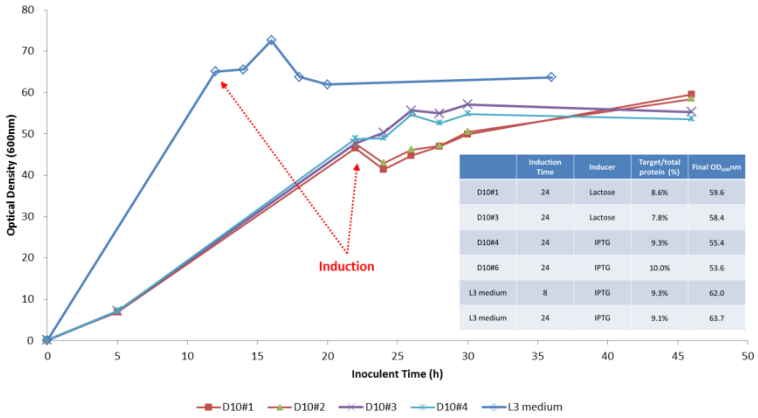
ENGINEERING OF *ESCHERICHIA COLI* PROTEIN EXPRESSION PROCESS DEVELOPMENT

Chih-Hsi Fan, Development Center for Biotechnology
chfan@dcb.org.tw
Yue-Chang Chou, Development Center for Biotechnology
Jen-Wei Chang, Development Center for Biotechnology
Neng-Hsien Chang, Development Center for Biotechnology
Wei-Hong Cheng, Development Center for Biotechnology
Ming-Hong Cyue, Development Center for Biotechnology
Wei-Kuang Chi, Development Center for Biotechnology

Key Words: *Escherichia coli*, DoE, protein drug, expression, fermentation

It almost 30% protein drugs are expression by *Escherichia coli*, because of rapid growth and high production yield. We have developed E.coli base system for recombinant protein expression, scFv, Fab and vaccine. In this study we introduce example about process development for nutrient components selection. Shaker flasks were used for different nitrogen and carbon components screening by DoE. Seven media formulations for *E. coli* fermentation were used in this study. By changing nitrogen and carbon source ratio, product titer of target protein could be optimized, at least 1.4 folds increased. The best result from shaker flask was used in 250 mL parallel fermenter and pH, dissolved oxygen, feeding/induction strategy were evaluated. The processes from seed culture to harvest only require 64 hours. The optimized time was reduced to 32 hours. The result showed that both target protein expression and cell density value were comparable, but the total process time was significantly reduced by half.



	Induction Time	Inducer	Target/total protein [%]	Final OD_{600nm}
D10#1	24	Lactose	8.6%	59.6
D10#3	24	Lactose	7.8%	58.4
D10#4	24	IPTG	9.3%	55.4
D10#6	24	IPTG	10.0%	53.6
L3 medium	8	IPTG	9.3%	62.0
L3 medium	24	IPTG	9.1%	63.7

Figure 1. The result of Escherichia coli Growth condition and target protein titer by different process.