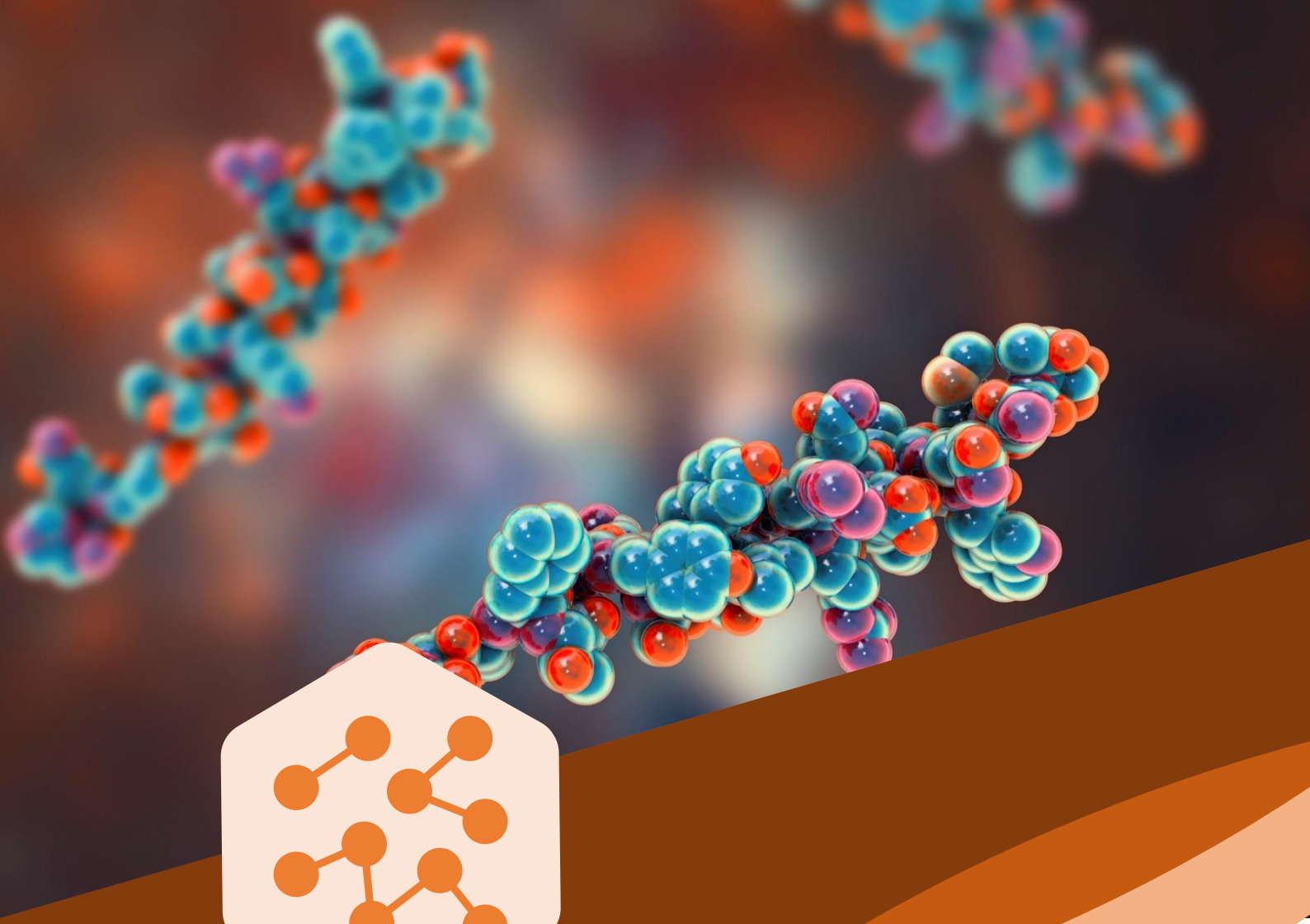


RECOMBINANT PEPTIDES

Cost competitive production of recombinant peptides

ISOMERASE

Recombinant peptides

Which recombinant peptides does Isomerase work on?

We have expertise and technologies to support cost-effective production of recombinant peptides (containing all natural amino acids) by fermentation.

Therapeutic peptides commonly function as hormones, growth factors, neurotransmitters, ion channel ligands or anti-infective agents. Most target cell surfaces due to membrane impenetrability and have poor *in vivo* stability. Increasingly, peptides are being developed as therapeutics. Chemical synthesis of peptides <50 residues is routine, is well suited to introducing non-canonical amino acids but can be costly and challenging, especially at scale. Synthesis is a great tool for generating research materials, but depending on the peptide length the cost of synthesis may be prohibitive, especially as each step will require independent optimisation followed by challenging and costly chromatographic purification. To help overcome the cost constraints of chemically synthesised peptides, Isomerase supports the production of peptides using recombinant biology technologies. We have expertise in cost effective production of native peptides by fermentation.

