

UC Irvine

UC Irvine Previously Published Works

Title

The Concise Guide to PHARMACOLOGY 2015/16: Overview

Permalink

<https://escholarship.org/uc/item/0b61k3qv>

Journal

British Journal of Pharmacology, 172(24)

ISSN

0007-1188

Authors

Alexander, Stephen PH

Kelly, Eamonn

Marrion, Neil

et al.

Publication Date

2015-12-01

DOI

10.1111/bph.13347

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at

<https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

THE CONCISE GUIDE TO PHARMACOLOGY 2015/16: Overview

Stephen PH Alexander¹, Eamonn Kelly², Neil Marrion², John A Peters³, Helen E Benson⁴, Elena Faccenda⁴, Adam J Pawson⁴, Joanna L Sharman⁴, Christopher Southan⁴, O Peter Buneman⁵, William A Catterall⁶, John A Cidlowski⁷, Anthony P Davenport⁸, Dorian Fabbro⁹, Grace Fan¹⁰, John C McGrath¹¹, Michael Spedding¹², Jamie A Davies⁴ and CGTP Collaborators

¹School of Biomedical Sciences, University of Nottingham Medical School, Nottingham, NG7 2UH, UK

²School of Physiology and Pharmacology, University of Bristol, Bristol, BS8 1TD, UK

³Neuroscience Division, Medical Education Institute, Ninewells Hospital and Medical School, University of Dundee, Dundee, DD1 9SY, UK

⁴Centre for Integrative Physiology, University of Edinburgh, Edinburgh, EH8 9XD, UK

⁵Laboratory for Foundations of Computer Science, School of Informatics, University of Edinburgh, Edinburgh, EH8 9LE, United Kingdom

⁶Department of Pharmacology, University of Washington, Seattle, WA 98195-7280, USA

⁷National Institute of Environmental Health Sciences, National Institutes of Health, Department of Health and Human Services, Research Triangle Park, NC 27709, USA

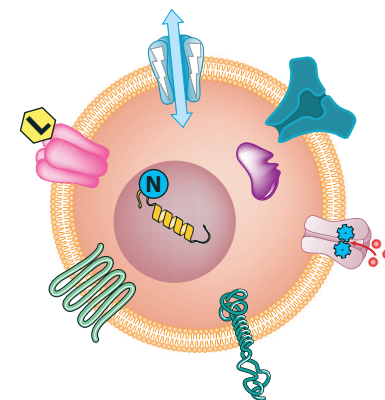
⁸Clinical Pharmacology Unit, University of Cambridge, Cambridge, CB2 0QQ, UK

⁹PIQUR Therapeutics, Basel 4057, Switzerland

¹⁰The Agnes Irwin School, Rosemont, Pennsylvania, USA

¹¹School of Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK

¹²Spedding Research Solutions SARL, Le Vésinet 78110, France



Abstract

The Concise Guide to PHARMACOLOGY 2015/16 provides concise overviews of the key properties of over 1750 human drug targets with their pharmacology, plus links to an open access knowledgebase of drug targets and their ligands (www.guidetopharmacology.org), which provides more detailed views of target and ligand properties. The full contents can be found at <http://onlinelibrary.wiley.com/doi/10.1111/bph.13347/full>. This compilation of the major pharmacological targets is divided into eight areas of focus: G protein-coupled receptors, ligand-gated ion channels, voltage-gated ion channels, other ion channels, nuclear hormone receptors, catalytic receptors, enzymes and transporters. These are presented with nomenclature guidance and summary information on the best available pharmacological tools, alongside key references and suggestions for further reading. The Concise Guide is published in landscape format in order to facilitate comparison of related targets. It is a condensed version of material contemporary to late 2015, which is presented in greater detail and constantly updated on the website www.guidetopharmacology.org, superseding data presented in the previous Guides to Receptors & Channels and the Concise Guide to PHARMACOLOGY 2013/14. It is produced in conjunction with NC-IUPHAR and provides the official IUPHAR classification and nomenclature for human drug targets, where appropriate. It consolidates information previously curated and displayed separately in IUPHAR-DB and GRAC and provides a permanent, citable, point-in-time record that will survive database updates.

Table of contents

5729 Overview

5734 Other Protein Targets

5734 Adiponectin receptors

5735 Blood coagulation components

5735 Non-enzymatic BRD containing proteins

5736 Carrier proteins

5737 CD molecules

5738 Methyllysine reader proteins

5739 Cytokines and growth factors

5739 Fatty acid-binding proteins

5741 Sigma receptors

5742 Tubulins

5744 G protein-coupled receptors

5746 Orphan and other 7TM receptors

5746 Class A Orphans

5756 Class C Orphans

5756 Taste 1 receptors

5757 Taste 2 receptors

5758 Other 7TM proteins

5759 5-Hydroxytryptamine receptors

5764 Acetylcholine receptors (muscarinic)

5766 Adenosine receptors

5768 Adhesion Class GPCRs

5770 Adrenoceptors

5774 Angiotensin receptors

5775 Apelin receptor

Searchable database: <http://www.guidetopharmacology.org/index.jsp>

Full Contents of ConciseGuide: <http://onlinelibrary.wiley.com/doi/10.1111/bph.13347/full>

