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International Union of Pharmacology: Approaches to the Nomenclature of Voltage-Gated Ion Channels

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This issue of Pharmacological Reviews includes a new venture in the collaboration between the International Union of Pharmacology (IUPHAR) and the American Society for Pharmacology and Experimental Therapeutics (ASPET), in that a new classification of voltage-gated ion channels is outlined in this issue of *Pharmacological Reviews*, which resolves much confusion in channel nomenclature. With approximately 140 related members, the family of voltage-gated ion channels and their structural relatives comprise one of the largest families of signal transduction proteins in the human genome. There has been a need for rationalization of the classification of the voltage-gated ion channels for some time, which has grown more acute as new families and family members have been added without systematic nomenclature or classification to guide authors in the field. The schemes presented here represent the work of several subcommittees, coordinated by W.A. Catterall, which produced the IUPHAR Compendium of Voltage-Gated Ion Channels (Catterall et al., 2002). The classifications of sodium (Na_V 1.1–1.9; Goldin et al., 2000) and calcium channels (Ca_V 1.1–1.4, Ca_V 2.1–2.3, Ca_V 3.1–3.3; Ertel et al., 2000) follow the scheme previously advanced for voltage-gated potassium channels (K_v) by Chandy and Gutman (1993). Chandy, Gutman, and several subcommittees organized by them have revised and extended this classification of potassium channels, including calcium-activated potassium channels (K_{Ca}), inwardly rectifying potassium channels (K_{ir}), and two-pore potassium channels (K_{2P}). A classification and nomenclature of the cyclic nucleotide-modulated channels, including both cyclic nucleotide-gated channels (CNG) and hyperpolarization-activated cyclic nucleotide-modulated channels (HCN), have been developed by a subcommittee chaired by F. Hofmann. Three subfamilies of the transient receptor potential (TRP) channels have been classified using the same general guidelines, with different alphanumeric designations appropriate for this protein family (TRPC, TRPV, and TRPM) by a subcommittee chaired by D. Clapham.

The subcommittees also produced data tables for each channel molecule, listing the molecular and genetic information, electrophysiological properties, channel distribution, pathophysiology, and pharmacology. However, these data tables are too voluminous for paper publication, and will benefit from regular updating, which is impossible in paper format. To address this problem, the nomenclature committee of IUPHAR (NC-IUPHAR), in conjunction with the European Bioinformatics Institute (EBI), has created two web sites, one for the voltage-gated ion channel classification (http://www.iuphar-db.org/iuphar-ic) and the other for receptor classification (http://www.iuphar-db.org/iuphar-rd), where the chapters of classification and their supporting data tables are freely available. The IUPHAR receptor database is a fully interactive database, whereas, for the present, the IUPHAR ion channel database is composed of downloadable pdf files. Development of an interactive format for the ion channel database is in progress. The literature citation of the voltage-gated ion channel database will be via reference to the summary articles in *Pharmacological Reviews*.

In this way IUPHAR extends its alliance with *Pharmacological Reviews*, publishing reviews and updates of classification and nomenclature, but keeps a freely addressable web site up to date as well. NC-IUPHAR will thus become much more proactive, listing many of the receptors and other drug targets in the human genome and curating the functional data. This is only possible with the help of multiple subcommittees, where motivated members of the scientific community are encouraged to enlist in the task of functionally annotating the receptor and ion channel sequences in the human genome. The authors of this Introduction thank their many colleagues who have served with insight and dedication on subcommittees to develop the

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classifications and nomenclatures of ion channels summarized in the articles that follow.

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