

A SUPERIOR RECOMBINANT MAMMALIAN PROTEIN EXPRESSION PLATFORM

BACKGROUND

Mammalian protein production platforms have had an enormous impact in many areas of basic and applied research as well as in the biotech industry. The number of blockbuster therapies that are recombinant mammalian proteins (biologics) is rising, although recombinant proteins are also important for diagnostic and a wide variety of research applications.

Expression systems are the cornerstone of every biologic therapeutic development programme. There is a significant market opportunity for cost-effective and labor-saving production of recombinant proteins targeting either clinical, diagnostic or R&D markets.

We have developed a highly efficient and novel vector platform for mammalian recombinant protein expression that is superior to existing approaches. To date, we have built up an impressive portfolio of recombinant proteins that we have synthesised for internal Manchester University research groups as well as external groups/companies for their own research applications. One of the main drivers for the development and optimisation of our mammalian expression platform is the need to produce a high number of proteins deemed to be either completely “unexpressable” or those that are produced at very low levels in alternative expression systems.

THE TECHNOLOGY

A novel protein expression vector construct used to express a range of proteins at very high yield in mammalian cells. The expression is based on the adherently grown HEK293 EBNA1 cell line, using our novel high efficiency expression vector system named pPEF. The expression system has been validated on CHO cells and proved to be similarly efficient. It has also been successfully used with HEK293T suspension cells which are normally not amenable to stable recombinant expression. One of our vectors has been specifically designed for stable transfections of HEK293T.

We have seen that our expression vector system can increase protein expression by up to 200-fold in when compared to alternative mammalian expression systems.

UMIP - REPUTATION AND VALUE THROUGH INTELLECTUAL PROPERTY®

Examples of recombinant proteins expressed in our novel system:

- Human secreted Phospholipase A2 Receptor 1 (PLA2R1) - aa 20-1397.
- Human secreted Thrombospondin Type-1 Domain-Containing Protein 7A (THSD7A) - aa 48-1606.
- Human secreted Vascular Adhesion Protein-1 (sVAP-1) - aa 29-763.
- Human secreted Heparanase 2 (HPSE2) - aa 42-592.
- Human secreted Noggin - aa 28-232.
- Human Rearranged During Transfection (RET) - aa 30-1114.
- Human secreted Matrix Metalloproteinase 12 (MMP-12) - aa 17-470.
- Human secreted Interferon Beta 1 (IFN β 1A) - aa 22-187.
- Human secreted Amyloid Precursor Protein alpha and beta forms (APP α and APP β) - aa 18-596 and aa 18-612.
- Trastuzumab (monoclonal antibody also known by the brand name Herceptin).

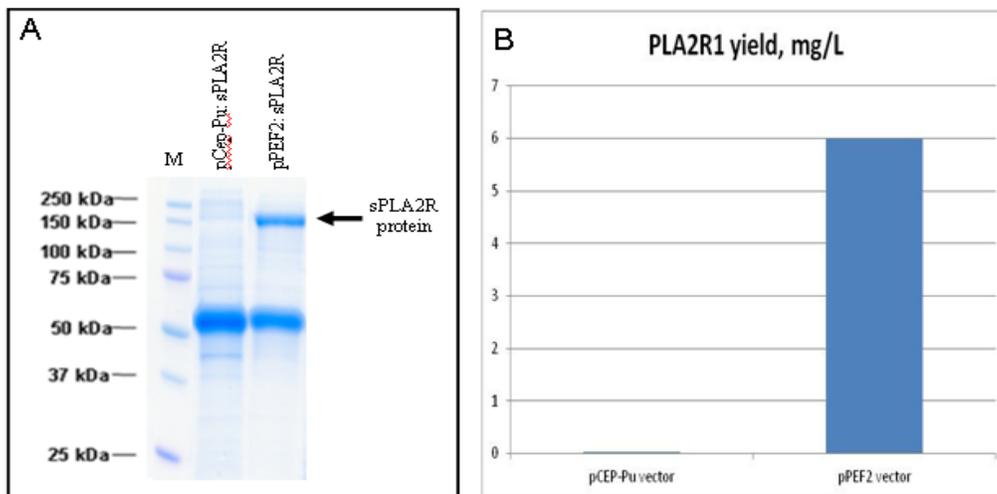


Figure 1: sPLA2R protein expression comparison study using pCep-Pu & pPEF2 vectors. Part 1A shows the SDS PAGE analysis of secreted protein harvested from stably transfected HEK293 cells. Part 1B shows the yield of purified protein obtained from the purification from 1 litre of cell media.