Overview 5729

- 5777 Bile acid receptor
 5778 Bombesin receptors
 5780 Bradykinin receptors
 5781 Calcitonin receptors
 5783 Calcium-sensing receptors
 5784 Cannabinoid receptors
 5785 Chemerin receptor
 5785 Chemokine receptors
 5791 Cholecystokinin receptors
 5792 Class Frizzled GPCRs
 5793 Complement peptide receptors
 5795 Corticotropin-releasing factor receptors
 5796 Dopamine receptors
 5798 Endothelin receptors
 5799 G protein-coupled estrogen receptor
 5800 Formylpeptide receptors
 5801 Free fatty acid receptors
 5803 GABAB receptors
 5805 Galanin receptors
 5806 Ghrelin receptor
 5807 Glucagon receptor family
 5809 Glycoprotein hormone receptors
 5810 Gonadotrophin-releasing hormone receptors
 5811 GPR18, GPR55 and GPR119
 5812 Histamine receptors
 5814 Hydroxycarboxylic acid receptors
 5815 Kisspeptin receptor
 5816 Leukotriene receptors
 5818 Lysophospholipid (LPA) receptors
 5819 Lysophospholipid (SIP) receptors
 5820 Melanin-concentrating hormone receptors
 5821 Melanocortin receptors
 5822 Melatonin receptors
 5823 Metabotropic glutamate receptors
 5826 Motilin receptor
 5827 Neuromedin U receptors
 5828 Neuropeptide FF/neuropeptide AF receptors
 5829 Neuropeptide S receptor
 5828 Neuropeptide W/neuropeptide B receptors
 5830 Neuropeptide Y receptors
 5832 Neurotensin receptors
 5833 Opioid receptors
 5835 Orexin receptors
 5836 Oxoglutarate receptor
 5836 P2Y receptors
 5838 Parathyroid hormone receptors
 5839 Platelet-activating factor receptor
 5840 Prokineticin receptors
 5841 Prolactin-releasing peptide receptor
 5842 Prostanoid receptors
- 5844 Proteinase-activated receptors
 5846 QRF1 receptor
 5846 Relaxin family peptide receptors
 5848 Somatostatin receptors
 5850 Succinate receptor
 5850 Tachykinin receptors
 5852 Thyrotropin-releasing hormone receptors
 5852 Trace amine receptor
 5854 Urotensin receptor
 5854 Vasopressin and oxytocin receptors
 5856 VIP and PACAP receptors
- 5870 Ligand-Gated Ion Channels**
 5871 5-HT₃ receptors
 5873 Acid-sensing (proton-gated) ion channels (ASICs)
 5875 Epithelial sodium channels (ENaC)
 5877 GABA_A receptors
 5882 Glycine receptors
 5885 Ionotropic glutamate receptors
 5891 IP₃ receptor
 5891 Nicotinic acetylcholine receptors
 5896 P2X receptors
 5898 Ryanodine receptor
 5900 ZAC
- 5904 Voltage-gated ion channels**
 5905 CatSper and Two-Pore channels
 5907 Cyclic nucleotide-regulated channels
 5909 Potassium channels
 5910 Calcium-activated potassium channels
 5912 Inwardly rectifying potassium channels
 5915 Two-P potassium channels
 5917 Voltage-gated potassium channels
 5920 Transient Receptor Potential channels
 5934 Voltage-gated calcium channels
 5936 Voltage-gated proton channel
 5937 Voltage-gated sodium channels
- 5942 Other ion channels**
 5943 Aquaporins
 5944 Chloride channels
 5944 CIC family
 5947 CFTR
 5948 Calcium activated chloride channel
 5949 Maxi chloride channel
 5950 Volume regulated chloride channels
 5952 Connexins and Pannexins
 5954 Sodium leak channel, non-selective
- 5956 Nuclear hormone receptors**
 5958 1A. Thyroid hormone receptors
 5959 1B. Retinoic acid receptors
 5960 1C. Peroxisome proliferator-activated receptors
 5961 1D. Rev-Erb receptors
 5962 1F. Retinoic acid-related orphans
 5963 1H. Liver X receptor-like receptors
 5964 1I. Vitamin D receptor-like receptors
 5965 2A. Hepatocyte nuclear factor-4 receptors
 5966 2B. Retinoid X receptors
 5967 2C. Testicular receptors
 5968 2E. Tailless-like receptors
 5969 2F. COUP-TF-like receptors
 5970 3B. Estrogen-related receptors
 5971 4A. Nerve growth factor IB-like receptors
 5972 5A. Fushi tarazu F1-like receptors
 5973 6A. Germ cell nuclear factor receptors
 5974 0B. DAX-like receptors
 5975 Steroid hormone receptors
 5975 3A. Estrogen receptors
 5976 3C. 3-Ketosteroid receptors
- 5979 Catalytic receptors**
 5981 Cytokine receptor family
 5981 IL-2 receptor family
 5983 IL-3 receptor family
 5983 IL-6 receptor family
 5985 IL-12 receptor family
 5985 Prolactin receptor family
 5986 Interferon receptor family
 5987 IL-10 receptor family
 5988 Immunoglobulin-like family of IL-1 receptors
 5989 IL-17 receptor family
 5990 GDNF receptor family
 5991 Integrins
 5994 Natriuretic peptide receptor family
 5996 Pattern recognition receptors
 5996 Toll-like receptor family
 5997 NOD-like receptor family
 5999 Receptor serine/threonine kinase (RSTK) family
 6000 Type I receptor serine/threonine kinases
 6001 Type II receptor serine/threonine kinases
 6001 Type III receptor serine/threonine kinases
 6002 RSTK functional heteromers
 6003 Receptor tyrosine kinases
 6004 Type I RTKs: ErbB (epidermal growth factor) receptor family
 6005 Type II RTKs: Insulin receptor family
 6005 Type III RTKs: PDGFR, CSFR, Kit, FLT3 receptor family
 6007 Type IV RTKs: VEGF (vascular endothelial growth factor)

receptor family	6040 M19: Membrane dipeptidase	6079 Lipoxygenases
6008 Type V RTKs: FGF (fibroblast growth factor) receptor family	6040 S1: Chymotrypsin	6080 Leukotriene and lipoxin metabolism
6008 Type VI RTKs: PTK7/CCK4	6041 T1: Proteasome	6081 GABA turnover
6009 Type VII RTKs: Neurotrophin receptor/Trk family	6042 S8: Subtilisin	6082 Glycerophospholipid turnover
6010 Type VIII RTKs: ROR family	6042 S9: Prolyl oligopeptidase	6082 Phosphatidylinositol kinases
6010 Type IX RTKs: MuSK	6042 Acetylcholine turnover	6083 1-phosphatidylinositol 4-kinase family
6010 Type X RTKs: HGF (hepatocyte growth factor) receptor family	6044 Adenosine turnover	6083 Phosphatidylinositol-4-phosphate 3-kinase family
6011 Type XI RTKs: TAM (TYRO3-, AXL- and MER-TK) receptor family	6045 Amino acid hydroxylases	6084 Phosphatidylinositol 3-kinase family
6012 Type XII RTKs: TIE family of angiopoietin receptors	6046 L-Arginine turnover	6084 Phosphatidylinositol-4,5-bisphosphate 3-kinase family
6012 Type XIII RTKs: Ephrin receptor family	6047 Arginase	6085 1-phosphatidylinositol-3-phosphate 5-kinase family
6013 Type XIV RTKs: RET	6047 Arginine:glycine amidinotransferase	6085 Type I PIP kinases (1-phosphatidylinositol-4-phosphate 5-kinase family)
6014 Type XV RTKs: RYK	6047 Dimethylarginine dimethylaminohydrolases	6086 Type II PIP kinases (1-phosphatidylinositol-5-phosphate 4-kinase family)
6014 Type XVI RTKs: DDR (collagen receptor) family	6048 Nitric oxide synthases	6087 Phosphoinositide-specific phospholipase C
6015 Type XVII RTKs: ROS receptors	6048 Carboxylases and decarboxylases	6088 Phospholipase A ₂
6015 Type XVIII RTKs: LMR family	6049 Carboxylases	6089 Phosphatidylcholine-specific phospholipase D
6016 Type XIX RTKs: Leukocyte tyrosine kinase (LTK) receptor family	6050 Decarboxylases	6090 Lipid phosphate phosphatases
6016 Type XX RTKs: STYK1	6052 Catecholamine turnover	6091 Haem oxygenase
6017 Receptor tyrosine phosphatases (RTP)	6055 Ceramide turnover	6092 Hydrogen sulphide synthesis
6018 Tumour necrosis factor (TNF) receptor family	6055 Serine palmitoyltransferase	6093 Hydrolases
	6056 Ceramide synthase	6093 Inositol phosphate turnover
6024 Enzymes	6057 Sphingolipid Δ^4 -desaturase	6094 Inositol 1,4,5-trisphosphate 3-kinases
6028 Protein Kinases (EC 2.7.x.x)	6058 Sphingomyelin synthase	6094 Inositol polyphosphate phosphatases
6028 Rho kinase	6058 Sphingomyelin phosphodiesterase	6094 Inositol monophosphatase
6029 Protein kinase C (PKC)	6059 Neutral sphingomyelinase coupling factors	6095 Lanosterol biosynthesis pathway
6029 Alpha subfamily	6059 Ceramide glucosyltransferase	6097 Nucleoside synthesis and metabolism
6029 Delta subfamily	6060 Acid ceramidase	6099 Sphingosine 1-phosphate turnover
6030 Eta subfamily	6060 Neutral ceramidases	6100 Sphingosine kinase
6030 FRAP subfamily	6061 Alkaline ceramidases	6100 Sphingosine 1-phosphate phosphatase
6031 CDK4 subfamily	6061 Ceramide kinase	6101 Sphingosine 1-phosphate lyase
6031 GSK subfamily	6062 Chromatin modifying enzymes	6101 Thyroid hormone turnover
6032 Polo-like kinase (PLK) family	6062 2.1.1.- Protein arginine N-methyltransferases	6103 1.14.11.29 2-oxoglutarate oxygenases
6032 STE7 family	6062 3.5.1.- Histone deacetylases (HDACs)	6103 2.4.2.30 poly(ADP-ribose)polymerases
6033 Abl family	6063 Cyclic nucleotide turnover	6104 2.5.1.58 Protein farnesyltransferase
6033 Ack family	6063 Adenylyl cyclases	6104 3.5.3.15 Peptidyl arginine deiminases (PADI)
6034 Janus kinase (JakA) family	6064 Soluble guanylyl cyclase	6104 RAS subfamily
6034 Src family	6065 Exchange protein activated by cyclic AMP (Epac)	6105 4.2.1.1 Carbonate dehydratases
6035 Tec family	6066 Phosphodiesterases, 3',5'-cyclic nucleotide	6105 5.99.1.2 DNA Topoisomerases
6035 RAF family	6069 Cytochrome P450	
6036 Peptidases and proteinases	6069 CYP1 family	6110 Transporters
6036 A1: Pepsin	6070 CYP2 family	6113 ATP-binding cassette transporter family
6037 A22: Presenilin	6070 CYP3 family	6113 ABCA subfamily
6037 C14: Caspase	6071 CYP4 family	6115 ABCB subfamily
6037 M1: Aminopeptidase N	6072 CYP5, CYP7 and CYP8 families	6116 ABCC subfamily
6038 M2: Angiotensin-converting (ACE and ACE2)	6072 CYP11, CYP17, CYP19, CYP20 and CYP21 families	6117 ABCD subfamily of peroxisomal ABC transporters
6038 M10: Matrix metalloproteinase	6073 CYP24, CYP26 and CYP27 families	6118 ABCG subfamily
6039 M12: Astacin/Adamalysin	6074 CYP39, CYP46 and CYP51 families	6119 F-type and V-type ATPases
6039 M28: Aminopeptidase Y	6075 Endocannabinoid turnover	6119 F-type ATPase
	6076 Eicosanoid turnover	6120 V-type ATPase
	6077 Cyclooxygenase	
	6077 Prostaglandin synthases	

