# Protein X-ray Crystallography Services at Domainex

domainex
the faster route to drug discovery

## Protein X-ray Crystallography at Domainex

Domainex is a multidisciplinary drug discovery company with an exceptional track record of drug candidate delivery. It has a world-class discovery team with the unrivalled track record of an average of one candidate drug delivered every year.

Domainex protein X-ray crystallography has supported a wide range of SBDD programmes including epigenetic targets, kinases, glycoproteins as protein-protein complexes.

Optional: Protein production to crystallographic standard

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Sparse matrix screening/ crystal optimisation/ crystal analysis

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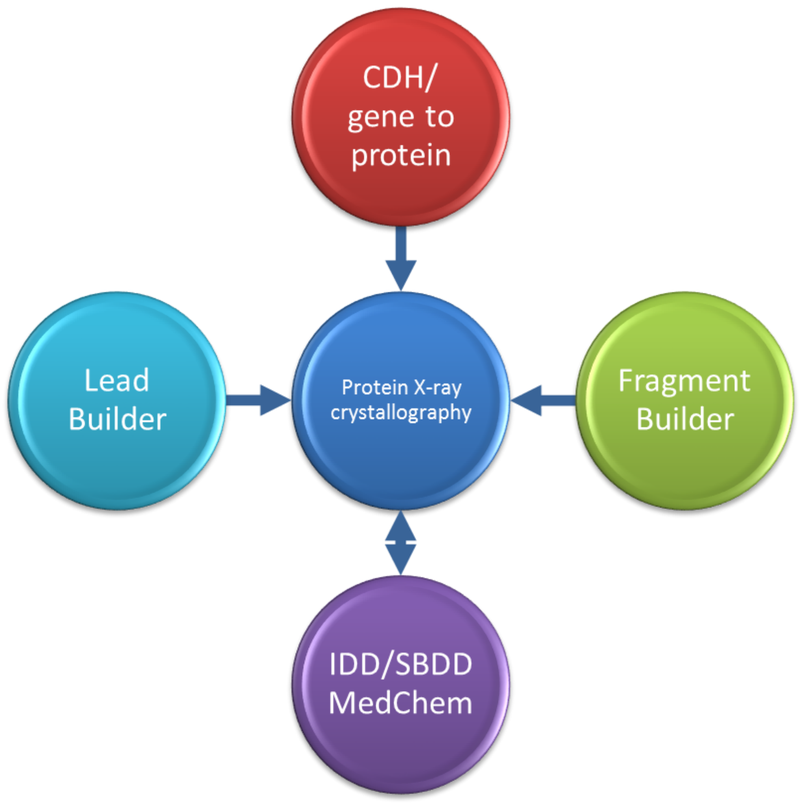
Structural refinement and modelling of collected datasets




Protein X-ray crystallography is a stand-alone service but can be combined seamlessly with other services (separate flyers available):

- –CDH (Combinatorial Domain hunting) – identification of novel soluble protein constructs
- –Routine protein production - E.*coli*, insect/mammalian expression
- –*FragmentBuilder* – our fragment screening platform
- –*LeadBuilder* – our virtual screening platform
- –Biological screening assays including cell, biochemical and biophysical assays
- –Medicinal chemistry – hit-to-lead/lead optimisation/drug candidate selection

## Case Study – CD73

CD73 (also known as ecto-50-nucleotidase, e5NT) is a eukaryotic extracellular glycoprotein with potential applications in the treatment of cancer and inflammation

- CD73 catalyses the hydrolysis of extracellular AMP to adenosine and plays a pivotal role in switching on adenosine signaling via the P1 receptors of the purinergic signaling pathway

Commercial protein not suitable for MST studies

- In-house protein production based on literature precedent (Knapp et al., 2012)
- Functional protein from inclusion bodies was produced in–house within 6 weeks after receipt of expression plasmid

In-house produced CD73 was used successfully for

- *A LeadBuilder* screening campaign (virtual screen followed by MST screen)
- STD-NMR to confirm ligand binding
- Biochemical assays
- Protein-ligand complex X-ray crystallography

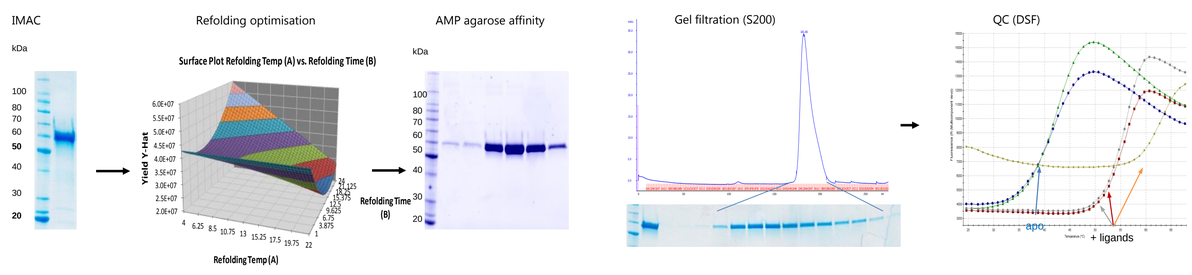
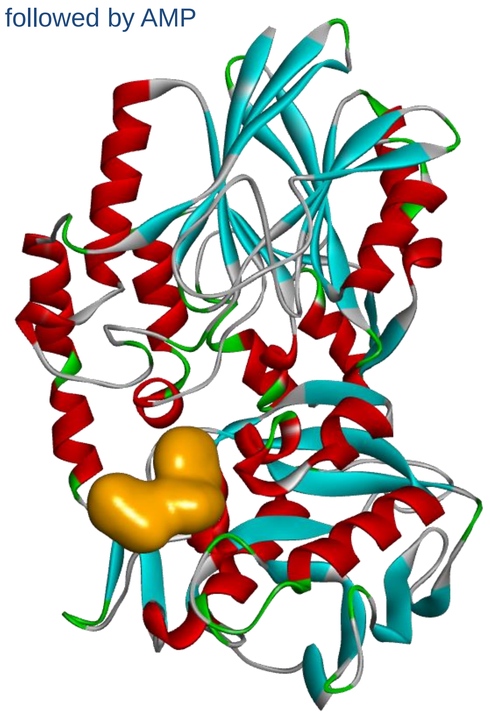



Fig 1: Purification of CD73 from inclusion bodies by refolding, followed by AMP affinity and size exclusion chromatography.

- CD73 was purified at crystallographic grade from inclusion bodies (Fig 1).
- Functional folding of the protein was confirmed by DSF, a $T_m$ shift was observed in the presence of a specific ligand.
- The protein-ligand complex structure of CD73-AMPCP was solved at 1.7Å.



## Contact

Domainex welcomes interest from any potential collaborators, industrial or academic. If you would like to learn more about applying our drug-discovery platform to your targets, please contact: **tom.mander@domainex.co.uk**
**www.domainex.co.uk**