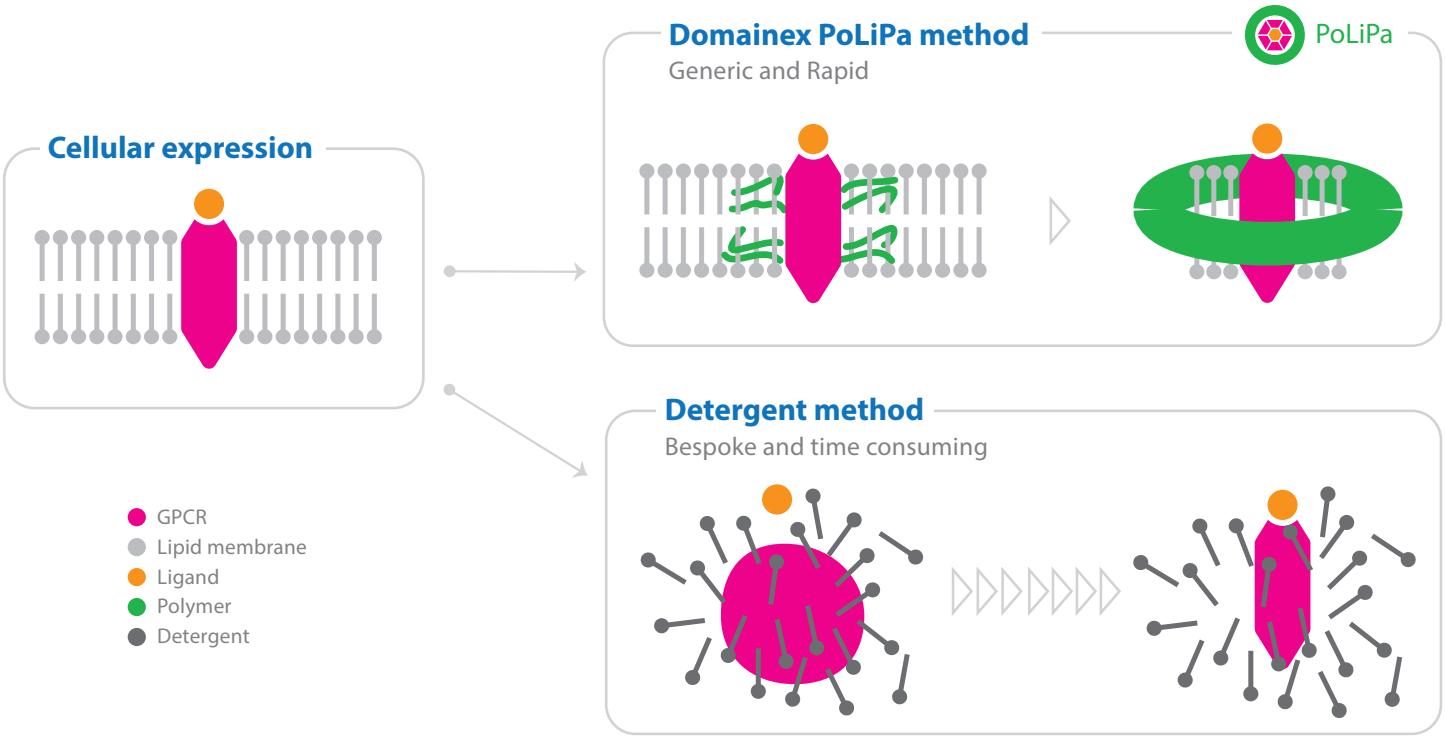
Innovative Polymer Lipid Particle (PoLiPa) technology

PoLiPa
Accelerating Membrane Protein Research

Accelerates G-Protein Coupled Receptor (GPCR) drug discovery

Domainex has established a generic platform to generate any purified GPCR without the need for thermostabilising mutations or detergents. This was achieved using Polymer Lipid Particle (PoLiPa) technology that can stabilise GPCRs, by encapsulating the target protein in a polymer that encloses a small disc of the native cell membrane lipids.



Advantages of soluble PoLiPa-GPCRs

Enables rapid and generic access to pure samples of GPCRs.

- Mutagenesis
- Detergent
- Refolding

PoLiPa-GPCRs are **pharmacologically intact** and **very stable** as they contain a disc of functionally important phospholipids. As such they can be used across multiple techniques and enable access to solution-based drug discovery methods.

domainex
the faster route to drug discovery

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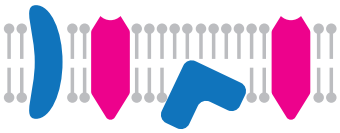
Generation of PoLiPa-GPCRs at Domainex

START

Expression



MONTH 2

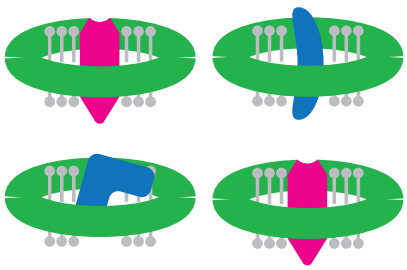
Activities

- Proprietory construct design
- Construct synthesis
- Expression in HEK293 cells
- Clonal selection

Criteria

- Cell surface expression >70% relative to positive cell line

Solubilisation



MONTH 3

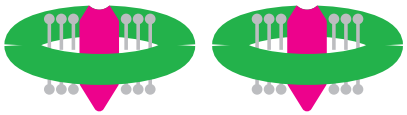
Activities

- Polymer selection and generation
- Solubilisation of cells with polymer

Criteria

- >90% receptor recovery

Purification



MONTH 4

Activities

- NiNTA purification
- SEC purification

Criteria

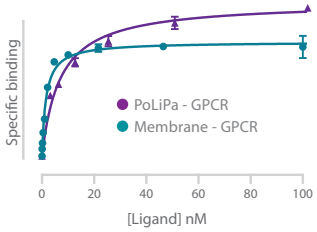
- >80% purity

Validation

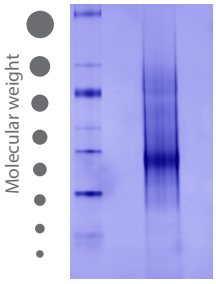
MONTH 4

Activities

Ligand observed LC-MS (LOMS)

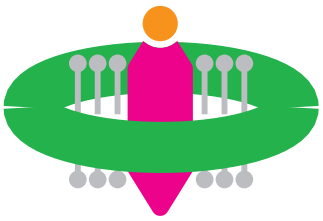


Native gels Coomassie



Criteria

- Expected pharmacology by LOMS
- >50% intact binding



Purified PoLiPa

FINISH

Applications

FBDD SBDD Biophysical characterisation Structural determination

DNA-encoded library screening Biologic hit ID Orphan receptor profiling

Development of this methodology was in collaboration with Prof. Tim Dafforn and with funding from the Innovate UK Biocatalyst Award.

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