6120	P-type ATPases	6145	SLC10 family of sodium-bile acid co-transporters	6172	SLC27 family of fatty acid transporters
6121	Na ⁺ /K ⁺ -ATPases	6147	SLC11 family of proton-coupled metal ion transporters	6173	SLC28 and SLC29 families of nucleoside transporters
6121	Ca ²⁺ -ATPases	6148	SLC12 family of cation-coupled chloride transporters	6173	SLC28 family
6122	H ⁺ /K ⁺ -ATPases	6149	SLC13 family of sodium-dependent sulphate/carboxylate transporters	6174	SLC29 family
6122	Cu ⁺ -ATPases	6150	SLC14 family of facilitative urea transporters	6176	SLC30 zinc transporter family
6122	Phospholipid-transporting ATPases	6151	SLC15 family of peptide transporters	6176	SLC31 family of copper transporters
6123	Major facilitator superfamily (MFS) of transporters	6152	SLC16 family of monocarboxylate transporters	6177	SLC32 vesicular inhibitory amino acid transporter
6123	SLC superfamily of solute carriers	6154	SLC17 phosphate and organic anion transporter family	6178	SLC33 acetylCoA transporter
6124	SLC1 family of amino acid transporters	6154	Type 1 sodium-phosphate co-transporters	6179	SLC34 family of sodium phosphate co-transporters
6124	Glutamate transporter subfamily	6155	Sialic acid transporter	6180	SLC35 family of nucleotide sugar transporters
6126	Alanine/serine/cysteine transporter subfamily	6155	Vesicular glutamate transporters (VGLUTs)	6181	SLC36 family of proton-coupled amino acid transporters
6127	SLC2 family of hexose and sugar alcohol	6156	Vesicular nucleotide transporter	6182	SLC37 family of phosphosugar/phosphate exchangers
6127	Class I transporters	6156	SLC18 family of vesicular amine transporters	6182	SLC38 family of sodium-dependent neutral amino acid transporters
6128	Class II transporters	6158	SLC19 family of vitamin transporters	6183	System A-like transporters
6129	Proton-coupled inositol transporter	6159	SLC20 family of sodium-dependent phosphate transporters	6183	System N-like transporters
6129	SLC3 and SLC7 families of heteromeric amino acid transporters (HATs)	6160	SLC22 family of organic cation and anion transporters	6184	Orphan SLC38 transporters
6130	SLC3 family	6160	Organic cation transporters (OCT)	6185	SLC39 family of metal ion transporters
6130	SLC7 family	6161	Organic zwitterions/cation transporters (OCTN)	6186	SLC40 iron transporter
6131	SLC4 family of bicarbonate transporters	6162	Organic anion transporters (OATs)	6187	SLC41 family of divalent cation transporters
6132	Anion exchangers	6163	Urate transporter	6187	SLC42 family of Rhesus glycoprotein ammonium transporters
6132	Sodium-dependent HCO ₃ ⁻ transporters	6163	SLC23 family of ascorbic acid transporters	6188	SLC43 family of large neutral amino acid transporters
6133	SLC5 family of sodium-dependent glucose transporters	6164	SLC24 family of sodium/potassium/calcium exchangers	6189	SLC44 choline transporter-like family
6134	Hexose transporter family	6165	SLC25 family of mitochondrial transporters	6190	SLC45 family of putative sugar transporters
6135	Choline transporter	6165	Mitochondrial di- and tri-carboxylic acid transporter subfamily	6191	SLC46 family of folate transporters
6136	Sodium iodide symporter, sodium-dependent multivitamin transporter and sodium-coupled monocarboxylate transporters	6166	Mitochondrial amino acid transporter subfamily	6192	SLC47 family of multidrug and toxin extrusion transporters
6137	Sodium <i>myo</i> -inositol cotransporter transporters	6167	Mitochondrial phosphate transporters	6192	SLC48 heme transporter
6138	SLC6 neurotransmitter transporter family	6167	Mitochondrial nucleotide transporter subfamily	6193	SLC49 family of FLVCR-related heme transporters
6138	Monoamine transporter subfamily	6168	Mitochondrial uncoupling proteins	6194	SLC50 sugar transporter
6139	GABA transporter subfamily	6169	Miscellaneous SLC25 mitochondrial transporters	6195	SLC51 family of steroid-derived molecule transporters
6141	Glycine transporter subfamily	6170	SLC26 family of anion exchangers	6195	SLC52 family of riboflavin transporters
6142	Neutral amino acid transporter subfamily	6170	Selective sulphate transporters	6196	SLCO family of organic anion transporting polypeptides
6144	SLC8 family of sodium/calcium exchangers	6170	Chloride/bicarbonate exchangers	6199	Patched family
6145	SLC9 family of sodium/hydrogen exchangers	6171	Anion channels		
		6171	Other SLC26 anion exchangers		

