

Action: BM0806

2009-2013

Recent Advances in Histamine Receptor H₄R Research

Participating countries: AT·CH·CZ·DE·DK·EL·ES·FI·FR·HU·IE·IL·IT·LT·NL·PL·SE·SI·SK·UK

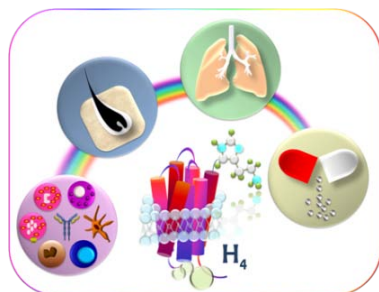
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BMBS



European Cooperation in
Science and Technology

Working Groups

WG1: Methodological approaches for H₄R systems investigation

Assessment and validation of methodologies targeting H₄R expression, distribution and characterization. Determination of the optimal experimental conditions for investigating H₄R functions in various species, cells, tissues and environments.

WG2: (Patho)physiological importance of H₄R systems

Identification of H₄R isoforms and elucidation of the molecular structure. Integration of data on H₄R-mediated signals. Elucidation of the H₄R role in models of allergy, inflammation, immune disorders, cancer & other conditions.

WG3: Pharmacological properties of new selective H₄R ligands

Design of selective H₄R ligands & compounds with additional properties. Pharmacological & physicochemical evaluation of new promising drug candidates targeting the H₄R.

WG4: Therapeutic potential of new H₄R histaminergic compounds

Set the standards for optimal translational research on H₄R systems as therapeutic targets & comparison with current treatments. Evaluation of clinical trials of H₄R ligands. Strategies and economic dimension of any novel therapeutic intervention.

Scientific background

The newly identified H₄R elicits a variety of effects depending on its differential expression, regulation and downstream signalling in various cell types and tissues. Despite the tissue and species differences in H₄R properties and the complex pharmacology of the H₄R ligands, experimental data strongly support the role of the H₄R in inflammation and immunomodulation. Preclinical evidence argues for H₄R therapeutic opportunities in treating inflammatory conditions such as allergies, asthma, dermatitis and possibly itch and pain, while the first H₄R antagonist has already entered clinical trials for allergic respiratory diseases.

Objectives defined in the MoU

The main objective is to foster a multidisciplinary approach to H₄R research and to focus on the current state of play pertaining to the basic understanding & the huge therapeutic potential of this important new drug target. The Action aims to set the standards & to defragment H₄R research; to facilitate training & mobility of young scientists; to promote translational research and collaborations between academia and industry; to increase awareness of health authorities and the general public.

Scientific deliverables obtained due to networking

Roßbach K *et al* (2009) The histamine H₄ receptor as a new target for treatment of canine inflammatory skin disease. *Vet Dermatol* 20:555–561.

Smits RA *et al* (2010) Synthesis and QSAR of quinazoline sulfonamides as highly potent human histamine H₄ receptor inverse agonists. *J Med Chem* 53:2390-400

Tiligada E *et al* (2009) Histamine H₃ and H₄ receptors as novel drug targets. *Expert Opin Investig Drugs* 18:1519-31.

Capacity building due to networking

- Close interdisciplinary networking of partners from academia, research, SMEs & pharmaceutical companies, including members from New Zealand & Argentina → innovative knowledge on H₄R functional expression & significant intellectual property on its biological function, in addition to its role in inflammatory & immune responses → result exploitation & precursors for Grant applications.
- Technology transfer, training and mobility of young scientists through Short Term Scientific Missions.
- Involvement of Early Stage & female Researchers in leading responsibilities.

COST Visibility

- Action's website: ~500 hits/month – total views >13300.
- Initiation of an internet *database of methods and tools* related to H₄R research.
- Strong links with the European Histamine Research Society (EHRS) & close collaboration with EAACI, BPS, FENS, SMEs, pharmaceutical industry & the non-COST countries New Zealand, Argentina and the USA.
- Joint publications, reports & special issues in international scientific journals; meetings organization; research grant proposals.
- The advancement of the first H₄R-targeting compounds to Phase IIa clinical trials supports translational research and the 'bench-to-bedside' concept.
- Training and mobility of young researchers through Short Term Scientific Missions. Award winning ESR presentations and STSMs.
- Participation of Action members in Committees.
- Public lectures to promote COST aims.