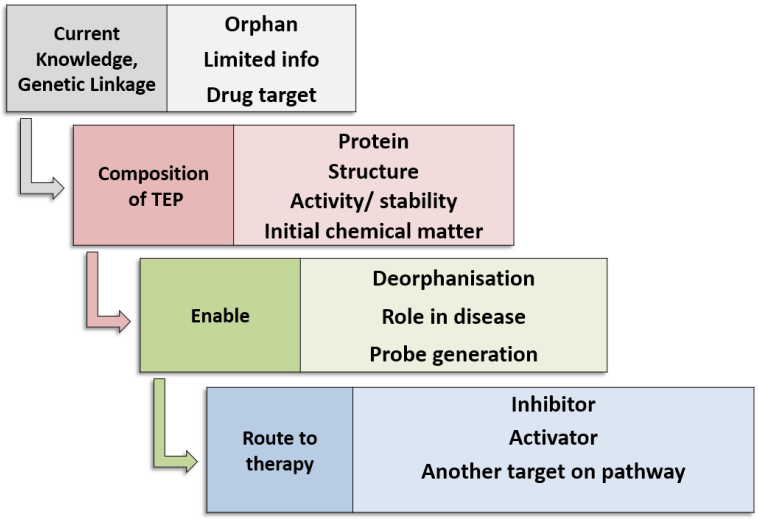
Human Family With Sequence Similarity 83 Member B (FAM83B)

A Target Enabling Package (TEP)

FAM83A-H are newly identified oncogenes characterised by a conserved DUF1669 domain. FAM83B can substitute for RAS to promote malignant transformation. Ablation of FAM83B or mutation of Lys230 inhibits malignant phenotypes, implicating FAM83B as potential therapeutic target. As part of this TEP, we solved the first crystal structures from the FAM83 family, including FAM83A and FAM83B. The structures of the DUF1669 domain reveal a phospholipase D-like fold lacking conservation of key catalytic residues. We deorphanise the FAM83 DUF1669 domain as a critical docking scaffold for binding of casein kinase 1 isoforms. Finally, using XChem fragment screening we report chemical fragments that bind to Lys230 in the central pocket of the DUF1669 and form starting points for potential drug development.

The Target Enabling Package (TEP) programme's foundation is built upon the recognition that genetic data is proving to be a powerful tool for target validation. As such, TEPs provide a critical mass of reagents and knowledge on a protein target to allow rapid biochemical and chemical exploration and characterisation of proteins with genetic linkage to key disease areas. TEPs provide an answer to the missing link between genomics and chemical biology, provide a starting point for chemical probe generation and therefore catalyse new biology and disease understanding with the ultimate aim of enabling translation collaborations and target/ drug discovery.



Future versions of this document will contain experimental data about the FAM83B TEP.

For more information regarding any aspect of TEPs and the TEP programmes, please contact teps@thesgc.org or visit https://thesgc.org/tep