Introduction

In order to allow clarity and consistency in pharmacology, there is a need for a comprehensive organisation and presentation of the targets of drugs. This is the philosophy of the IUPHAR/BPS Guide to PHARMACOLOGY presented on the online free access database (<http://www.guidetopharmacology.org/>). This database is supported by the British Pharmacological Society (BPS), the International Union of Basic and Clinical Pharmacology (IUPHAR), the Wellcome Trust and the University of Edinburgh. Data included in the Guide to PHARMACOLOGY are derived in large part from interactions with the subcommittees of the Nomenclature

Committee of the International Union of Basic and Clinical Pharmacology (NC-IUPHAR). The Editors of the Concise Guide have compiled the individual records, in concert with the team of Curators, drawing on the expert knowledge of these latter subcommittees. The tables allow an indication of the status of the nomenclature for the group of targets listed, usually previously published in Pharmacological Reviews. In the absence of an established subcommittee, advice from several prominent, independent experts has generally been obtained to produce an authoritative consensus on nomenclature, which attempts to fit in within the gen-

eral guidelines from NC-IUPHAR. This current edition, the Concise Guide to PHARMACOLOGY 2015/16, is the latest snapshot of the database in print form, following on from the Concise Guide to PHARMACOLOGY 2013/14. It contains data drawn from the online database as a rapid overview of the major pharmacological targets. Thus, there are fewer targets presented in the Concise Guide (1761) compared to the online database (2761, as of August 2015). The priority for inclusion in the Concise Guide is the presence of quantitative pharmacological data. This means that often orphan family members are not presented in the Con-

cise Guide, although structural information is available on the online database. An expansion in the current version of the Concise Guide is the increased inclusion of approved drugs, which reflects the aim of the online database to reflect the clinical exploitation of human molecular targets. Although many of these agents are much less selective than the tool compounds listed to define individual targets or groups of targets, we have included them for the significant interest associated with their use and mechanisms of action. The emphasis on approved drugs means that the online database has been expanded to include 8024 ligands (as of August 2015), meaning that additional records now appear in the Concise Guide, primarily in the enzymes section. The organisation of the data is tabular (where appropriate) with a standardised format, where possible on a single page, intended to aid understanding of and comparison within a particular target group. The Concise Guide is intended as an initial resource, with links to additional

reviews and resources for greater depth and information. Pharmacological and structural data focus primarily on human gene products, wherever possible, with links to HGNC gene nomenclature and UniProt IDs. In a few cases, where data from human proteins are limited, data from other species are indicated. Pharmacological tools listed are prioritised on the basis of selectivity and availability. That is, agents (agonists, antagonists, inhibitors, activators, etc.) are included where they are both available (by donation or from commercial sources, now or in the near future) AND the most selective. This edition of the Concise Guide is divided into nine sections, which comprise pharmacological targets of similar structure/function. These are G protein-coupled receptors, ligand-gated ion channels, voltage-gated ion channels, other ion channels, catalytic receptors, nuclear hormone receptors, enzymes, transporters and other protein targets. A new aspect of the Concise Guide 2015/16 is that each of these sections contains a

complete listing of the families available for inspection on the online database, identifying those families reported in the Concise Guide by their page numbers. We hope that the Concise Guide will provide for researchers, teachers and students a state-of-the-art source of accurate, curated information on the background to their work that they will use in the Introductions to their Research Papers or Reviews, or in supporting their teaching and studies.

We recommend that any citations to information in the Concise Guide are presented in the following format:

Alexander SPH *et al.* (2015). The Concise Guide to PHARMACOLOGY 2015/16: Overview. *Br J Pharmacol* XXX.

In this overview are listed protein targets of pharmacological interest, which are not G protein-coupled receptors, ligand-gated ion channels, voltage-gated ion channels, ion channels, nuclear hormone receptors, catalytic receptors, transporters or enzymes.

A dedication

This Edition of the Concise Guide to PHARMACOLOGY is dedicated to Tony Harmar (1951–2014). Tony was a friend and colleague, who was involved with IUPHAR for over 15 years and worked on the IUPHAR database for over a decade at Edinburgh, working hard to establish the curators as a team

of highly informed and informative individuals imbued with Tony's passion and dogged determination to focus on high-quality data input, ensuring high-quality data output. With time and the resources of the BPS and Wellcome Trust, combined with the expertise of the NC-IUPHAR committee mem-

bers mentioned above, Tony established the online database at <http://www.guidetopharmacology.org/> as the exceptional resource it is today.

Acknowledgements

We are extremely grateful for the financial contributions from the British Pharmacological Society, the International Union of Basic and Clinical Pharmacology, the Wellcome Trust (099156/Z/12/Z), which support the website and the University of Edinburgh, who host the [guidetopharmacology.org](http://www.guidetopharmacology.org) website. We are also tremendously grateful to the long list of collaborators from NC-IUPHAR subcommittees and beyond, who have assisted in the construction of the Concise Guide to PHARMACOLOGY 2015/16 and the online database www.GuideToPHARMACOLOGY.org

Conflict of interest

The authors state that there are no conflicts of interest to disclose.

© 2015 The Authors. *British Journal of Pharmacology* published by John Wiley & Sons Ltd on behalf of The British Pharmacological Society.

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Other Protein Targets

Family structure

5734	Adiponectin receptors	5739	Fatty acid-binding proteins	–	R4 family
–	B-cell lymphoma 2 (Bcl-2) protein family	–	Heat shock proteins	–	R7 family
5735	Blood coagulation components	–	Immunoglobulins	–	R12 family
–	Bromodomain-containing proteins	–	Inhibitors of apoptosis (IAP) protein family	–	Reticulons
5735	Non-enzymatic BRD containing proteins	–	Kelch-like proteins	–	Ribosomal factors
5736	Carrier proteins	–	Kinesins	5741	Sigma receptors
5737	CD molecules	–	Mitochondrial-associated proteins	5742	Tubulins
–	Chromatin-interacting transcriptional repressors	–	Notch receptors	–	Tumour-associated proteins
5738	Methyllysine reader proteins	–	Pentaxins	–	WD repeat-containing proteins
–	Circadian clock proteins	–	Serum pentaxins		
5739	Cytokines and growth factors	–	Regulators of G protein signaling (RGS) proteins		
–	EF-hand domain containing	–	RZ family		

Adiponectin receptors

Other protein targets → Adiponectin receptors

Overview: Adiponectin receptors (**provisional nomenclature**, [ENSMF00500000270960](#)) respond to the 30 kDa complement-related protein hormone adiponectin (also known as *ADIPOQ*: adipocyte, C1q and collagen domain-containing protein; ACRP30, adipose most abundant gene transcript 1; apM-1; gelatin-binding protein: [Q15848](#)) originally cloned from adipocytes [49]. Although sequence data suggest 7TM domains,

immunological evidence indicates that, contrary to typical 7TM topology, the carboxyl terminus is extracellular, while the amino terminus is intracellular [86]. Signalling through these receptors appears to avoid G proteins. Adiponectin receptors appear rather to stimulate protein phosphorylation via AMP-activated protein kinase and MAP kinase pathways [86], possibly through the protein partner *APPL1* (adaptor protein, phosphotyrosine in-

teraction, PH domain and leucine zipper containing 1, [Q9UKG1](#) [52]). The adiponectin receptors are a class of proteins (along with membrane progesterin receptors), which contain seven sequences of aliphatic amino acids reminiscent of GPCRs, but which are structurally and functionally distinct from that class of receptor.

