

# Cell-line Engineering of Chinese Hamster Ovary Cells for Low-temperature Culture

TAN Hong Kiat<sup>a</sup>, Miranda Yap<sup>b</sup>, Daniel I.C.Wang<sup>c</sup>

<sup>a</sup> Singapore-MIT Alliance, 4 Engineering Drive 3, National University of Singapore, Singapore-117576

<sup>b</sup> Bioprocessing Technology Centre, Kent Ridge Crescent, National University of Singapore, Singapore-119260.

<sup>c</sup> Massachusetts Institute of Technology, Cambridge, Massachusetts.

*Abstract* – Developments in mammalian cell culture and recombinant technology has allowed for the production of recombinant proteins for use as human therapeutics. Mammalian cell culture is typically operated at the physiological temperature of 37 °C. However, recent research has shown that the use of low-temperature conditions (30-33°C) as a platform for cell-culture results in changes in cell characteristics, such as increased specific productivity and extended periods of cell viability, that can potentially improve the production of recombinant proteins. Furthermore, many recent reports have focused on investigating low-temperature mammalian cell culture of Chinese hamster ovary (CHO) cells, one of the principal cell-lines used in industrial production of recombinant proteins.

Exposure to low ambient temperatures exerts an external stress on all living cells, and elicits a cellular response. This cold-stress response has been observed in bacteria, plants and mammals, and is regulated at the gene level. The exact genes and

molecular mechanisms involved in the cold-stress response in prokaryotes and plants have been well studied. There are also various reports that detail the modification of cold-stress genes to improve the characteristics of bacteria or plant cells at low temperatures. However, there is very limited information on mammalian cold-stress genes or the related pathways governing the mammalian cold-stress response.

This project seeks to investigate and characterise cold-stress genes that are differentially expressed during low-temperature culture of CHO cells, and to relate them to the various changes in cell characteristics observed in low-temperature culture of CHO cells. The gene information can then be used to modify CHO cell-lines for improved performance in the production of recombinant proteins.