GLUCOCORTICOIDS MODULATE CHO CELL GLYCOSYLATION IN CHEMICALLY-DEFINED MEDIA

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Key Words: glycosylation, chemically-defined media, glucocorticoid, product quality, cell signaling

Product quality attributes are critical to the therapeutic activity of manufactured biologics. One key quality attribute is glycosylation, which can dramatically affect antibody activity, specificity, and/or immunogenicity. As such, a high priority during drug development is to control the glycosylation profile. Glycosylation is significantly influenced by the composition of cell culture media, including sugars, amino acids, vitamins, trace metals, and even metabolic waste products. Formulation of chemically-defined growth and feed media provides the ability to fine tune the concentrations of media components that regulate glycosylation through metabolic shifts and cell signaling. For example, some of the current strategies for modulating glycosylation involve combinations of guanosine, uridine, MnCl2, galactose, and other sugars. While these components can be adjusted to alter glycosylation, they can also negatively impact cell growth or productivity. Therefore, identifying a broad array of glycosylation control strategies is necessary for tailoring media to different cell lines. Glucocorticoids are a class of compounds commonly found in cell culture media that have demonstrated viability enhancing properties in growth of CHO cells. This class of steroid hormones regulates programmed cell death in CHO cells by triggering increased expression of the anti-apoptotic gene Tsc22d3 [Jing et al., Biotechnol Prog. 2012; 28:490496]. Using our chemically-defined media system, we demonstrate an additional property of glucocorticoids as a regulator of antibody glycosylation in CHO cell culture. Our results show reductions in fucosylated and galactosylated glycan species and a concomitant increase in mannosylated glycan species. This is notable because fucosylation and mannosylation affect potency if the mechanism of action relies on antibodydependent, cell-mediated cytotoxicity (ADCC) and galactosylation affects potency if the mechanism of action relies on complement-dependent cytotoxicity (CDC). Therefore, understanding the effect of glucocorticoids on glycosylation is important for tuning cell culture media in the pursuit of more desirable product quality attributes of biologics