Nomenclature	Adipo1 receptor	Adipo2 receptor
HGNC, UniProt	<i>ADIPOR1</i> , Q96A54	<i>ADIPOR2</i> , Q86V24
Rank order of potency	globular adiponectin (<i>ADIPOQ</i> , Q15848) > adiponectin (<i>ADIPOQ</i> , Q15848)	globular adiponectin (<i>ADIPOQ</i> , Q15848) = adiponectin (<i>ADIPOQ</i> , Q15848)

Comments: T-Cadherin (*CDH13*, [P55290](#)) has also been suggested to be a receptor for (hexameric) adiponectin [35].

Further Reading

- Buechler C *et al.* (2010) Adiponectin receptor binding proteins—recent advances in elucidating adiponectin signalling pathways. *FEBS Lett.* **584**: 4280-6 [PMID:20875820]
- Dalamaga M *et al.* (2012) The role of adiponectin in cancer: a review of current evidence. *Endocr. Rev.* **33**: 547-94 [PMID:22547160]
- Goldstein BJ *et al.* (2009) Protective vascular and myocardial effects of adiponectin. *Nat Clin Pract Cardiovasc Med* **6**: 27-35 [PMID:19029992]
- Juhl C *et al.* (2012) Molecular tools to characterize adiponectin activity. *Vitam. Horm.* **90**: 31-56 [PMID:23017711]
- Shetty S *et al.* (2009) Adiponectin in health and disease: evaluation of adiponectin-targeted drug development strategies. *Trends Pharmacol. Sci.* **30**: 234-9 [PMID:19359049]
- Sun Y *et al.* (2009) Adiponectin, an unlocking adipocytokine. *Cardiovasc Ther* **27**: 59-75 [PMID:19207481]
- Thundyil J *et al.* (2012) Adiponectin receptor signalling in the brain. *Br. J. Pharmacol.* **165**: 313-27 [PMID:21718299]

Blood coagulation components

Other protein targets → Blood coagulation components

Overview: Coagulation as a patho/physiological process is interpreted as a mechanism for reducing excessive blood loss through the generation of a gel-like clot local to the site of injury. The process involves the activation, adhesion (see [Integrins](#)), degranulation and aggregation of platelets, as well as proteins circulating in the plasma. The coagulation cascade involves multiple proteins being converted to more active forms from less active precursors, typically through proteolysis (see [Proteases](#)). Listed here are the components of the coagulation cascade targeted by agents in current clinical usage.

Nomenclature	coagulation factor V (proaccelerin, labile factor)	coagulation factor VIII, procoagulant component	serpin peptidase inhibitor, clade C (antithrombin), member 1
HGNC, UniProt	F5 , P12259	F8 , P00451	SERPINC1 , P01008
Selective activators	–	–	heparin (pK _d 7.8) [25], fondaparinux (pK _d 7.5) [65], dalteparin [34], danaparoid [15, 58], enoxaparin [17], tinzaparin [19]
Selective antagonists	drotrecogin alfa (Inhibition) [40, 41]	drotrecogin alfa (Inhibition) [40, 41]	–

Further Reading

Astermark J (2015) FVIII inhibitors: pathogenesis and avoidance. *Blood* **125**: 2045-2051 [PMID:25712994]

Non-enzymatic BRD containing proteins

Other protein targets → Bromodomain-containing proteins → Non-enzymatic BRD containing proteins

Overview: bromodomains bind proteins with acetylated lysine residues, such as histones, to regulate gene transcription. Listed herein are examples of bromodomain-containing proteins for which sufficient pharmacology exists.

Nomenclature	bromodomain adjacent to zinc finger domain, 2A	bromodomain adjacent to zinc finger domain, 2B	CREB binding protein	polybromo 1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4 SMARCA4, P51532
HGNC, UniProt	BAZ2A, Q9UIF9	BAZ2B, Q9UIF8	CREBBP, Q92793	PBRM1, Q86U86	
Selective inhibitors	GSK2801 (p <i>K_d</i> 6.6) [73]	GSK2801 (Binding) (p <i>K_d</i> 6.9) [73]	I-CBP112 (p <i>K_d</i> 6.8) [72]	PFI-3 (Binding) (p <i>K_d</i> 7.3) [79]	PFI-3 (Binding) (p <i>K_d</i> 7.1) [79]

Further Reading

- Brand M *et al.* (2015) Small molecule inhibitors of bromodomain-acetyl-lysine interactions. *ACS Chem Biol* **10**:22-39 [PMID:25549280]
- Filippakopoulos P and Knapp S (2014) Targeting bromodomains: epigenetic readers of lysine acetylation. *Nat Rev Drug Discov* **13**: 337-356 [PMID:24751816]
- Gallenkamp D *et al.* (2014) Bromodomains and their pharmacological inhibitors. *ChemMedChem* **9**: 438-464 [PMID:24497428]
- Sanchez R *et al.* (2014) The bromodomain: from epigenome reader to druggable target. *Biochim Biophys Acta* **1839**: 676-685 [PMID:24686119]

Carrier proteins

Other protein targets → [Carrier proteins](#)

Overview: TTR is a homo-tetrameric protein which transports thyroxine in the plasma and cerebrospinal fluid and retinol (vitamin A) in the plasma. Many disease causing mutations in the protein have been reported, many of which cause complex dissociation and protein mis-assembly and deposition of toxic aggregates amyloid fibril formation [66]. These amyloidogenic mutants are linked to the development of pathological amyloidoses, including familial amyloid polyneuropathy (FAP) [1, 13], familial amyloid cardiomyopathy (FAC) [37], amyloidotic vitreous opacities, carpal tunnel syndrome [57] and others. In old age, non-mutated TTR can also form pathological amyloid fibrils [85]. Pharmacological intervention to reduce or prevent TTR dissociation is being pursued as a therapeutic strategy. To date one small molecule kinetic stabilising molecule (tafamidis) has been approved for FAP, and is being evaluated in clinical trials for other TTR amyloidoses.

Nomenclature	transthyretin
Common abbreviation	TTR
HGNC, UniProt	TTR, P02766

CD molecules

Other protein targets → CD molecules

Overview: Cluster of differentiation refers to an attempt to catalogue systematically a series of over 300 cell-surface proteins associated with immunotyping. Many members of the group have identified functions as enzymes (for example, see [CD73 ecto-5'-nucleotidase](#)) or receptors (for example, see [CD41 integrin, alpha 2b subunit](#)). Many CDs are targeted for therapeutic gain using antibodies for the treatment of proliferative disorders. A full listing of all the Clusters of Differentiation is not possible in the Guide to PHARMACOLOGY; listed herein are selected members of the family targeted for therapeutic gain.

