## Cell-line Engineering for Low-temperature Growth

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Abstract—In the chemical industry, the rates of reactions are usually enhanced by the use of high-temperature and high-pressure conditions. This chemical engineering approach is rarely applied in the biotechnology field. Firstly, most biochemical reactions take place in an aqueous phase, which makes them relatively insensitive to changes in pressure. Secondly, they form a tightly regulated network, with distinct pathways that operate optimally at relatively low temperatures of about of 25-40°C. Beyond this range, higher temperatures would denature the proteins in the cell, leading to eventual cell death.

Mammalian cells are integral the biotechnology field for production of human therapeutics. Bio-reactors for mammalian cells are typically operated at 370C. The effects of temperature down-shifting have been well-investigated and documented for several mammalian cell-lines and recombinant products. Although the rate of growth of cells is reduced, the productivity of recombinant protein is increased at lower temperatures. Apoptosis and nutrient requirements are reportedly reduced at lower temperatures also.

As such, it is advantageous to investigate the effects of mammalian cell culture at down-shifted temperatures, with the ultimate aim of improving recombinant protein production and quality.

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