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Enzymes as drug targets: curated pharmacological information in the Guide to PHARMACOLOGY

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Enzymes constitute a significant proportion of the druggable genome. In order to fully exploit their potential as drug targets it is vital that database tools exist to provide easily-navigable access to relevant genetic, biochemical and pharmacological information. The Guide to PHARMACOLOGY portal (http://www.guidetopharmacology.org/, abbreviated as GtoPdb) is an open access, expert-driven resource providing manually curated information on human drug targets and the substances that act on them. Database content has recently been expanded to include information on enzymatic drug targets. We have included the >500 protein kinases constituting the human kinome, 180 peptidases/proteases and >90 chromatin modifying enzymes. For curation of the two latter target families we chose to restrict target inclusion to proteins with published pharmacological data. For each of these three new target groups we have curated quantitative data on their interactions with approved drugs and investigational and research compounds. For each target GtoPdb includes information on enzyme nomenclature, substrates, reactions, cofactors, inhibitors, links to relevant external resources and references, and expert submitted overviews of their functions and (patho)physiology. For the subset of targets with significant clinical importance we are developing detailed expert-curated summaries from the primary literature, covering a wide range of relevant topics. In addition to the chemistry and specialist database links found on our regular ligand pages, approved drug curation includes pharmacological data mapped to primary molecular target(s), clinical use information, approval details, a summary of the drug's molecular mechanism of action (mmoa) and links to external resources (e.g. http://www.drugs.com/, http://www.ema.europa.eu/ema/ and https://www.medicines.org.uk/emc/) which provide extensive additional information for each drug including approved indications, formulation, dosage, pharmacokinetics/pharmacodynamics and details of the marketing authorisation holder. The GtoPdb now includes >1100 distinct enzymes, adding to existing information on >1600 other targets which include receptors, ion channels, transporters and other proteins. Adding these enzyme families marks a significant milestone in our mission to provide expert-curated information for all the human targets of current prescription medicines and prospective targets of novel therapeutics *via* the GtoPd. This is a unique resource which should appeal to scientists from a range of disciplines and aid further exploration of enzymes as drug targets.