Nomenclature	CD2	CD3e molecule, epsilon (CD3-TCR complex)	CD20 (membrane-spanning 4-domains, subfamily A, member 1)	CD33	CD52	CD80	CD86	cytotoxic T-lymphocyte-associated protein 4 (CD152)
Common abbreviation	–	–	–	–	–	–	–	CTLA-4
HGNC, UniProt	CD2 , P06729	CD3E , P07766	MS4A1 , P11836	CD33 , P20138	CD52 , P31358	CD80 , P33681	CD86 , P42081	CTLA4 , P16410
Selective inhibitors	–	–	–	–	–	abatacept [84], belatacept [16]	abatacept [84], belatacept [16]	–
Selective antagonists	alefacept (Inhibition) [56, 89]	–	–	–	–	–	–	–
Antibodies	–	catumaxomab (Binding) [46], muromonab-CD3 (Binding) [24], otelixizumab (Binding) [7]	ofatumumab (Binding) (pK_d 9.9) [47], rituximab (Binding) (pK_d 8.5) [78], ibritumomab tiuxetan (Binding), obinutuzumab (Binding) [2, 68], tositumomab (Binding)	lintuzumab (Binding) (pK_d ~10) [8], gemtuzumab ozogamicin (Binding) [6]	alemtuzumab (Binding) [22]	–	–	ipilimumab (Binding) (pK_d >9) [28], tremelimumab (Binding) (pK_d 8.9) [30]

Nomenclature	programmed cell death 1 (CD279)
Common abbreviation	PD-1
HGNC, UniProt	PDCD1 , Q15116
Antibodies	pembrolizumab (Binding) ($pK_d \sim 10$) [9], nivolumab (Binding) (pK_d 9.1) [29, 42, 43]
Comments	The endogenous ligands for human PD-1 are programmed cell death 1 ligand 1 (PD-L1 <i>aka</i> CD274 (CD274 , Q9NZQ7)) and programmed cell death 1 ligand 2 (PD-L2; PDCD1LG2). These ligands are cell surface peptides, normally involved in immune system regulation. Many types of cancer cells evolve mechanisms to evade control and elimination by the immune system. Such mechanisms can include inhibition of so-called 'immune checkpoints', which would normally be involved in the maintenance of immune homeostasis. An increasingly important area of clinical oncology research is the development of new agents which impede these evasion techniques, thereby switching immune vigilance back on, and effecting immune destruction of cancer cells. Three molecular targets of checkpoint inhibitors which are being extensively pursued are cytotoxic T-lymphocyte antigen 4 (CTLA4), programmed cell death 1 (PD-1), and programmed cell death ligand 1 (PD-L1). Using antibody-based therapies targeting these pathways, clinical responses have been reported in various tumour types, including melanoma, renal cell carcinoma [64] and non-small cell lung cancer [39, 51]. pembrolizumab is the first-in-class, anti-PD-1 antibody to be approved by the US FDA, with ongoing clinical trials for nivolumab (<i>e.g.</i> NCT01673867 , NCT01721746) and pidilizumab (NCT02077959 , NCT01952769).

Methyllysine reader proteins

Other protein targets → [Chromatin-interacting transcriptional repressors](#) → [Methyllysine reader proteins](#)

Overview: Methyllysine reader proteins bind to methylated proteins, such as histones, allowing regulation of gene expression.

Nomenclature	l(3)mbt-like 3 (Drosophila)
HGNC, UniProt	L3MBTL3 , Q96JM7
Selective agonists	UNC1215 (pK_d 6.9) [38]

Further Reading

- Liu K *et al.* (2015) Epigenetic targets and drug discovery Part 2: Histone demethylation and DNA methylation. *Pharmacol Ther* **151**: 121-140 [PMID:25857453]
- Musselman CA *et al.* (2014) Towards understanding methyllysine readout. *Biochim Biophys Acta* **1839**: 686-693 [PMID:24727128]
- Thinnies CC *et al.* (2014) Targeting histone lysine demethylases - progress, challenges, and the future. *Biochim Biophys Acta* **1839**: 1416-1432 [PMID:24859458]

Cytokines and growth factors

Other protein targets → Cytokines and growth factors

Overview: cytokines and growth factors are a group of small proteins released from cells, which act upon the same cell or neighbouring cells, often with a role in immune regulation and/or proliferation. Listed herein are examples of cytokines and growth factors targeted for therapeutic benefit.

Nomenclature	interleukin 1, beta	tumor necrosis factor	vascular endothelial growth factor A
HGNC, UniProt	<i>IL1B</i> , P01584	<i>TNF</i> , P01375	<i>VEGFA</i> , P15692
Antagonists	–	–	affibercept (Inhibition) [10, 11, 82]
Selective antagonists	–	etanercept (Inhibition) [18, 23]	pegaptanib (Inhibition) [26, 61]
Antibodies	gevokizumab (Binding) (pK_d 12.5) [36, 53, 71], canakinumab (Binding) (pK_d 10.5) [27], rilonacept (Binding) [32, 55]	golimumab (Inhibition) (pIC_{50} 10.7) [77], infliximab (Inhibition) (pK_d 8.7) [44], adalimumab (Inhibition) (pK_d >8) [75], certolizumab pegol (Inhibition) [60]	ranibizumab (Inhibition) (pK_d ~9.8) [3], bevacizumab (Inhibition) (pIC_{50} 8–8.3) [3]

Fatty acid-binding proteins

Other protein targets → Fatty acid-binding proteins

Overview: Fatty acid-binding proteins are low molecular weight (100–130 aa) chaperones for long chain fatty acids, fatty acyl CoA esters, eicosanoids, retinols, retinoic acids and related metabolites and are usually regarded as being responsible for allowing the otherwise hydrophobic ligands to be mobile in aqueous media. These binding proteins may perform functions extracellularly (*e.g.* in plasma) or transport these agents; to the nucleus to interact with nuclear receptors (principally PPARs and retinoic acid receptors [76]) or for interaction with metabolic enzymes. Although sequence homology is limited, crystallographic studies suggest conserved 3D structures across the group of binding proteins.

Nomenclature	fatty acid binding protein 1, liver	fatty acid binding protein 2, intestinal	fatty acid binding protein 3, muscle and heart	fatty acid binding protein 4, adipocyte	fatty acid binding protein 5 (psoriasis-associated)
HGNC, UniProt	<i>FABP1</i> , P07148	<i>FABP2</i> , P12104	<i>FABP3</i> , P05413	<i>FABP4</i> , P15090	<i>FABP5</i> , Q01469
Rank order of potency	stearic acid, oleic acid > palmitic acid, linoleic acid > arachidonic acid, α -linolenic acid [69]	stearic acid > palmitic acid, oleic acid > linoleic acid > arachidonic acid, α -linolenic acid [69]	stearic acid, oleic acid, palmitic acid > linoleic acid, α -linolenic acid, arachidonic acid [69]	oleic acid, palmitic acid, stearic acid, linoleic acid > α -linolenic acid, arachidonic acid [69]	–
Comments	A broader substrate specificity than other FABPs, binding two fatty acids per protein [83].	Crystal structure of the rat FABP2 [74].	Crystal structure of the human FABP3 [87].	–	Crystal structure of the human FABP5 [33].

