Protein Functional Families to characterise drug-target interactions.

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The quest for “magic bullets” has been the driving force in drug discovery during the last two decades. However, the increasing rate of drug failure over this period has occurred concurrently with the assumption that a drug is a selective ligand for a single target. It now seems likely that polypharmacology is the rule rather than the exception [1].

Our previous research shows that protein domains are a good proxy for drug targets, and that drug polypharmacology emerges as a consequence of the multi-domain composition of proteins [2]. In this study, we investigate further the idea that the domain is the druggable entity within a protein target. We have identified a specific class of domains (CATH Functional Families) as the best currently available for identifying drug-target interactions. We show how this opens a new direction in target identification with potential application in drug repurposing.

1. Hopkins, AL. (2008) Network pharmacology: the next paradigm in drug discovery. Nat Chem Biol; 4: 682
2. Moya-García AA & Ranea JAG (2013) Insights into polypharmacology from drug-domain associations. Bioinformatics 29: 1934–1937)