What problems do we help partners with?

Generating proof of concept recombinant processes

We can generate recombinant strains and processes to produce peptides for partners when supplied with no more than the amino acid sequence, for example where the manufacture process was previously synthetic.

Supply of recombinant peptides

We can conduct lab/pilot scale manufacture of peptides for partners, to supply mg to gram level quantities.

Process optimisation (USP and DSP)

We have expert bioprocess scientists and engineers that routinely manage a breadth of commercial peptide products. We know what good looks like, and how to reach target specifications quickly and robustly through proprietary enhanced development toolkits.

Technical transfer to scaled manufacturers

During the peptide process development program, we can generate all the technical documentation including technology books, quality reports, risk registers and ideal control strategies for mitigating failure modes and control of critical process parameters (CPPs) and critical material attributes (CMAs) in the process. We then work closely with the manufacturing facility teams to enable efficient process familiarisation and implementation for successful biomanufacturing.

What technologies and capabilities do we use?

Biology

Isomerase specialises in the production and modification of peptides using recombinant technologies, using both *E. coli* (prokaryotic) and *Pichia* (eukaryotic) strains.

Peptide manufacturing methods: Our proprietary recombinant peptide manufacture methods can be used to produce peptides (especially those >20 amino acids in length) at scale cheaper than synthetic processes.	**Purification processes:** This is enabled by technologies using easily removable protein tags which aid the DSP and purification process. These can be used to generate recombinant peptide expression constructs which can be cost-effectively expressed and purified and with targeted amino acid sequence.