Nomenclature	fatty acid binding protein 6, ileal	fatty acid binding protein 7, brain	peripheral myelin protein 2	fatty acid binding protein 9, testis	fatty acid binding protein 12
HGNC, UniProt	FABP6 , P51161	FABP7 , O15540	PMP2 , P02689	FABP9 , Q0Z7S8	FABP12 , A6NFH5
Comments	Able to transport bile acids [88].	Crystal structure of the human FABP7 [4].	<i>In silico</i> modelling suggests that FABP8 can bind both fatty acids and cholesterol [50].	–	–

Nomenclature	retinol binding protein 1, cellular	retinol binding protein 2, cellular	retinol binding protein 3, interstitial	retinol binding protein 4, plasma	retinol binding protein 5, cellular
HGNC, UniProt	RBP1 , P09455	RBP2 , P50120	RBP3 , P10745	RBP4 , P02753	RBP5 , P82980
Rank order of potency	–	stearic acid > palmitic acid, oleic acid, linoleic acid, α -linolenic acid, arachidonic acid [70]	–	–	–

Nomenclature	retinol binding protein 7, cellular	retinaldehyde binding protein 1	cellular retinoic acid binding protein 1	cellular retinoic acid binding protein 2
HGNC, UniProt	RBP7 , Q96R05	RLBP1 , P12271	CRABP1 , P29762	CRABP2 , P29373
Rank order of potency	–	11- <i>cis</i> -retinal, 11- <i>cis</i> -retinol > 9- <i>cis</i> -retinal, 13- <i>cis</i> -retinal, 13- <i>cis</i> -retinol, all- <i>trans</i> -retinal, retinol [14]	tretinoin > alitretinoin stearic acid > palmitic acid, oleic acid, linoleic acid, α -linolenic acid, arachidonic acid [70]	–

Comments: Although not tested at all FABPs, [BMS309403](#) exhibits high affinity for FABP4 (pIC₅₀ 8.8) compared to FABP3 or FABP5 (pIC₅₀ <6.6) [20, 81]. [HTS01037](#) is reported to interfere with FABP4 action [31]. Multiple pseudogenes for the FABPs have been identified in the human genome.

Further Reading

- Chmurzyńska A. (2006) The multigene family of fatty acid-binding proteins (FABPs): function, structure and polymorphism. *J. Appl. Genet.* **47**: 39-48 [PMID:16424607]
- Furuhashi M *et al.* (2008) Fatty acid-binding proteins: role in metabolic diseases and potential as drug targets. *Nat Rev Drug Discov* **7**: 489-503 [PMID:18511927]
- Kralisch S *et al.* (2013) Adipocyte fatty acid binding protein: a novel adipokine involved in the pathogenesis of metabolic and vascular disease? *Diabetologia* **56**: 10-21 [PMID:23052058]
- Schroeder F *et al.* (2008) Role of fatty acid binding proteins and long chain fatty acids in modulating nuclear receptors and gene transcription. *Lipids* **43**: 1-17 [PMID:17882463]
- Storch J *et al.* (2010) Tissue-specific functions in the fatty acid-binding protein family. *J. Biol. Chem.* **285**: 32679-83 [PMID:20716527]
- Yamamoto T *et al.* (2009) Classification of FABP isoforms and tissues based on quantitative evaluation of transcript levels of these isoforms in various rat tissues. *Biotechnol. Lett.* **31**: 1695-701 [PMID:19565192]

Sigma receptors

Other protein targets → Sigma receptors

Overview: Although termed ‘receptors’, the evidence for coupling through conventional signalling pathways is lacking. Initially described as a subtype of opioid receptors, there is only a modest pharmacological overlap and no structural convergence with the G protein-coupled receptors. A wide range of compounds, ranging from psychoactive agents to antihistamines, have been observed to bind to these sites, which appear to be intracellular.

Nomenclature	sigma non-opioid intracellular receptor 1	$\sigma 2$
HGNC, UniProt	SIGMAR1 , Q99720	–
Agonists	–	PB-28 (pK _i 8.3) [5], 1,3-ditolyguanidine (pK _i 7.4) [45] – Guinea pig
(Sub)family-selective agonists	(RS)-PPCC (pK _i 8.8) [67]	–
Selective agonists	PRE-084 (pIC ₅₀ 7.4) [80], (+)-SK&F10047	–
Antagonists	(-)-pentazocine	SM 21 (pIC ₅₀ 7.2) [48]
Selective antagonists	NE-100 (pIC ₅₀ 8.4) [62], BD-1047 (pIC ₅₀ 7.4) [54]	–
Labelled ligands	[³H]pentazocine (Agonist)	[³H]-di-o-tolyguanidine (Agonist)
Comments	–	There is no molecular correlate of the $\sigma 2$ receptor.

Comments: [\(-\)-pentazocine](#) also shows activity at opioid receptors.

Further Reading

- Dubrovsky B. (2006) Neurosteroids, neuroactive steroids, and symptoms of affective disorders. *Pharmacol. Biochem. Behav.* **84**: 644-55 [PMID:16962651]
- Guitart X *et al.* (2004) Sigma receptors: biology and therapeutic potential. *Psychopharmacology (Berl.)* **174**: 301-19 [PMID:15197533]
- Matsumoto RR *et al.* (2003) Sigma receptors: potential medications development target for anti-cocaine agents. *Eur. J. Pharmacol.* **469**: 1-12 [PMID:12782179]
- de Medina P *et al.* (2011) Importance of cholesterol and oxysterols metabolism in the pharmacology of tamoxifen and other AEBS ligands. *Chem. Phys. Lipids* **164**: 432-7 [PMID:21641337]

Tubulins

Other protein targets → Tubulins

Overview: Tubulins are a family of intracellular proteins most commonly associated with microtubules, part of the cytoskeleton. They are exploited for therapeutic gain in cancer chemotherapy as targets for agents derived from a variety of natural products: taxanes, colchicine and vinca alkaloids. These are thought to act primarily through β -tubulin, thereby interfering with the normal processes of tubulin polymer formation and disassembly.

Nomenclature	tubulin, alpha 1a	tubulin, alpha 4a	tubulin, beta class I	tubulin, beta 3 class III	tubulin, beta 4B class IVb	tubulin, beta 8 class VIII
HGNC, UniProt	TUBA1A , Q71U36	TUBA4A , P68366	TUBB , P07437	TUBB3 , Q13509	TUBB4B , P68371	TUBB8 , Q3ZCM7
Inhibitors	–	–	vinblastine (pIC ₅₀ 9), vincristine	–	–	–
(Sub)family-selective inhibitors	–	–	eribulin (pIC ₅₀ 8.2) [59], paclitaxel (Mitotic cell cycle arrest in A431 cells) (pEC ₅₀ 8.1) [63], colchicine (pIC ₅₀ 8) [12], cabazitaxel, docetaxel, ixabepilone	–	–	–

Further Reading

- Kaur R *et al.* (2014) Recent developments in tubulin polymerization inhibitors: An overview. *Eur J Med Chem* **87**: 89-124 [PMID:25240869]
- Lu Y *et al.* (2012) An overview of tubulin inhibitors that interact with the colchicine binding site. *Pharm. Res.* **29**: 2943-71 [PMID:22814904]
- Perdiz D *et al.* (2011) The ins and outs of tubulin acetylation: more than just a post-translational modification? *Cell. Signal.* **23**: 763-71 [PMID:20940043]
- Schappi JM *et al.* (2014) Tubulin, actin and heterotrimeric G proteins: coordination of signaling and structure. *Biochim. Biophys. Acta* **1838**: 674-81 [PMID:24071592]
- Song Y *et al.* (2015) Post-translational modifications of tubulin: pathways to functional diversity of microtubules. *Trends Cell Biol.* **25**: 125-36 [PMID:25468068]
- Yu I *et al.* (2015) Writing and Reading the Tubulin Code. *J. Biol. Chem.* **290**: 17163-72 [PMID:25957412]

