Annotation and integration of endogenous peptide ligands for GPCRs on the IUPHAR Database

Veny Lukito, Joanna Sharman, Helen Benson, Vincent Bombail, Chidochangu Mpamhanga, Adam Pawson, Anthony Harmar. *The University of Edinburgh, University/BHF Centre for Cardiovascular Science, The Queen's Medical Research Institute, Edinburgh, EH16 4TJ, UK*

Bioactive peptides play critical roles in regulating a wide array of biological processes, and are of considerable biological, medical and industrial importance. To date, no single resource provides searchable, easily-navigable details of all the bioactive endogenous peptide ligands that act at G protein-coupled receptors (GPCRs), together with their associated biological activity data. Instead, such information must be sought in abstracts and full-length peer-reviewed articles, and/or obtained by interrogating fragmented public sources which generally contain an overwhelming amount of data that is cumbersome to navigate. IUPHAR-DB (www.iuphar-db.org) is an open access database providing detailed, expert-driven annotation of the pharmacology of drug target systems from peer-reviewed primary literature sources. The database is maintained by a team of curators, with guidance from the International Union of Basic and Clinical Pharmacology (IUPHAR) Committee on Receptor Nomenclature and Drug Classification (NC-IUPHAR) and an international network of ~700 expert contributors. By adopting a formal approach, IUPHAR-DB has now sought to address the gap in information on endogenous peptide ligands in bioactivity databases that focus on pharmacological space. We now provide detailed, manually-curated information on ~500 endogenous peptide ligands that act at members of ~39 GPCR families, presented in a user-friendly format. For each peptide, the human, mouse and rat sequence was compared and species variation annotated. Information on precursor proteins and their encoding genes were collected, and the mature peptides linked to their precursor proteins. A critical component of the annotation process involved identifying bona fide endogenous peptide ligands and curating their sequences and available information on predicted and experimentally confirmed post-translational modifications. The peptides were linked to their receptors and listed in a separate table on the receptor pages; a separate ‘Endogenous peptides’ tab has also been created on the ‘Ligand List’ page of the database. Additional sources of data are provided with direct links to the corresponding pages in relevant public databases including UniProt, HGNC, MGI, and RGD. Future plans include implementing tools for sequence-based searching and clustering of related peptides based on sequence similarity. A joint initiative between NC-IUPHAR and the British Pharmacological Society (BPS) has led to the recent launch of a new open access portal, www.guidetopharmacology.org, which integrates IUPHAR-DB and the BPS Guide to Receptors and Channels (GRAC) and currently documents quantitative pharmacological information on over half of the targets of current licensed drugs.