

COST ACTION BM0806: RECENT ADVANCES IN HISTAMINE RECEPTOR H4R RESEARCH

Scientific Report – Workshop of Working Group 4

BioMEDCHEM on Histamine H4 Receptor - New Compounds for Translational Steps

JOHANN WOLFGANG GOETHE-UNIVERSITY FRANKFURT AM MAIN, GERMANY

TUESDAY OCTOBER 6 2009

A total of 72 participants, including numerous doctoral and post-doctoral fellows, from 11 different countries attended this inaugural meeting of Working Group 4 (WG4) of the COST Action BM0806. After welcome from Prof Tiligada (COST chair); Prof Schubert-Zsilavecz (Vice-President of the Goethe University) and Prof Stark (Chairman of WG4), the meeting consisting of 8 plenary and 4 selected presentations began.

Prof Tiligada gave an excellent introduction to the field and in particular the role of histamine in inflammation and immunomodulation. Prof Ennis described the presence of H4R on several cell types involved in inflammation and presented data indicating that H4R antagonists may prove useful in the treatment of allergy and asthma – at least in murine models. Dr Kiss described innovative methods to discover new H4 ligands through the use of virtual screening. Prof Buschauer elegantly demonstrated his findings that several of the compounds developed as H2R agonists were also (partial) agonists at the H3R and H4R. This led to the development of a highly selective H4R agonist. Dr Rayan also described a method of data mining – Intelligent Learning Engine Technology – the use of which has led to the development of a focused library for development of H4R antagonists. Dr Smits described the research procedure to optimize the affinity of an H4R antagonist based on an active structure. This approach increased the affinity by 3400 fold. Dr de Graaf utilized *in silico* guided site directed mutagenesis together with quantitative structure-activity relationships to examine the ligand-binding pocket of the H4 receptor. Dr Alfon described an H4R antagonist, developed at his company, which was active in two murine asthma models. Prof Seifert nicely explained his *in vitro* test model for H4 receptors with the co-expression of different G proteins and the synergistic roles of H1 and H4 receptors as potential benefit in asthma therapy. Prof Radeke gave a look into related immunomodulatory roles of sphingolipids and their influence on dendritic cells. With the last lecture of this workshop the vice-chair Dr Chazot showed the species heterogeneity of H4 receptor distribution in different brain regions and their potential impact on the translational research from animal models to human trials.

Taking all together this has been a very stimulating and successful workshop lecturing topical state-of-the-art H4 receptor research with the meeting of different European co-operation partners and the establishment of new co-operations.

M. Ennis, H. Stark (WG 4)