NAD$^+$ SUPPLEMENTATION IMPROVES MABS PRODUCTIVITY IN CHO CELLS VIA A GLUCOSE METABOLIC SHIFT

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Aerobic glycolysis and its by-product lactate accumulation are usually associated with adverse culture phenotypes such as poor cell viability and productivity. Because of the unclear understanding of the causes and accompanying biological processes, regulation of aerobic glycolysis has been an ongoing challenge in culture process development for therapeutic protein production. NAD$^+$ is a coenzyme and co-substrate in energy metabolism that plays a key role to promote the conversion of inefficient glycolysis into efficient oxidative phosphorylation pathway. However, the effect of NAD$^+$ treatment on CHO cell lines for biopharmaceutical production has not been reported yet. In this work, we aimed to elucidate the influence of NAD$^+$ on cell culture performance by examining metabolic shift and mAb productivity. The supplementation of NAD$^+$ increased the intracellular concentration of NAD$^+$ and promoted SIRT3 expression. Antibody titer and the specific productivity of NAD$^+$-treated cultures at the growth phase increased by up to 1.8 and 1.9-folds, respectively, with marginal restrictions on cell growth. NAD$^+$ significantly reduced the accumulation of reactive oxygen species as well as the degree of glycolysis, determined by lactate accumulation versus glucose consumption ($Y_{Lac/Glc}$). In contrast, OXPHOS capacity and amino acid consumption rate increased significantly. Collectively, our data indicated that NAD$^+$ treatment to the CHO cultures may improve therapeutic protein productivity in bioprocessing via inducing an energy metabolic shift.

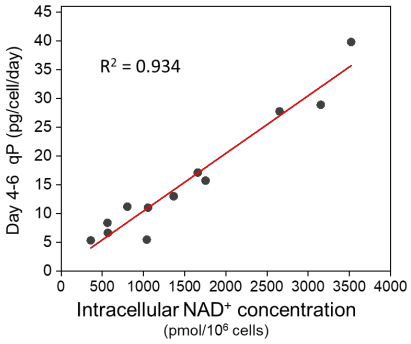

Figure 1 – Intracellular NAD+ concentration and specific antibody productivity of two cell lines treated with various concentrations of NAD$^+$