



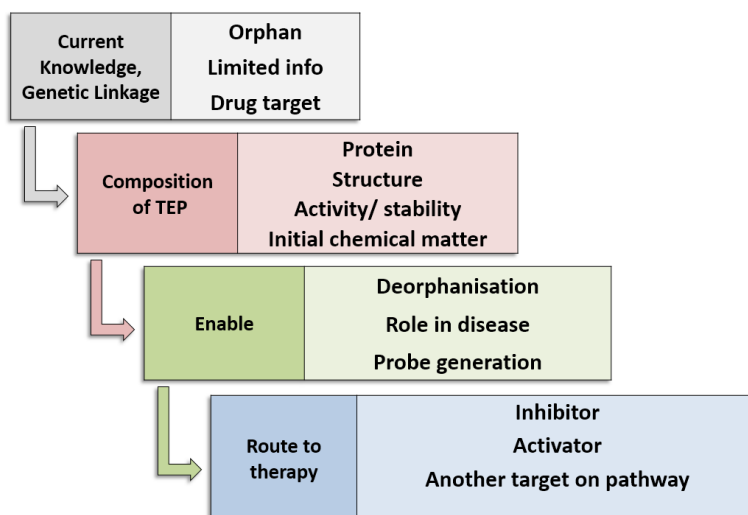
Human 5'-Aminolevulinate synthase, erythroid-specific (ALAS2)



A Target Enabling Package (TEP)

Erythroid specific 5'-Aminolevulinate synthase (ALAS2) catalyses the first and rate-determining step in haem biosynthesis during erythroid development. This TEP provides the structural biology tools to facilitate two aspects of ALAS2 research: (i) understanding how mutations in the ALAS2 C-terminus, a region unique to higher eukaryotes, lead to over-activity of the enzyme associated with a gain-of-function disorder; and (ii) providing chemical starting points to explore metabolic intervention of ALAS2, as substrate reduction therapy for the group of porphyria disorders that are associated with haem biosynthetic steps downstream of ALAS2.

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 ALAS2 TEP.

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