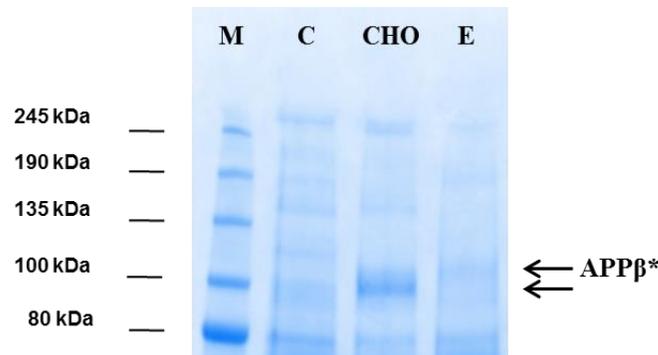


Figure 2. Comparative expression of human amyloid precursor protein beta form (APP β) in HEK293 EBNA1 and CHO-K1 stable cell lines using the PEF2 vector. Secreted proteins were separated by 4-20% gradient SDS-PAGE and stained with Coomassie blue. Enhanced yield of APP β is observed in CHOs.

* The difference in APP β size between HEK293EBNA1 and CHO-K1 is due to variability in the glycosylation pattern between the two species.

M – Protein size marker

C – control, conditioned serum free media untransfected CHO-K1

CHO – conditioned serum free media from CHO-K1 cells stably expressing APP β

E – conditioned serum free media from HEK293 EBNA1 cells stably expressing APP β

APPLICATIONS

Our technology and expertise is applicable for research applications in small academic labs all the way to biotechnology and pharmaceutical companies. Recombinant proteins have numerous uses for research, diagnostic and therapeutic applications.

KEY BENEFITS

- Our novel vector construct has commercial potential as it demonstrates generic high expression capability in mammalian cells. We have tested this across a range of proteins and it consistently outperforms existing standard vectors.
- We have expressed a comprehensive and growing range of proteins using our novel mammalian expression technology that includes growth factors, kinases, enzymes and transcription factors.

UMIP - REPUTATION AND VALUE THROUGH INTELLECTUAL PROPERTY®

THE UNIVERSITY OF MANCHESTER INTELLECTUAL PROPERTY UMIP®

- We have a bank of expression constructs for research applications in academia and the biotechnology/pharmaceutical industries.
- The vector system excels in producing proteins that are not available or poorly described in the literature.
- Our novel expression system provides high production efficiency at an early stage, shrinking the time and expense involved in lengthy scale up procedures: our system does not require individual clonal selection thereby omitting a very tedious, lengthy and costly stage.
- Resulting stable cell lines ensure the highest yields which are not lost after multiple passage numbers or freeze-thaw events.
- Our vectors are very good at expressing large proteins in the 50-200kDa range, which makes them stand apart from competing expression systems.

INTELLECTUAL PROPERTY

Patent pending.

OPPORTUNITY

We are seeking partnership and collaboration opportunities for our novel expression vector platform with a view to eventually licensing the technology. We are also happy to discuss bespoke supply of proteins for R&D purposes.

Whilst the current technology platform has been deployed to great effect for the production of difficult to express targets, we wish to further exemplify it in compliant and scalable processes using accepted target recombinants, to be able to compete in the development and production of large scale biotherapeutics - the market which provides the greatest opportunity and financial reward. We would therefore welcome the opportunity to discuss potential collaboration to carry out these activities.

CONTACT

Laura Etchells, Enterprise Development Manager, UMIP. ✉: laura.etchells@umip.com

☎: +44 (0) 161 606 7264

UMIP - REPUTATION AND VALUE THROUGH INTELLECTUAL PROPERTY®