HYPEROSMOTIC STRESS ABD RECOMBINANT ANTIBODY PRODUCTION IN CHO CELLS: CHARACTERIZATION AND GENE EXPRESSION INVESTIGATION

by

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An Abstract of a Thesis Submitted to the Graduate

Faculty of Rensselaer Polytechnic Institute

in Partial Fulfillment of the

Requirements for the degree of

MASTER OF SCIENCE

Major Subject: BIOCHEMISTRY & BIOPHYSICS

The original of the complete thesis is on file
In the Rensselaer Polytechnic Institute Library

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Rensselaer Polytechnic Institute
Troy, New York
April, 2011
(For Graduation May, 2011)

ABSTRACT

Increasing demand for antibodies for use in research and clinical practices has led to large-scale cultures of recombinant antibody-producing Chinese hamster ovary (CHO) cells. The current industrial culture conditions expose CHO cells to hyperosmotic stress. Previous literature shows that this stress results in altered antibody production but the mechanisms behind this phenomenon are poorly understood. In an effort to shed light on these processes, we examined two CHO cell lines, producing the same recombinant monoclonal antibody at different rates, and subjected them to hyperosmotic stress for 48 hours. During this time, we monitored growth, extracellular metabolite concentrations, and antibody production. Using this information, we further characterize the effects of osmotic stress on recombinant protein producing CHO cells. The different cell lines allowed us to also identify differences between high and low antibody producers. Further characterization at the level of gene expression was completed by identifying genes of interest through previous experiments and novel bioinformatics analysis. The novel bioinformatics techniques used require the biological confirmation presented here to fine tune the methodology and create programs that can reliably identify up and down regulated genes. From the identified genes, we were able to identify three that show differential expression under hyperosmotic stress or across cell lines. Further characterization of antibody-producing cell lines and the development of bioinformatics to help with this process is essential to understanding the expression of valuable recombinant proteins and may lead to the increased efficiency of production required for monoclonal antibodies to be used in therapeutic areas. The understanding of expression changes also may allow for more rational engineering of antibody-producing CHO cells in the future.