References

1. ANDRADE C. (1952) [12978172]
2. Alduaij W *et al.* (2011) [21378274]
3. Baca M *et al.* (1998) Anti-vegf antibodies. Patent number: WO1998045331. Assignee: Genentech Inc., Priority date: 07/04/1997. Publication date: 15/10/1998.
4. Balendiran GK *et al.* (2000) [10854433]
5. Berardi F *et al.* (1996) [8568804]
6. Bernstein ID. (2000) [10720144]
7. Bolt S *et al.* (1993) [8436176]
8. Caron PC *et al.* (1992) [1458463]
9. Carven GJ *et al.* (2010) Antibodies to human programmed death receptor PD-1. Patent number: US20100266617. Assignee: Organon NV. Priority date: 13/06/2008. Publication date: 21/10/2010.
10. Chang AA *et al.* (2013) [24144450]
11. Chu QS. (2009) [19236257]
12. Cifuentes M *et al.* (2006) [16504507]
13. Coelho T. (1996) [8894411]
14. Crabb JW *et al.* (1998) [9541407]
15. Cziraky MJ *et al.* (1993) [8137606]
16. El-Charabaty E *et al.* (2012) [22992146]
17. Eriksson BI *et al.* (1995) [7667822]
18. Feldman M *et al.* (1998) [9865320]
19. Friedel HA *et al.* (1994) [7528134]
20. Furuhashi M *et al.* (2007) [17554340]
21. Garcia-Calvo M *et al.* (2005) [15928087]
22. Ginaldi L *et al.* (1998) [9593475]
23. Goldenberg MM. (1999) [10090426]
24. Goldstein G. (1987) [3105134]
25. Gotti R *et al.* (2013) [23598032]
26. Gragoudas ES *et al.* (2004) [15625332]
27. Gram H *et al.* (2008) Antibodies to human IL-1 β . Patent number: US7446175. Assignee: Novartis Ag. Priority date: 22/08/2000. Publication date: 04/11/2008.
28. Halk EL *et al.* (2001) Human ctla-4 antibodies and their uses. Patent number: WO2001014424. Assignee: Medarex Inc. Priority date: 24/08/1999. Publication date: 01/03/2001.
29. Hall RD *et al.* (2013) [23302904]
30. Hanson DC *et al.* (2004) Human monoclonal antibodies to CTLA-4. Patent number: US6682736 B1. Assignee: Abgenix, Inc., Pfizer Inc., Priority date: 22/12/1998. Publication date: 27/01/2004.
31. Hertz AV *et al.* (2009) [19754198]
32. Hoffman HM *et al.* (2008) [18668535]
33. Hohoff C *et al.* (1999) [10493790]
34. Holmer E *et al.* (1986) [3744129]
35. Hug C *et al.* (2004) [15210937]
36. Issafras H *et al.* (2014) [24194526]
37. Jacobson DR *et al.* (1997) [9017939]
38. James LI *et al.* (2013) [23292653]
39. Johnson DB *et al.* (2014) [25096781]
40. Kanji S *et al.* (2001) [11714212]
41. Kapur S *et al.* (2001) [11463021]
42. Kline J *et al.* (2010) [21154117]
43. Korman AJ *et al.* (2006) Human monoclonal antibodies to programmed death 1(pd-1) and methods for treating cancer using anti-pd-1 antibodies alone or in combination with other immunotherapeutics. Patent number: WO2006121168. Assignee: Ono Pharmaceutical Co. Priority date: 09/05/2005. Publication date: 02/03/2015.
44. Le J *et al.* (1997) Methods of treating TNF- α -mediated Crohn's disease using chimeric anti-TNF antibodies. Patent number: US5656272. Assignee: New York University Medical Center, Centocor, Inc., Priority date: 18/03/1991. Publication date: 12/08/1997.
45. Lever JR *et al.* (2006) [16463398]
46. Linke R *et al.* (2010) [20190561]
47. Liu Q. (2013) Fully human antibodies against human cd20. Patent number: WO2013007052. Assignee: Qingfa Liu. Priority date: 13/07/2011. Publication date: 17/01/2013.
48. Mach RH *et al.* (1999) [10096443]
49. Maeda K *et al.* (1996) [8619847]
50. Majava V *et al.* (2010) [20421974]
51. Malas S *et al.* (2014) [24969320]
52. Mao X *et al.* (2006) [16622416]
53. Masat L *et al.* (2009) IL-1 β binding antibodies and fragments thereof. Patent number: US7531166. Assignee: Xoma Technology, Ltd. Priority date: 27/02/2015. Publication date: 12/03/2010.
54. Matsumoto RR *et al.* (1995) [8566098]
55. McDermott MF. (2009) [19649332]
56. Mitchell P. (2002) [12089534]
57. Murakami K *et al.* (1999) [10403814]
58. Nakase J *et al.* (2009) [19398784]
59. Narayan S *et al.* (2011) [21324687]
60. Nesbitt A *et al.* (2007) [17636564]
61. Nimjee SM *et al.* (2005) [15660527]
62. Okuyama S *et al.* (1993) [7901723]
63. Ouyang X *et al.* (2006) [16377187]
64. Pal SK *et al.* (2014) [24892254]
65. Paolucci F *et al.* (2002) [12383040]
66. Penchala SC *et al.* (2013) [23716704]
67. Prezzavento O *et al.* (2007) [17328523]
68. Reslan L *et al.* (2013) [23537278]
69. Richieri GV *et al.* (1994) [7929039]
70. Richieri GV *et al.* (2000) [10852718]
71. Roell MK *et al.* (2010) [20410301]
72. SGC. I-CBP112 - a CREBBP/EP300-selective chemical probe. Accessed on 03/03/2015. thesgc.org.
73. SGC. GSK2801: A Selective Chemical Probe for BAZ2B/A bromodomains. Accessed on 03/03/2015. thesgc.org.
74. Sacchetti JC *et al.* (1989) [2671390]
75. Salfeld JG *et al.* (2001) Human antibodies that bind human TNF α . Patent number: US6258562. Assignee: Basf Aktiengesellschaft. Priority date: 09/02/1996. Publication date: 10/07/2001.
76. Schroeder F *et al.* (2008) [17882463]
77. Shealy DJ *et al.* (2010) [20519961]
78. Stein R *et al.* (2004) [15102696]
79. Structural Genomics Consortium. PFI-3: Selective chemical probe for SMARCA bromodomains. Accessed on 10/11/2014. <http://www.thesgc.org>.
80. Su TP *et al.* (1991) [1658302]
81. Sulsky R *et al.* (2007) [17502136]
82. Tang PA *et al.* (2013) [24179482]
83. Thompson J *et al.* (1997) [9054409]
84. Vicente Rabaneda EF *et al.* (2013) [23899231]
85. Westermark P *et al.* (1990) [2320592]
86. Yamauchi T *et al.* (2003) [12802337]
87. Young AC *et al.* (1994) [7922029]
88. Zwicker BL *et al.* (2013) [23603607]