



A novel platform for the advanced production of therapeutic proteins

The efficient expression of a therapeutic protein in microbial or mammalian cells is often a bottleneck in the production of biopharmaceuticals. To address this, MSD (formerly Avecia Biologics) has developed novel technology for the efficient expression of proteins.

## Features and benefits

*Speed, flexibility and breadth of application...*

- **Fast track process creation and development**  
*Reduced time to clinic, Reduced time to market*
- **High yield protein production**  
*Class leading fermentation productivity, Potential for reduced cost of goods*
- **Versatility**  
*Can produce a wide range of biotherapeutic proteins using a family of expression systems*
- **Regulatory compliance**  
*Well characterised systems with full development history*



## A novel technology

The pAVEway™ platform is based on a set of unique protein expression plasmids, which have been developed by MSD. Using a novel configuration of operators, promoters and repressors, we have created a range of vectors which provide tightly controlled production of the target proteins, whilst allowing very high expression levels.

These vectors are complemented by a range of host strains. By choosing the appropriate combination of plasmid, host strain and fermentation conditions, very high titres have been demonstrated for soluble, insoluble or secreted proteins.

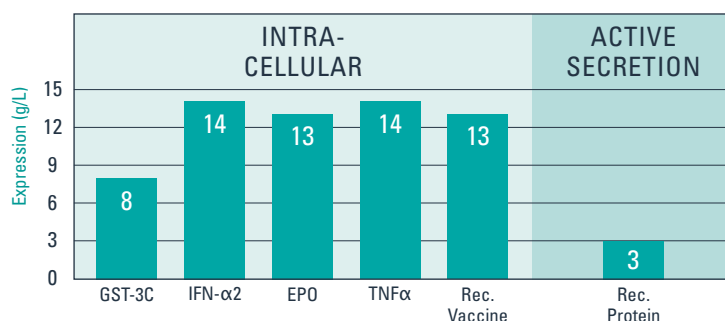




## pAVEway™ delivers fast track process definition

MSD makes the pAVEway™ protein production platform available as a service to our clients for cGMP manufacturing of their protein. Starting from the gene of interest, MSD and the customer will discuss the preferred route of expression. We will express the protein in a pre-defined set of pAVEway™ vectors, clone these in a range of corresponding host strains and grow these in a selection of optimised conditions. This allows rapid selection of an optimal expression system and early definition of the upstream production process.

Activity	Week 1	Week 2	Week 3	Week 4
Vector construction				
Shake flask experiments				
Fermentation				



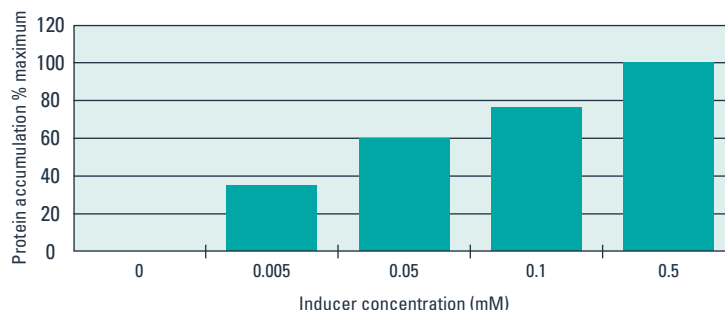
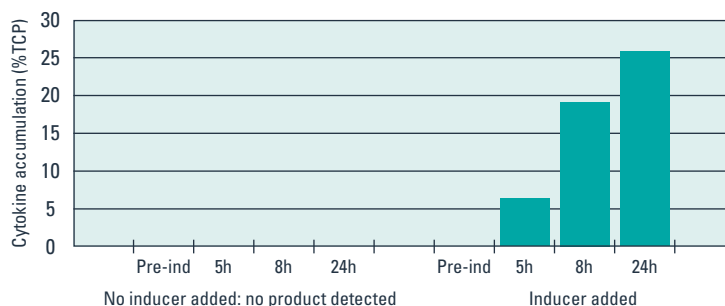
Examples of fast process definition leading to high expression levels. The titres shown were achieved in the **first evaluation** of recombinants using a pre-established generic fermentation process. Further intensification can be achieved.

## pAVEway™ delivers high yields

Using the pAVEway™ platform, very high fermentation yields have been achieved for a wide range of proteins, as exemplified above. To achieve this, pAVEway™ combines two unique features.

Firstly, the basic expression levels can be fully suppressed (see graph right), so that no protein is produced before induction. This allows high expression levels even for proteins that would normally impair the growth of the host cells.

A second characteristic of the pAVEway™ technology is the ability to modulate the expression levels by varying the concentration of inducer (see graph bottom right). The expression kinetics can thus be tightly regulated to match the folding capabilities of the host cell, enabling the soluble expression of proteins of high folding complexity.



## pAVEway™ delivers versatility

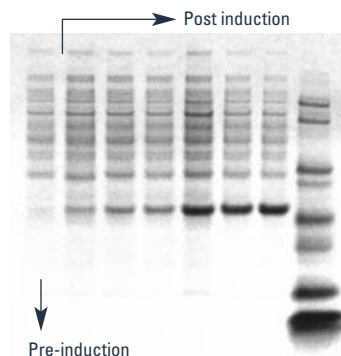
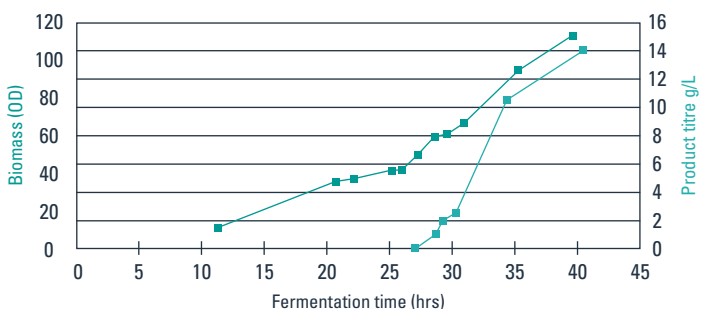
The pAVEway™ platform consists of a range of vectors for soluble, secreted and insoluble expression, which can be selected according to the specific customer requirements. An overview of the systems available for *E.coli* is given in the table below:

*E.coli* expression systems of the pAVEway™ Advanced Protein Expression platform

Features	System (vector/hosts/fermentation platform)				
	1	2	3	4	5
High level productivity	✓	✓	✓	✓	Moderate
High expression levels	✓	✓	✓	✓	Moderate
Tight control of basal expression	Moderate	✓	✓	✓	✓
Modulation to maximise accumulation and partitioning into soluble, insoluble (inclusion body), periplasmic secretion	✓	✓	✓	✓	✓
Fermentation titres achieved in first evaluation with generic system	12-14g/L	8-14g/L	6-8g/L	6-8g/L	2-3g/L
Benefits	High cytoplasmic titre of soluble and inclusion body proteins	High cytoplasmic titre of soluble and inclusion body proteins. High titre of simple monomeric proteins	High cytoplasmic titre of soluble and inclusion body proteins. High level secretion of simple monomeric proteins	High cytoplasmic titre of soluble protein. High level secretion of simple monomeric proteins	High level secretion of complex/multi-meric proteins

pAVEway™ also offers a solution high level expression in *Pseudomonas* and other micro-organisms, thereby paving the way for the optimal expression of therapeutic proteins.

### *Pseudomonas*: high titre fermentation - recombinant enzyme



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