterization of H4R-mediated effects in *in vivo* models of inflammation. Studies on the affinity of H4R ligands toward H4R species variants will be helpful in the ligand selection for studies in animal models.

“Histaminergic system and pain. Therapeutic opportunities for H3 and H4 receptor antagonists”

(Symposium at FENS Meeting, Amsterdam 2010)

- 1) Passani B, Blandina P. University of Florence, Italy. **Histaminergic system and the CNS**
- 2) Nickolls S. Pfizer Inc, UK. **The effects of histamine H3 and H4 receptor antagonists in preclinical pain models.**
- 3) Alfon J, Sanchez-Gomez S, Cabellos J, Ardanaz N, et al Palau Pharma, Barcelona, Spain. **A novel histamine 4 receptor antagonist for asthma devoid of CNS side effects in rat**