6 September 2013

Dear Adhesion GPCR researcher

Regarding: **Change in nomenclature for the Adhesion GPCRs**

Currently we are using different names for several of these genes. This has been observed by IUPHAR nomenclature committee (NC-IUPHAR) and they initiated talks about a revised and unified nomenclature of the Adhesion-GPCR class. I was contacted in this context by NC-IUPHAR and together with the leadership of the Adhesion GPCR Consortium (Jörg Hamann, Tobias Langenhan and Gabriela Aust) started working on this. After touching base with colleagues within the Adhesion-GPCR consortium, we suggested minor changes and a harmonization of the current nomenclature in line with the discussion we had on this topic within the Adhesion GPCR Consortium last year. The NC-IUPHAR committee, however, responded that we should look into a unified nomenclature for the entire family that has worked well for, for example, the Frizzled family of GPCR.

We were all reluctant in the beginning as this is a painful operation. However, after discussing the alternatives, we eventually came to the conclusion that in the long run it would be advantageous to have a unified nomenclature and that it is better to do this sooner than later. One large advantage is that this family of proteins will have a unique and clearly identifiable symbol that is in line with common structural and functional features. Moreover, a nomenclature allowing clear designation of subfamilies and subtypes therein would be very useful for all the work that is ahead in naming orthologues and paralogues in a number of species. This is particularly important as several of the branches of Adhesion GPCRs are ancient in evolutionary terms and there are several additional subtypes, not found in humans, that need naming.

Naming by NC-IUPHAR usually takes consideration of the ligands that interact with the receptors. It is however clear to all of us in this case that nomenclature based on ligands will not be easily established for this family for long time ahead as several receptors are likely to bind many different ligands and classical ligand-receptor terms do not always apply.

We have thus worked up a proposal (see enclosed) after testing several both shorter and longer alternatives against other names in the literature/databases during the summer time. The core abbreviation is suggested to be the first three letters in the common Adhesion term and then a G for the G protein-coupled receptor, ie ADHG. Then the nine main families have a number 1-9 and then each subtype is named A, B and C etc. We have not included R in the gene name based on advise from the NC-IUPHAR but receptor or R can be added in text when addressing the receptor protein.

We fully understand some may think this is confusing/unnecessary and there may be sentimental values towards the old names. My team worked for example hard in close relationship with HUGO nomenclature committee (HGNC) to name 14 of the

Adhesion GPCRs, resulting in the GPRXXX names. It is important, however, to acknowledge that the old name will be used for considerable time. We recommend to write in the following way (using a sentence from the review from our last workshop): "CD97 (ADHG2A) interacts, through different regions in its extracellular subunit, with at least four other molecules.....". Or the other way around "ADHG2A (CD97)" as the new names will get acceptance. It would be very important to use both old and new names in the abstracts of all papers for considerable time to allow crosslinking the old and new designations.

Our current plan is to bring this proposal up at next NC-IUPHAR meeting in October (by me and Jörg Hamann) and if NC-IUPHAR accepts the proposal, it will be forwarded to the NC-IUPHAR member representative at HGNC for insertion in the databases as the official names.

We welcome comments and will respond to all requests for further clarification and the rationale of doing this now. This process has not been easy for us, and we do not expect it to be easier for you either but we ask for your consideration of the matter and a balanced evaluation of advantages versus drawbacks of the nomenclature revision. To aid in this process, we provide some talking points that we feel carry the positive impact of a revised nomenclature would generate:

- identification of any Adhesion GPCR homolog belonging to the same receptor/protein class through the prefix ADHG
- Homologs/subtypes within a family are clearly associated by the family number ADHGx
- phylogenetic relationships between Adhesion GPCR homologs are visible through closer family numbers

Best regards,

Helgi Schiöth, member of the board of the Adhesion GPCR Consortium and corresponding member of NC-IUPHAR.

Helgi B. Schiöth
Professor in Pharmacology
Head, Unit of Functional Pharmacology
Dept. of Neuroscience, Uppsala University
Box 593, Husargatan 3
751 24 Uppsala
Sweden

Fax: +46 18 511540
Tel: +46 18 4714160
Email: helgis@bmc.uu.se

PS: After further extensive discussion – both within the AGC and with IUPHAR – the core abbreviation suggested now is ADGR for Adhesion G protein-coupled receptor (Jörg Hamann – 2 February 2014).