

Recent Advances in Histamine Receptor H₄R Research

BMBS



Participating countries: AT, CH, DE, DK, ES, FI, FR, GR, HU, IE, IL, IT, LT, NL, PL, SE, SI, UK
 Chair of the Action: Ekaterini Tiligada, GR, aityliga@med.uoa.gr
 COST Science Officer: Kalliopi Kostelidou, kkostelidou@cost.esf.org

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Figure 1: H₄R is principally expressed on haematopoietic cells and plays a key role in immune and inflammatory responses



Figure 2: Management Committee members, London (UK) - 17.12.2009

Objectives:

- to create a formal network of European experts with the goal to foster a multi-disciplinary approach to H₄R research
- to focus on the current state of play pertaining to the basic understanding & the huge therapeutic potential of this important new drug target
- to overcome H₄R research fragmentation by enhancing communication, facilitating collaborations & building up strong links between academia, research & industry
- to broaden interdisciplinary training & mobility of young European scientists
- to promote H₄R translational research & to attract industrial partners interested in the commercial exploitation of the results
- to set the standards & to develop a forum for free exchange of ideas & data leading to a template for best practice
- to increase the awareness of the general public & to disseminate the information on H₄R to clinicians, medicines policy makers & health authorities

Working Group 1: Methodological approaches for H₄R systems investigation

- Assessment & validation of methodologies targeting H₄R distribution & characterization (*in vivo*, *in vitro*, *in situ*, *in silico*, molecular, cellular, genomic, transcriptomic studies)
- Development of assays to identify qualitative & quantitative modifications of H₄R expression & distribution in disease states
- Determination of the optimal experimental conditions for the investigation of the mechanisms associated with H₄R functions & interactions in a range of cells & tissues under environments that define physiology & pathophysiology

Working Group 2: (Patho)physiological importance of H₄R systems

- Identification of H₄R isoforms & elucidation of the molecular structure
- Integration & critical evaluation of data, derived mainly from basic research, on the complex H₄R-mediated signals in various cell types & conditions
- Elucidation of the role of the H₄R in models of allergy, inflammation, immune disorders, cancer & other conditions

Working Group 3: Pharmacological properties of new selective H₄R ligands

- Design of selective H₄R ligands using traditional & modern tools for drug development
- Design of H₄R ligands with additional properties (imaging, pharmacological profiling)
- Pharmacological & physicochemical evaluation of new promising drug candidates targeting the H₄R (SAR, dose-response relationships, ADMET properties)

Working Group 4: Therapeutic potential of new H₄R histaminergic compounds

- Set the standards for optimal translational research on H₄R systems
- The H₄R as a target for the treatment of inflammatory diseases, allergy & cancer: comparison with current therapeutic approaches
- Evaluation of current & potential clinical trials of H₄R ligands
- Strategies & economic dimension of any novel therapeutic intervention

Main Achievements:

- Close collaboration with the European Histamine Research Society (EHRS)
- Joint publications & research grant proposals
- Non-COST countries New Zealand & Argentina joined the Action
- European industries *Pfizer* (UK) & *Palau Pharma* (ES) and the SME *Griffin Discoveries* (VU University Amsterdam, NL) are members of the Action
- First H₄R-targeting compounds entered clinical trials
- Mobility & training of young researchers through Short Term Scientific Missions
- Organisation of
 - WG4 Workshop 'BioMedChem on Histamine H₄ Receptor: New Compounds for Translational Steps' Frankfurt, DE (October 2009)
 - WG1/3 Meeting & Symposium 'The histamine H₄ receptor: new multi-use therapeutic target' London, UK (British Pharmacological Society Meeting, December 2009)
 - WG2 Workshop 'Histamine H₄ Receptor: Where we are and where we are going...' Florence, IT (January 2010)
 - Joint Conference with the EHRS, Durham, UK (April 2010)