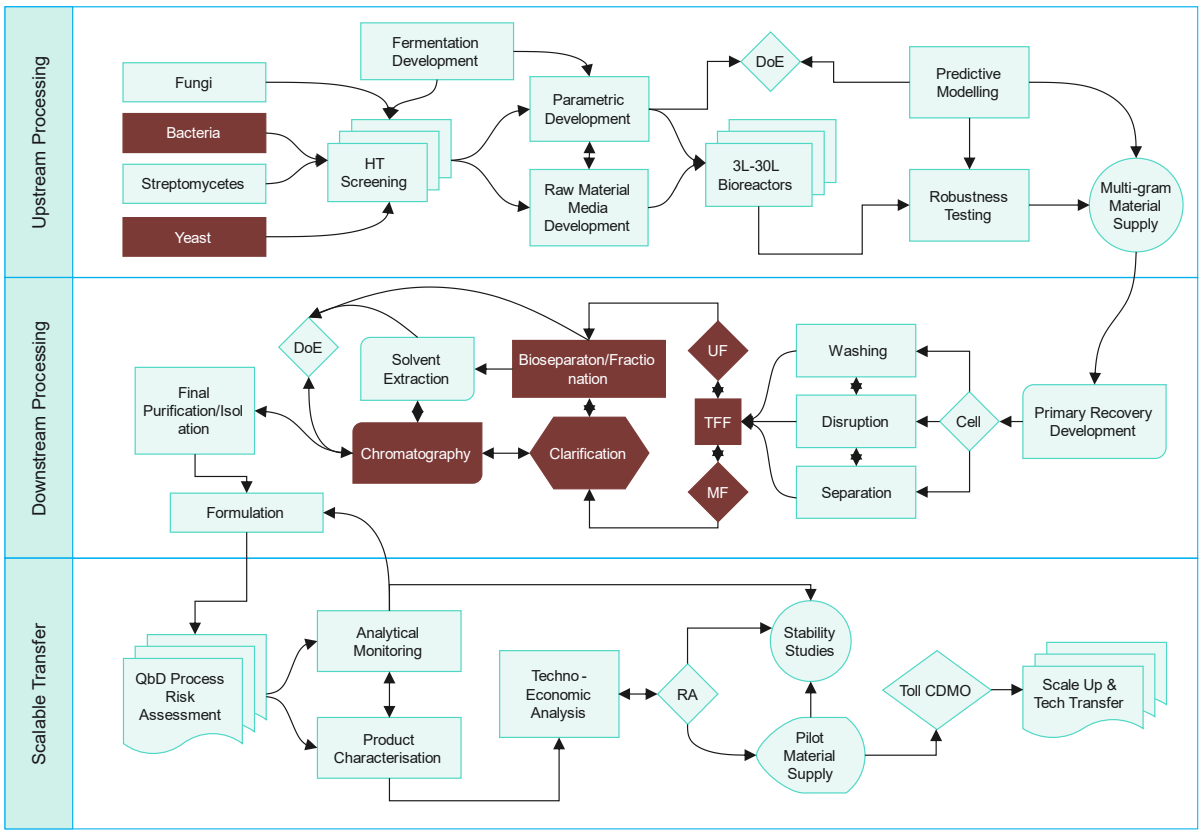
Bioprocess and Chemical development

We understand that recombinant peptides may have characteristics of both small molecules and larger protein products. Leveraging our extensive ability in both areas of bioproduction, we can develop and intensify peptide biomanufacturing processes at both a micro and macro level. This can involve refining product chemistry sensitivity, optimising upstream production and downstream purification pathways, and bolstering the stability of these fragile poly-chains during scalable fermentation and recovery-isolation procedures. Thus, we ensure that recombinant production is still advantageous and sustainable for innovators.

USP development:
We have robust drop in solutions for peptide manufacture. The processes are fine tuned for your peptide of choice. The fermentation methods ensure efficient cost-effective scalable growth with high yields. Trust us to innovate and streamline your biotechnological processes for enhanced productivity and success.

DSP development:
We have drop in robust DSP platforms that align with our biological approach to peptide manufacture. These methods are designed to not require expensive chromatography in most circumstances. The processes are fine tuned for your peptide of choice. Isomerase excels in developing platforms for primary recovery purification and product isolation, and activities are developed with robustness and scalability in mind for producing high-quality bio-products.

Scalable Transfer:
With the product specifications and commercial constraints in mind throughout our development platforms we build de-risked informative and detailed technical transfer dossiers to enable ensure process commercialisation



* **CDMO** Contract Development Manufacturing Organisation, **DoE** Design of Experiment, **HT** High Throughput, **MF** Microfiltration, **QbD** Quality by Design, **RA** Risk Assessment, **TFF** Tangential Flow Filtration, **UF** Ultrafiltration.

What advice can Isomerase provide as consultants?

Isomerase offers a range of consultancy services including the following.

Techno-economic Analysis (TEA)

Isomerase specialises in providing comprehensive techno-economic analysis (TEA) for natural product manufacturing. Our knowledge of the specific process from the cell energetics to industrial production systems enables us to accurately model using leading commercial software ensuring optimal decision making and compliance needs. We excel in advising on CAPEX/OPEX needs or sourcing CDMOs that are tailored to our partners' specific processes.

Process Risk Assessment

Isomerase uses proprietary systems to apply a risk profile to ‘as is’ innovator processes and targeting the ‘to be’ process. Using quality by design (QbD) tools we define and characterise the product critical quality attributes (CQAs), perform extensive risk assessment and map all process parameters and materials to the quality specifications. We define what is critical to quality (CTQ) and generate bespoke control strategies to remove and reduce risk for our partner processes.

What proprietary innovations can Isomerase add to projects?

Lower cost recombinant peptide production methods

Isomerase has developed and filed patents for technologies to support low-cost recombinant manufacture of peptides which avoids the use of expensive chromatography steps in the DSP.

Pichia Strains

Isomerase has developed fast and robust engineering tools for *Pichia* and has generated a growing collection of proprietary *Pichia* strains, including *Mut*$^{+}$ and *Mut*^{S} (useful for tuning expression in methanol-induced systems), auxotrophic mutants (enabling increased antibiotic-free plasmid retention) and protease knockouts (reducing breakdown of desired protein products) and methods for methanol-free production.

Upon a Partner’s request, Isomerase can use our proprietary *Pichia* strains to produce proteins for them. No license is needed if the project deliverable is the protein produced. When the deliverable is Isomerase’s *Pichia* strain engineered to make the protein of interest a product-specific license is needed. The licencing terms consider the amount the Partner has already spent with Isomerase. Licenses to Isomerase’s *Pichia* strains from companies not otherwise working with Isomerase are also available but on commercial terms.

What are representative examples of past projects?

CASE STUDY

RECOMBINANT PEPTIDE PRODUCTION PROCESS AND TECHNOECONOMIC ANALYSIS

Request

Partner requested to generate a recombinant process to therapeutic peptides previously only produced using synthetic chemistry and conduct technoeconomic comparison.

Our approach

A series of target sequences were supplied by the client. *E. coli* strains expressing these peptides along with a proprietary tag was developed. 2L and 30L USP and DSP processes were run, and test samples of material generated and supplied. A techno-economic analysis was carried out to compare anticipated costs through development and at different scales.

Value added

Recombinant peptide was supplied to the partner along with a technoeconomic analysis, enabling them to assess the process against their existing synthetic routes.

Ways to contact Isomerase

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