

The Functional Therapeutic Chemical Classification System

Samuel Croset^{1,*}, John Overington², Dietrich Rebholz-Schuhmann³

1 Samuel Croset Dept/Program/Center, Institution Name, City, State, Country

2 John Overington Dept/Program/Center, Institution Name, City, State, Country

3 Dietrich Rebholz-Schuhmann Dept/Program/Center, Institution Name, City, State, Country

*** E-mail: Corresponding croset@ebi.ac.uk**

Abstract

The abstract of the paper should be succinct; it must not exceed 300 words. Authors should mention the techniques used without going into methodological detail and should summarize the most important results. While the abstract is conceptually divided into three sections (Background, Methodology/Principal Findings, and Conclusions/Significance), please do not apply these distinct headings to the abstract within the article file. Please do not include any citations and avoid specialist abbreviations.

Author Summary

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Introduction

The introduction [1] should put the focus of the manuscript into a broader context. As you compose the introduction, think of readers who are not experts in this field. Include a brief review of the key literature. If there are relevant controversies or disagreements in the field, they should be mentioned so that a non-expert reader can delve into these issues further. The introduction should conclude with a brief statement of the overall aim of the experiments and a comment about whether that aim was achieved.

Functional Therapeutic Chemical Classification System (FTC) is a taxonomy (ontology) representing the mode of action of approved drugs in the human body. It can be pictured as a toolbox classifying the therapeutic agents based on their functionality in the human body. FTC categories are automatically built based on Gene Ontology terms. FTC categories are also equivalent to arbitrary definitions such as drug that perturbs some (protein that involved-in some (regulation of biological process)). A knowledge base created by integrating the content of DrugBank and some GO annotations assists to automatically assign compounds into FTC categories based on the satisfaction of the definition. The FTC is evaluated against the Anatomical Therapeutic Chemical Classification System by assigning equivalences between classes. The knowledge base can be queried in order to retrieve implicit information about the involvement of approved drugs into biological processes. Drug repurposing hypotheses can be formulated out of the evaluation. The FTC can serve as starting point for analysis or projects requiring a structured vocabulary representing the mode of action. The source code of the FTC as well as the data are publicly available for free to anyone.

The indication of a drug depends on the effects induced by the molecule when administrated in a biological system. For instance, a molecule such as the Ximelagatran is indicated as anticoagulant because it directly inhibits the catalytic activity of the thrombin, enzyme itself involved in the blood coagulation. In order to speak of this therapeutic effect (anticoagulant), people sometimes refer to the **mode of action** of an active compound. Wikipedia gives us the following definition for it: A mode of action describes a functional or anatomical change, at the cellular level, resulting from the exposure of a living organism to a substance.

Characterising the mode of action of drugs is interesting for the following reasons: It is a central link between the molecular structure of a drug and its indication towards a disease. Drugs with similar mode of actions could be used to treat similar conditions. It abstracts away from the chemical structure and allows to reason over the effects of the compound in the body. The mode of action of a drug is a feature against which compounds can be classified. It can capture polypharmacology. Most of the drugs are not magic bullets and produce various side effects. A drug can have several mode of actions, representing the different processes the drug is perturbing directly or indirectly. A representation of the mode of action helps to better understand and analyse the behaviour of an agent in the human body.

Although the **mode of action** is an old and useful notion in the drug discovery community (see number of results for this PubMed search, no resources were previously fully dedicated to it. The aim of the FTC is to fill this gap.

The FTC can be seen as a toolbox designed to fix dysfunctioning biological systems. It features over 20'000 compartments (categories) inside which approved drugs are automatically classified, based on facts from various databases. FTC categories represent the mode of action of compounds in the human system. The resource can be used for various tasks where a structured vocabulary is needed, such as compound annotation, drug repurposing analysis and anything else you can think of!

Results

The results section should provide details of all of the experiments that are required to support the conclusions of the paper. There is no specific word limit for this section, but details of experiments that are peripheral to the main thrust of the article and that detract from the focus of the article should not be included. The section may be divided into subsections, each with a concise subheading. Large datasets, including raw data, should be submitted as supporting files; these are published online alongside the accepted article. The results section should be written in the past tense.

Subsection 1

Subsection 2

Discussion

The discussion should spell out the major conclusions of the work along with some explanation or speculation on the significance of these conclusions. How do the conclusions affect the existing assumptions and models in the field? How can future research build on these observations? What are the key experiments that must be done? The discussion should be concise and tightly argued. The results and discussion may be combined into one section, if desired.

Materials and Methods

This section should provide enough detail for reproduction of the findings. Protocols for new methods should be included, but well-established protocols may simply be referenced. While we do encourage

authors to submit all appendices, detailed protocols, or details of the algorithms for newer or less well-established methods, please do so as Supporting Information files. These are not included in the typeset manuscript, but are downloadable and fully searchable from the HTML version of the article.

Acknowledgments

People who contributed to the work but do not fit the criteria for authors should be listed in the Acknowledgments, along with their contributions. You must also ensure that anyone named in the Acknowledgments agrees to being so named.

Details of the funding sources that have supported the work should be confined to the funding statement provided in the online submission system. Do not include them in the Acknowledgments.

References

1. Krötzsch M, Siman F, Horrocks I (2012) A Description Logic Primer. *Language* abs/1201.4: 1–16.

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Tables

Tables should be included at the end of the manuscript file and cited sequentially in the text. All tables should have a concise title. Footnotes can be used to explain abbreviations. Citations should be indicated using the same style as outlined above. Tables should not occupy more than one printed page; larger tables can be published as online supporting information. Tables must be cell-based; do not use picture elements, text boxes, tabs, or returns in tables. Please ensure that all tables conform to our Guidelines for Figure and Table Preparation when preparing them.